The essential and optimal analgesic and anti-inflammatory medicines for athletes at the Olympic Games

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Abstract

Background. At every Olympic Games, a comprehensive set of medications is selected to be provided through the polyclinic pharmacy and wider medical services primarily for the treatment of athletes. This is known as the games formulary, and usually consists of 200-300 different types of drugs chosen to meet the expected medical needs encountered in this unique sport setting. This formulary constitutes the list of medicines that are available for prescribing for athletes at the event by both local physicians and visiting international team physicians.

At the Olympic Games this formulary has always been constructed on a games-by-games and country-by-country basis, and thus has usually reflected the national formulary and availability of medicines used by the host country. This process has inevitably led to significant variations and inconsistent standards in medicines provision between games in terms of efficacy, quality, safety, and costs of service delivery, even though the athlete population being served has remained relatively consistent in terms of their pharmacological needs.

In 2019, the International Olympic Committee (IOC) published the first *Olympic and Paralympic Model Formulary* (OPF),[1] which for the first time presented a standardised set of medications required to be available at every Olympic and Paralympic Games starting from the Tokyo 2020 Olympic Games, but was also implemented prior to this at the Minsk 2019 European Games. The OPF provides all healthcare providers from both the host country and visiting teams with a consistent, safe, and clinically relevant selection of medicines to prescribe to athletes during the games. The OPF must be representative of the medications athletes are taking and what physicians are prescribing to them during the games, while at the same time reflecting a set of consistent and dependable treatment options which are both safe and effective.

Aims. The overall aims of this study were to:

i) Determine whether the OPF meets both the clinical needs of the athlete population, and the prescribing expectations of team physicians relating to the treatment of musculoskeletal sports injury with medicines for pain and/or inflammation (PI) during international games;

ii) Present a revised and optimised set of essential PI medications for the Olympic Games, which will inform future editions of the OPF, and;

iii) Establish a quantitative, reproducible approach to the selection of medicines for the OPF which can be implemented for future games to enable continual updating of the OPF over time to reflect the changing medication needs of athletes.

Methods. This research was carried out in two phases (Phase One, proof-of-concept pilot study: European Games, Minsk 2019, and Phase Two: Olympic Games, Tokyo 2020 Summer Olympic Games and Beijing 2022 Olympic Winter Games).

Phase One involved a qualitative review of data collected from four sources including: i) doping control forms (n=999), ii) pharmacy dispensing reports from the athlete village pharmacy (n=471), iii) medication importation declarations by National Olympic Committee (NOC) teams (n=36), and iv) survey of team physicians (n=60).

Phase Two involved a quantitative analysis to determine a revised recommended list of PI medications for the OPF. It included the collection of actual medication-use data of Olympic athletes (n=6155) from 3 separate sources to establish the prevalence, including: i) doping control forms, ii) pharmacy dispensing reports from the athlete village pharmacy, and iii) injection declaration forms required submitted according to the *IOC Needle Policy*. Validation of the results included two further data sources: iv) medication importation declarations by NOC teams (n=156), and v) survey of team physicians (n=382).

Results. Phase One at the European Games showed that 23.1% (n=231) of athletes selected for testing declared the use of one or more PI medications in the previous 7 days on the doping control forms. Of all PI medications declared by athletes, 80.0% (n=252) were listed on the OPF, with NSAIDs accounting for the majority of all PI medications declared (70.8%,

n=223). Of all PI medications imported as team stock, 36% were listed on the OPF, but 44% could be covered by a suitable alternative medication in the same therapeutic class for the same indication. Of all physicians completing the team physician survey, 68.3% (n=41) indicated 75-100% of PI medications they prescribed were covered by the OPF. This pilot study identified use of a number of PI medications taken by athletes documented to have significant safety concerns, including metamizole, piroxicam and nimesulide.

Phase Two showed the overall prevalence of PI medication use by Olympic athletes was 36.7%. NSAIDs were the most used class of PI medication, with 27% of athletes reporting use. Female athletes had a higher prevalence of PI medication use compared to male athletes (f: 44.1%; m: 30.0%; $p<0.001$). The prevalence of PI medication use was higher in older athletes aged 30-34 (42.0%), and in athletes from the Pacific region, where over half (52.2%) of athletes reported using PI medications. Sports with the highest prevalence of PI medication use included: weightlifting (65.6%), gymnastics (58.1%), handball (55.0%) and volleyball/beach volleyball (54.5%). With the exception of corticosteroids for intra-articular use, there was no significant difference between the prevalence of PI medication use between the Tokyo and Beijing Olympic Games. Further use of PI medications by athletes with safety concerns were identified, including rofecoxib, nimesulide and metamizole.

By systematically applying a prevalence-based threshold for inclusion, a revised list of 48 PI medications was recommended (9 new, 13 deleted). This was validated through review of the imported team medications, with the most frequently stocked medications in 94% (n=17) of PI categories represented. Furthermore, the team physician survey demonstrated that the revised list covers the most frequently prescribed medication in each PI category. If the revised list of PI medications was implemented in the same athlete study population (n=6155) across the Tokyo 2020 and Beijing 2022 Olympic Games, it would lead to a 7% improvement in terms of numbers of athletes who could have their exact PI medication requirements met by the OPF (n=244).

Discussion and Conclusion. The research led to the determination of the prevalence of PI medication use by athletes at the Olympic Games. It also led to a revised and optimal set of

PI medications to be listed in the official OPF that can better serve the actual medical needs of athletes, which is aligned to the prescribing expectations of team physicians. It led to a key finding of the current use of drugs with harmful risks to athlete health. Through this study, a systematic, reproducible, and quantitative approach was developed which can be used to continually determine the optimal and essential set of medicines to be available for the treatment of pain and inflammation for athletes at all future Olympic Games.

Declaration

I, Mark Campbell Stuart, confirm that all the work presented is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Mark Campbell Stuart

10 October 2023

Impact Statement

Through my PhD research, I have successfully conducted an extensive investigation into the selection and optimisation of medications for treating pain and/or inflammation in athletes at the Olympic Games. The research will result in a refined and highly optimised formulary directly translating into better standards of athlete care, efficient pharmacy service delivery, and safety for athletes at the Olympic Games. Moreover, the translational impact of this research will not only standardise pharmacy provision at the Olympic Games but also ensure continuous improvement and adaptation for years to come.

Key findings

The Olympic and Paralympic Model Formulary (OPF) will see substantial enhancements and improvements due to my research, including greater applicability to Olympic athletes, better alignment with physician preferences, and standardisation of medical care and medicines availability across different Olympic Games. The findings will be implemented for the Paris 2024 Olympic Games.

The study identified several drugs with known harmful risks that are still being prescribed. These findings necessitate immediate education and action to protect athlete health. The research has led to recommendations for excluding specific drugs from the OPF known to have safety concerns, in order to protect athletes from potential harm.

I have also developed the Formulary Medication Match Website, an innovative online visualisation tool that allows for continual updates and improvements to the formulary for future Olympic Games.

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Abbreviations

BCO	Blood Collection Officer
CI	Confidence Interval
DCF	Doping Control Form
DCO	Doping Control Officer
EOC	European Olympic Committees
IDCO	International Doping Control Officer
IF	International Federation
IOC	International Olympic Committee
IPC	International Paralympic Committee
ITA	International Testing Agency
NOC	National Olympic Committee
NPC	National Paralympic Committee
NSAID	Non-steroidal anti-inflammatory drug
OCOG	Organising Committee of the Olympic Games
OPF	Olympic and Paralympic Model Formulary
PI	Pain and Inflammation
SD	Standard Deviation
TUE	Therapeutic Use Exemption
WADA	World Anti-Doping Agency
WHO	World Health Organization

Table of Contents

CHAPTER 1: INTRODUCTION

1.1 DEVELOPMENT OF THE OLYMPIC & PARALYMPIC MODEL FORMULARY

1.1.1 Background

At the Olympic Games, medicines are provided through a number of channels. The medical teams accompanying the athletes will usually import a comprehensive selection of medicines for use by their own team doctors, and individuals on long-term medication will usually bring personal supplies of medicines for the duration of the event. Host countries will provide comprehensive medical facilities within the athlete village polyclinic, with a fully stocked outpatient pharmacy serving the medicine needs of both the athlete and non-athlete population living in the village. The athlete village pharmacy can be accessed by both visiting team doctors and local healthcare providers. In addition, a selection of medicines is provided at every sport competition venue for use by the doctors of the host country for first-response and emergency care.[2]

The Olympic medical services are fully integrated into the local hospital and emergency services infrastructure of the host country, with systems in place to move sick and injured patients between facilities according to their clinical needs. The scope of medicines provision therefore reflects the type of care expected at the various sites where they are kept. At competition venues, the medicines cover first response care for both emergency medical incidents and minor ailments, with follow-up treatment provided through either ambulance, designated hospital, or athlete village polyclinic services. At the athlete village polyclinic, the medicines provided cover a comprehensive range of conditions relating to musculoskeletal sports injury and illness in athletes, as well as a range of conditions encountered in primary care.[3]

The games formulary

At every major multi-sport games a comprehensive set of stock medicines is selected to be provided through both the polyclinic pharmacy and wider games medical services for the

treatment of athletes and officials. This set of medicines is known as the games formulary which is published in each games' pharmacy guide handbook and usually consists of 200-300 different types of medicines chosen to meet the expected medical scenarios encountered in this unique setting. This formulary constitutes the list of medicines that are available for prescribing at the event by both local physicians of the host country providing medical care on behalf of the organising committee, and accessible by visiting international team physicians to prescribe for athletes and other members of their own delegation.

1.1.2 The need for a standardised formulary

The IOC mandates that all healthcare, which includes pharmacy provision, provided at the Olympic Games must embody the core principles of the *Olympic Movement Medical Code*,[4] which are as follows:

- Protect the health of the athlete
- Minimise risk of harm to the athlete
- Protect athletes in their relationships with physicians and other healthcare providers
- Mandate best medical practice in the provision of healthcare
- Embody the rules and ethics of the *World Anti-Doping Code*[5]

Prior to 2019, the medicines formulary for each Olympic Games was always compiled and published through the medical and pharmacy services of each host country organising committee with expert input from the IOC Medical and Scientific Commission, as specified in the *IOC Olympic Games Guide on Medical Services*.[3] The formulary was always constructed on a games-by-games and country-by-country basis. Although this system had generally worked to provide an adequate formulary for previous games, the selection of medicines was greatly dependent on various factors including local medicines availability, local clinical practice, national treatment guidelines of the host country, national medicines formularies, and personal treatment preferences of the medical advisors of the host country. This inevitably led to significant variations and inconsistent standards in medicines provision between games in terms of clinical efficacy, quality, safety, and costs of service delivery, even though the

athlete population being served has remained relatively consistent in terms of their pharmacological needs. The variations in medicines provision are clearly apparent through the published formularies for each edition of the Olympic Games.[6-11]

Through review of numerous Olympic Games pharmacy reports prior to 2019, it was evident that some aspects of the medicines provision at the Olympic Games needed improvement to ensure the Olympic Movement Medical Code was implemented to the highest standards at every games. The table below highlights examples of actual issues encountered at recent Olympic Games, which were identified and documented by the IOC Medical and Scientific Commission.[12-14] Many of these issues stemmed from the inconsistent and potentially misinformed selection process of medicines for the games formulary, and which could have conceivably be prevented through the implementation of a standardised medicines formulary.

Table 1 Medication issues which could be potentially prevented through a model formulary.

Olympic Games	**Issues which could potentially be prevented through a model formulary**
PyeongChang 2018	Appropriate selection of analgesic medications for treatment of severe pain after traumatic injury were not available at most competition venues. Medications containing a prohibited beta-2-agonist (tretoquinol), and a prohibited stimulant (tuaminoheptane) were available for prescribing at competition venues, presenting a potential risk of inadvertent doping to athletes.
Rio 2016	Several medicines commonly used in sports medicine globally were locally unavailable in Brazil, including some types of oral and topical NSAIDs. Incorrect information about the status of WADA prohibited substances was printed in games pharmacy guide, which needed to be recalled and republished mid-games. An excessive range and quantity of medications was provided at competition venues, which were not used, resulting in unnecessary cost, wastage, and logistical supply challenges.

	Some drugs stocked at competition venues for emergency use were outside the professional scope of practice of many of the medical workforce working at the venues.
Sochi 2014	Clinically appropriate analgesic medications for the treatment of severe pain after traumatic injury were not readily accessible on the field of play in some competition venues. Some drugs provided on the formulary were used in Russia, but not commonly used internationally, and better alternatives existed in terms of clinical safety and toxicity profiles (e.g. phenobarbital). A very limited selection of medications for minor ailments and symptomatic treatment for colds and flu was provided, and the treatment options did not reflect treatments widely prescribed internationally.
London 2012	Some venue drugs intended for emergency use, particularly rapid sequence intubation, were outside the scope of practice of some doctors working at those venues. The quantities of medications provided at competition venues exceed what was actually used, resulting in medication wastage and unnecessary costs. Some venue drugs were never used. Some duplication of medicines in the same therapeutic class were provided on the formulary, which could have been further rationalised to reduce costs.
Beijing 2008	Traditional Chinese herbal medicines were available for issue by the organising committee doctors, despite cautions by the World Anti-Doping Agency on the use of unregulated dietary supplements and the possibility of contamination, plus limited clinical evidence or understanding of safety profiles to support their use.

In 2018, the development of a new model formulary for the Olympic Games was recommended by the IOC Medical and Scientific Commission,[12] with support from the International Paralympic Committee (IPC) to also implement the model formulary for the Paralympic Games.

1.1.3 Supporting the strategy of the Olympic Movement

In 2014, the IOC passed a list of 40 reforms aimed at making the hosting of the Olympic games cheaper to stage and more attractive to host countries. These reforms formed the *Olympic Agenda 2020*, which was the strategic roadmap for the future of the Olympic Movement. Some of the key areas addressed by *Olympic Agenda 2020* included a new philosophy to invite potential candidate cities to present a project that fits their sporting, economic, social, and environmental long-term planning needs. But it also focussed on strengthening the principles of good governance and ethics, and the protection of the clean athlete.[15] It was these areas that particularly applied to the medical and pharmacy services of the Olympic Games, and so were embedded in the mission of the OPF from the outset.

The creation of the OPF supported the *Olympic Agenda 2020*[15] in the following strategic ways:

- Strengthening good medical governance and ethics relating to drug use and drug management at every games
- Protecting the health of the athlete through provision of safe, effective, and evidence-based drug treatment options and drug prescribing and administration guidance to both local and international physicians
- Empowering organising committee medical services to deliver excellent clinical care based on international best practice
- Reducing variability of medical care and standards between games
- Significantly reducing wastage and the costs of delivering the medical service through a rational selection of effective medicines for Olympic venues and villages
- Supporting clean athletes to remain doping-free through provision of trusted information about prescribed medications and the WADA regulations that apply to them

1.1.4 Methods used to create the first OPF

The format and guiding principles for the development of the first edition of the OPF were based on the World Health Organization (WHO) *Essential Medicines List* and *WHO Model*

Formulary, which consist of over 400 drugs deemed essential for addressing the most important public health needs globally, and which serves as a guide for the development of both national and institutional essential medicine lists.[16 17] The OPF was an adaptation of the WHO Essential Medicines List, but enhanced to cover a wider range of drugs used in sports medicine for athletes. The WHO list was also rationalised to reflect the likely specific needs of clients groups at the games, while recognising the temporary and short-term nature of the games medical service, public health issues relating to mass public gatherings, and access to existing healthcare infrastructure and sources of medicines supply in the host city.[18 19]

In addition, the OPF was developed using the London 2012 Olympic and Paralympic Games medicines formulary as a primary reference, which had been previously developed through a rigorous process involving a substantial review of previous games formularies, and pharmacy dispensing data. The development of the London 2012 formulary[7] represented the first time that previous games drug usage data had been used to inform the selection of medicines for a games formulary in a data-driven and systematic way.[14] The formularies and pharmacy dispensing data from the following games were included in this review: Sydney 2000 Olympic Games;[8] Manchester 2002 Commonwealth Games;[20] Melbourne 2006 Commonwealth Games;[21] Beijing 2008 Olympic and Paralympic Games;[9] and the Vancouver 2010 Olympic and Paralympic Games.[10] The format, drug naming conventions, and presentation of prescribing information for London 2012 was based on the British National Formulary.[14 22] The final pharmacy dispensing reports from the London 2012 Olympic and Paralympic Games were used to assess whether the medications on the formulary were used, or not used, during the games to further refine the draft list for the OPF prior to wider consultation.[2]

The determination of the necessary therapeutic drug classes for the OPF was also guided by the principles and scope of care required to be provided by Olympic organising committees, as outlined in the *IOC Olympic Games Guide on Medical Services*.[3] This guide states that the drug stock at competition venues must enable immediate first response and stabilisation of the patient onsite, prior to the transfer of the patient to the ambulance, where emergency pre-hospital medications can be administered if required. The range of drugs kept in the emergency bags on the field of play, versus the stock drugs in the venue medical rooms and

in the onsite ambulances needs to reflect the care pathway of a patient in the venue environment.[3] The OPF therefore contains a specific sub-list of essential emergency medicines which should be available for use by specialist emergency medicine providers at all venues. These lists are based on current international protocols for emergency resuscitation.[23] In addition, it contained the recommended list of medicines to be available from the medical stations at competition venues for the first-response treatment of common minor ailments and sports injury.

Conversely, the development of the OPF included consideration of what therapeutic categories not to include. It specifically identified those clinical conditions which were outside of the scope of the games medical service, but which would require referral to existing hospital services on a case-by-case basis. Clinical conditions not covered by the OPF include rare conditions, chronic long-term conditions, and those requiring specialist hospital treatment or monitoring. The OPF did, however, include a few examples of common medicines that are used for chronic conditions, based on some demand at previous games. However, the initiation of treatment of medicines for chronic conditions is not common in the games environment and should usually be undertaken through the patient's usual medical care provider.[18 24]

Finally, IOC consensus statements on pain management in athletes and use of nutritional supplements in elite athletes were reviewed to also inform the selection of analgesic and other treatment options relevant to the athlete population.[25 26]

1.1.5 International consultation and peer review

It was important that the new OPF met the needs of the all the clinical disciplines represented through the games medical services, and that it was relevant and could be adopted by the host countries of the known upcoming Olympic and Paralympic Games at the time of publication, which were: Japan (Tokyo 2020), Switzerland (Lausanne 2020 Winter Youth Olympics), China (Beijing 2022), France (Paris 2024), and USA (Los Angeles 2028). The OPF

would also be applicable to the Paralympic Games and so also needed to meet the clinical need of athletes with disabilities and impairments.

A group of international expert clinical advisors was established to peer review the OPF prior to final publication and consisted of current members of the IOC Medical and Scientific Commission Games Group, representing clinical experts in sports medicine, emergency medicine, pharmacy, dentistry, physical therapy, and public health, from various countries. The advisory group also included medical experts of the IPC Medical Committee and pharmacists and physicians working on the upcoming Olympic and Paralympic Games in Japan and China.

The feedback from the peer review process was considered by the editors of the OPF.[1] Most issues raised were related to the selection of drugs for emergency medicine to meet the scope of care provided at the games, and requests for the inclusion of specific drug examples that were used commonly in some regions of the world. Any outstanding issues were discussed at a face-to-face meeting of a sub-group of experts convened during the PyeongChang 2018 Olympic Winter Games, where a consensus on the final composition of the first OPF was agreed.

The final proposed OPF was then reviewed and ratified by the Medical Directors of the IOC and IPC and the first edition was officially published by the IOC in March 2019 in time for implementation at the Tokyo 2020 Olympic and Paralympic Games.[1]

1.1.6 Format of the OPF

The OPF is divided into 23 sections based on the following therapeutic categories.

Table 2 Therapeutic categories of the OPF

OLYMPIC & PARALYMPIC MODEL FORMULARY 2019	
Section	Therapeutic Category
1	**MEDICINES FOR PAIN AND INFLAMMATION**
1.1	Non-opioids and NSAIDs
1.2	Opioid analgesics
1.3	Medicines for neuropathic pain
1.4	Corticosteroids for intra-articular use
1.5	Local anaesthetics
1.6	Anaesthetic agents for dental procedures
2	**ANTI-ALLERGIC MEDICINES**
3	**ANTICONVULSANTS & ANTISPASMODICS**
4	**ANTI-INFECTIVE MEDICINES**
4.1	Antibacterials
4.2	Antifungal medicines
4.3	Antiviral medicines
4.4	Antiretrovirals
5	**ANTIMIGRAINE MEDICINES**
6	**IRON SUPPLEMENTS**
7	**MEDICINES AFFECTING COAGULATION**
8	**CARDIOVASCULAR MEDICINES**
8.1	Antianginal medicines
8.2	Antihypertensive/heart failure medicines
8.3	Antithrombotic medicines
8.4	Lipid-lowering medicines
9	**DIURETICS**
10	**DERMATOLOGICAL MEDICINES, TOPICAL**
10.1	Antifungal medicines
10.2	Anti-infective medicines
10.3	Anti-inflammatory and anti-pruritic medicines
10.4	Acne treatment
10.5	Paracidal and scabicidal preparations
10.6	Keratolytics
10.7	Emollient, barrier and sun protection preparations
10.8	Tissue adhesives

10.9	Massage and physical therapy preparations
11	**ANTISEPTICS AND DISINFECTANTS**
11.1	Antiseptics
11.2	Disinfectants
11.3	Water quality testing
12	**GASTROINTESTINAL MEDICINES**
12.1	Anti-secretory medicines
12.2	Antacids
12.3	Antiemetic and antispasmodic medicines
12.4	Laxatives
12.5	Medicines for diarrhoea
12.6	Probiotics
13	**CONTRACEPTIVES, HORMONES & ENDOCRINE MEDICINES**
13.1	Contraceptives
13.1.1	Combined oral contraceptives
13.1.2	Progestogen only contraceptive
13.1.3	Emergency oral contraceptive
13.2	Progestogens
13.3	Insulins and other medicines for diabetes
13.4	Thyroid hormones
14	**IMMUNOLOGICALS**
15	**OPHTHALMOLOGICAL PREPARATIONS**
15.1	Anti-infective agents
15.2	Artificial tears
15.3	Hay fever symptom relief
15.4	Anti-inflammatory agents
15.5	Local anaesthetics
15.6	Mydriatics
15.7	Diagnostic agents
16	**MEDICINES FOR MENTAL HEALTH AND BEHAVIOURAL DISORDERS**
16.1	Medicines for depressive disorders
16.2	Medicines for anxiety disorders
17	**MEDICINES FOR SLEEP DISORDERS**
18	**MEDICINES ACTING ON THE RESPIRATORY TRACT**
18.1	Anti-asthmatic agents and medicines for COPD
18.2	Antitussive medicines
19	**DILUENTS FOR INJECTION & STERILE CLEANING**
20	**EAR, NOSE AND THROAT MEDICINES**
21	**MEDICINES FOR TREATMENT OF ORAL CONDITIONS**
22	**MEDICINES FOR HAEMORRHOIDS AND PRURITUS ANI**

23	**EMERGENCY & PRE-HOSPITAL CARE MEDICINES**
23.1	General anaesthetics
23.2	Pre-operative medication and sedation for short-term procedures
23.3	Inhalational medicines
23.3.1	Oxygen
23.3.2	Gases for analgesia and sedation
23.4	Medicines used in anaphylaxis
23.5	Antiarrhythmic and cardiac arrest medicines
23.6	Muscle relaxants (peripherally acting)
23.7	Parenteral fluids

The following table presents an extract of the first edition of the OPF relating to the section on pain and inflammation to illustrate the format. It also shows how the status of the medication according to the *WADA List of Prohibited Substances and Methods* as of 1 January 2019 [27] is presented in the document, whether a needle-use declaration must be submitted according to the *IOC Needle Policy,*[28] [29] and whether the medication is recommended to be kept as stock at competition venues.

Table 3 Extract of the pain and inflammation section of the first edition of the OPF

		Primary indication and notes	WADA Status	Needle-use declaration required [N]	Venue stock [V]
1. MEDICINES FOR PAIN AND INFLAMMATION					
1.1 Non-opioids and non-steroidal anti-inflammatory drugs (NSAIDs)					
Acetylsalicylic acid (Aspirin)	**Tablet or soluble tablet:** 300 mg to 500 mg	Mild to moderate pain; pyrexia (*see Section 8.3 for anti-thrombotic use*)	Not Prohibited		**V**
Celexoxib*	**Tablet:** 200 mg	Mild to moderate pain; pain with inflammation; where other NSAIDS are not tolerated or not appropriate	Not Prohibited		
	*Or other oral COX-2 inhibitor				
Ibuprofen	**Oral liquid:** 200 mg/5 mL	Mild to moderate pain; pain with inflammation; pyrexia	Not Prohibited		
	Tablet: 200 mg; 400 mg	Mild to moderate pain; pain with inflammation; pyrexia; dysmenorrhea	Not Prohibited		**V**
Naproxen*	**Tablet:** 250 mg or 500 mg	Pain and inflammation in musculoskeletal conditions; dysmenorrhea	Not Prohibited		**V**
	*Or other oral NSAID such as meloxicam, ketorolac, or loxoprofen				
Paracetamol (Acetaminophen)	**Oral liquid:** 120 mg/5 mL	Mild to moderate pain; pyrexia	Not Prohibited		**V**
	Suppository: 100 or 200 mg	Mild to moderate pain; pyrexia	Not Prohibited		**V**
	Tablet: 500 mg	Mild to moderate pain; pyrexia	Not Prohibited		**V**
	Soluble tablet: 500 mg	Mild to moderate pain; pyrexia	Not Prohibited		**V**
Ketorolac*	**Injection:** 30 mg/1 mL	Short-term management of moderate to severe acute pain	Not Prohibited	**N**	**V**

	*Or other injectable NSAID such as diclofenac 75 mg/2 mL				
Diclofenac*	**Topical gel:** 1%	Relief of pain in musculoskeletal conditions	Not Prohibited		**V**
	*Or other topical NSAID such as ibuprofen or naproxen				
	Tablet: 50 mg	Relief of pain in musculoskeletal conditions	Not Prohibited		**V**
	Suppositories: 50 mg or 100 mg	Pain and inflammation in musculoskeletal disorders	Not Prohibited		
1.2 Opioid analgesics					
Codeine phosphate*	**Tablet:** 30 mg	Moderate to severe pain	Not Prohibited		
	*Or other non-prohibited oral opioid for moderate to severe pain such as dihydrocodeine or hydromorphone				
Codeine + Paracetamol*	**Tablet:** 8mg to 30 mg (codeine phosphate) + 500 mg paracetamol	Mild to moderate pain	Not Prohibited	**N**	**V**
	*or other combination analgesic containing paracetamol plus a non-prohibited opioid				
Morphine	**Injection:** 10 mg (morphine hydrochloride; or morphine sulfate) in 1 mL ampoule	Emergency analgesia for serious injury with severe pain	**PROHIBITED**	**N**	**V**
Tramadol	**Injection:** 100 mg/2 mL	Moderate to severe pain	Not Prohibited	**N**	**V**
	Capsule: 50 mg	Moderate to severe pain	Not Prohibited		**V**
1.3 Medicines for neuropathic pain					
	Tablet: 10mg	Neuropathic pain	Not Prohibited		

Amitriptyline hydrochloride*	*Or other tricyclic antidepressant suitable for neuropathic pain such as nortriptyline				
Gabapentin*	**Tablet:** 300 mg	Neuropathic pain	Not Prohibited		
	*Or other second-line neuropathic pain agent such as pregabalin or duloxetine				
1.4 Corticosteroids for intra-articular use					
Triamcinolone	**Injection:** 20 mg/1 mL (as hexacetonide or acetonide)	Local inflammation of the joints	Not Prohibited by intra-articular routes but **PROHIBITED** by IV, IM routes	**N**	
Hydrocortisone sodium phosphate	**Injection:** 100 mg/1 mL; or 100mg/2mL	Local inflammation of the joints	Not Prohibited by intra-articular routes but **PROHIBITED** by IV, IM routes	**N**	
1.5 Local anaesthetics					
Lidocaine*	**Injection:** 1% (as hydrochloride) in vial	Acute pain management	Not Prohibited	**N**	**V**
	*Or other injectable local anaesthetic such as bupivicaine 0.5%				
	Topical gel, spray or patch: 2% to 8% (as hydrochloride)	Surface anaesthesia	Not Prohibited		
Lidocaine + Epinephrine (adrenaline)*	**Injection:** 1% (as hydrochloride or sulfate) + epinephrine 1:200 000 in vial	Local anaesthesia (caution: not for use for peripheral injuries)	Not Prohibited	**N**	
	*Or other combination local anaesthetic with vasoconstrictor for injection such as bupivacaine + epinephrine				

The status of medicines according to the WADA *List of Prohibited Substances and Methods* as of 1 January 2019 [27] are also provided in the OPF. Prohibited medicines included in the OPF for legitimate therapeutic use, with a valid Therapeutic Use Exemption include the following:

Table 4 Prohibited medicines in the 2019 OPF

PROHIBITED AT ALL TIMES	PROHIBITED IN-COMPETITION	PROHIBITED IN PARTICULAR SPORTS
S3. BETA-2 AGONISTS	**S6. STIMULANTS**	**P1. BETA-BLOCKERS**
Formoterol inhaler*	Epinephrine (adrenaline)	Bisoprolol tablet
Salbutamol inhaler*		Metoprolol tablet
Salbutamol nebuliser	**S7. NARCOTICS**	Nebivolol tablet
Salmeterol inhaler*	Fentanyl injection	
	Morphine injection	
S4. HORMONE AND METABOLIC MODULATORS		
Insulin injection	**S9. GLUCOCORTICOIDS**	
Intermediate-acting insulin	Beclometasone tablet	
	Dexamethasone injection	
S5. DIURETICS AND MASKING AGENTS	Dexamethasone tablet	
Bendroflumethiazide tablet	Hydrocortisone injection***	
Bumetamide tablet	Hydrocortisone rectal	
Furosemide tablet	Prednisolone tablet	
Glucose injectable solution**	Triamcinolone injection***	
Hydrochlorothiazide tablet		
Mannitol injectable solution		
Sodium chloride injectable solution**		
Spironolactone tablet		

*Note that formoterol, salbutamol and salmeterol by inhalation are not prohibited if taken as prescribed according to the manufacturer's recommended dosage schedule. However, salbutamol in emergency doses or nebuliser will almost always result in levels above the accepted urinary threshold.

** intravenous infusions or intravenous injections are prohibited above 100 mL per 12 hour period regardless of any accompanying medication. A TUE should be requested if an intravenous injection above 100 mL is used.

***These may not be prohibited depending on the route of administration, for example, intra-tendinous or intra-articular injections. Glucocorticoids are prohibited by oral, intravenous, intramuscular injection or rectal routes.

1.1.7 Adapting the OPF for host countries

In addition to providing the list of essential medicines for the games, the OPF also provides guidance for organising committees on how to implement the model formulary, which includes some flexibility to account for local medicines availability. Some alternative drug examples are listed on the OPF if the primary one is unavailable, but if required, an alternative medicine within the same pharmacological class, and with the same clinical indication can be substituted if the primary or alternative options presented by the OPF are unavailable locally. The OPF guidance also allows for additional medicines to be added if required in response to specific environmental or public health risks that may be present and unique to the host country.[1]

1.1.8 The future

The OPF established the first standardised approach to the selection of drug treatment options for all future Olympic and Paralympic Games. It informs the essential list of medicines that are required to be available through the polyclinic medical services and at all competition and non-competition venues. The OPF provides a framework for selection of medicines based on current best clinical evidence, while representing the clinical needs of athletes and the prescribing preferences of visiting team physicians from around the world.[1] Regular revision and updating of this formulary is, however, essential to ensure its continued relevance to current medical practice and reflect the medications athletes require at the time of the games.

The research undertaken for this PhD sets out a unique method of review for the sections of the OPF relating to treatments for pain and inflammation due to sports injury, which incorporates a much wider pool of athlete drug usage data than was originally used for the development of the first edition. It is envisioned that the approach taken in this PhD study will be able to be applied to review and update the entire OPF for the subsequent edition.

1.2 ANALGESIC AND ANTI-INFLAMMATORY MEDICINES IN SPORTS MEDICINE

1.2.1 Types of pain associated with sports injury

There are four categories of pain, described as nociceptive, neuropathic, inflammatory or central sensitisation.[30] The duration of pain associated with sport injury may be described as acute (up to 6 weeks), sub-acute (6-12 weeks) or chronic (3 months or longer).[31]

In the context of sports medicine, each category of pain can be described as follows. 1) Nociceptive pain is the most common type of pain athletes experience from sports injury; it is used to describe the pain from physical damage or potential damage to the body and can be present with or without inflammation. 2) Inflammatory pain is the spontaneous hypersensitivity to pain that occurs in response to the damage of tissue and the resulting inflammation. This type of pain is often associated with acute traumatic sport injury with accompanying inflammation and swelling. 3) Neuropathic pain is caused by damage or disease affecting the somatosensory nervous system. Such pain may be a result of spinal cord injury, and thus may be seen in athletes with physical impairments. 4) Central sensitisation represents pain due to the enhancement in neuronal responsiveness or reduced inhibition within the central nervous system, without an identifiable noxious stimulus, inflammation, or neural damage. This may manifest as myofascial pain in an athlete.[39-50]

1.2.2 Types of sports injury

Sports injury is generally described as a new or recurring musculoskeletal complaint incurred during sports competition or training which requires medical attention, regardless of the potential absence from competition or training.[32] Sports injury is commonly categorised into three main categories: 1) acute traumatic injuries, 2) overuse injuries, and 3) subacute recurrent injuries and chronic degenerative conditions. These are described as follows.

Acute traumatic injury refers to a single event that leads to a singular macrotrauma of previously healthy tissue.[33] Acute injuries are commonly caused in sport by a collision, fall,

twist, or sudden impact, where pain is immediately felt. Most commonly, tears and sprains of the ligament and muscles are the consequence of such injuries, which demand immediate medical attention. Anti-inflammatory drugs are used to reduce the inflammatory response in such injuries, with oral NSAID drugs most frequently used for this purpose.[34]

Overuse injuries occur from repetitive submaximal loading of the musculoskeletal system when an inadequate period of rest has prevented structural adaptation.[35 36] Risk factors for these injuries include previous injury, training workload, intense and repetitive training and competition schedules, and inappropriate equipment use or technique.[35 37]

Subacute recurrent injuries and chronic degenerative conditions are closely related and often result from overuse injuries. A recurrent injury is defined as the same type and at the same site of a previous injury, which occurs after an athlete's return to the sport after the original incident.[38] Chronic soft-tissue injury, for example tendonitis, can start as mild pain without imposing any physical limitations. Chronic inflammation is often treated through rest, physical therapy, and NSAIDs. Local glucocorticoid injections are sometimes used for such injuries.[34]

1.2.3 The context of analgesic and anti-inflammatory drugs in sport

The world's elite athletes at the Olympic Games are in peak physical condition and represent some of the healthiest and fittest people on the planet. For most, participation at the event will be the highlight of their career and the culmination of years of intense training. However, in this environment where athletes push themselves to their maximum limits, sports injury is common, often resulting in painful and inflammatory conditions requiring immediate treatment; at the Rio 2016 Olympic Games, 8% of athletes reported an injury, 9% of athletes reported an injury during the Tokyo 2020 Olympic Games, and 10% of athletes reported an injury during the Beijing 2022 Olympic Winter Games.[39 40 41]

Patterns of drug use

The types and patterns of drug use seen in this environment are often very different to those observed in the general population. There have been a small number of studies conducted at

previous major games and other sporting events looking at medication declarations on doping control forms, applications for TUEs to use prohibited medications, games time needle declaration forms, and games pharmacy dispensing reports in order to understand of the use of drugs by elite athletes in this setting.[42 43-58] This PhD research project is unique from these previous studies as it combines multiple sources of known athlete drug usage data, providing a more comprehensive understanding of drug use by athletes at these international games than ever before.

The way analgesic and anti-inflammatory drugs are prescribed to athletes in the context of high-performance sport varies between clinicians, as does the intended use, which can range from immediate treatment of acute pain and inflammation, through to pain prevention, or performance continuation or improvement. In a survey on pain management of international team physicians conducted at the Rio 2016 Olympic Games, 61% (n=107) of physicians reported routine prescribing of analgesics or anti-inflammatory medications in greater than 10% of athlete patients. In the same survey, 50% of physicians considered acute pain and inflammation to be the most important factor when prescribing analgesic and anti-inflammatory medications, with 7% considering prevention of pain, inflammation and delayed-onset muscle soreness to be important, and 6% considering performance or endurance improvement to be an important factor when prescribing analgesic and anti-inflammatory medications to elite athletes.[25] It is also widely reported in studies looking at drug use in elite athletes that because of their intense training and competition regimens, athletes are more likely to use multiple analgesic agents compared to the general population, and be using them prophylactically before competition for prevention of pain.[42 55 59]

Driving factors for athletes to take analgesic medications

One of the primary factors driving athlete's use of analgesic and anti-inflammatory medications in sports includes the pressure to perform and the ambition to return to play quickly after an injury. Often athletes compete in a culture where playing through pain is the norm, and who have easy access to many common medications either through their team physician or through self-prescribing via local community pharmacies. The widespread availability and acceptance of drugs such as NSAIDs may lead to their routine use, sometimes

based on inadequate understanding of the potential risks and side-effects that might be involved. Other factors that drive analgesic medication use may include psychological reasons, including when athletes experience competitive anxiety and so may feel more confident and less anxious about their injury or pain when they know it is being managed with medication.[60] The decision to use analgesics may also be influenced by peer or sport-culture practices where physiotherapists, coaches, teammates, or other athlete support personnel may encourage the use or misuse of analgesics.[61]

The decision for an athlete to take analgesic or anti-inflammatory medications can be significantly influenced by the desire to maintain performance levels and potentially prolong the career of an athlete, and as such athletes may disregard potential long-term health risks for any opportunity to compete and win in their sport.[62] Athletes are often under immense pressure to maintain performance levels, and continue to compete despite serious injury, and so may resort to strong analgesia options such as opioids for quick and immediate pain relief, disregarding the potential serious risk of addiction and further injury.[62] These risks to health due to some PI medications are one of the reasons some drugs are prohibited in sport, for the primary aim to protect the health of the competing athlete.[5]

At the international elite level of competition at the Olympic Games, athletes may be subject to doping control testing. As such, when considering potential analgesic treatment options, both athletes and prescribers must be aware of the regulations pertaining to drug use in sport as governed by the World Anti-Doping Agency (WADA). Some opioid analgesic medications, including morphine, fentanyl and oxycodone, and glucocorticoids by some routes of administration, are listed on the *WADA List of Prohibited Substances and Methods*, and prohibited to be taken by athletes during competition.[63] However, when the use of such medications is deemed essential for the treatment of a medical condition for an athlete, an exemption to use the prohibited medication can be applied for through the athlete's national anti-doping organisation, international sport federation, or the major event organiser (such as the IOC), which is referred to as a Therapeutic Use Exemption (TUE).

A TUE is a formal authorisation allowing an athlete to use, for therapeutic purposes, a substance or method that is otherwise prohibited. Athletes may apply for a TUE if they have a documented medical condition that requires treatment with a prohibited substance or method. The process involves a thorough review by a TUE committee consisting of three physicians familiar with sports medicine and pharmacology. To be granted a TUE, the athlete must demonstrate that:

1. The use of the prohibited substance or method is necessary to treat a diagnosed medical condition, supported by relevant medical documentation.
2. The therapeutic use of the substance does not enhance their performance beyond restoring their normal health.
3. There are no reasonable therapeutic alternatives than the use of the prohibited substance or method.

The application for a TUE must usually be made in advance of use, except in emergency situations where the application can be made retrospectively (known as a "Retroactive TUE”). The athlete, in collaboration with the prescribing physician, is required to submit a detailed medical file, including the diagnosis, medical history, and the proposed treatment plan. The review process is undertaken by the TUE Committee who decide whether the athlete can take the prohibited medication for their medical treatment, or whether they should seek an alternative permitted treatment.

Once granted, a TUE is typically valid for a specific period. If an athlete with a TUE is subject to doping control, they must declare the use of the medication on their doping control form, and the presence of the substance in their sample will not be considered an Anti-Doping Rule Violation if the use is consistent with the terms of their TUE. The TUE process fairly recognises that some athletes have legitimate medical conditions requiring treatment with prohibited substances. The process of granting a TUE is rigorous, and must be undertaken in accordance with the *WADA International Standard for Therapeutic Use Exemptions*.[64]

1.2.4 Prescribing considerations for acute pain management at major games

Major international multi-sport events, such as the Olympic Games will almost always have a comprehensive medical service providing medical care for athletes at competition and training venues. This will include provision of a medical room stocked with medications including analgesia, and access to emergency medical services and ambulance at every competition venue. Access to analgesia for acute pain management will always be available at competition venues.[1 18]

When an acute injury occurs during competition or training, depending on the level of pain, athletes may be treated with a single dose of analgesia administered immediately at the venue, with follow-up care and ongoing analgesia being provided from either the polyclinic in the athlete village, or from the local hospital depending on the severity of the injury. The decision to treat an athlete to enable return to play in the elite sport environment can be a difficult and complex judgement faced by team physicians at major games. Any pain relief that allows competition to continue should not create further risk of making the injury worse for the athlete.[25] However, in this setting the decision to return the athlete to play versus the risk of causing further injury is often evaluated against the fact that the Olympic event will be a once-in-a-lifetime opportunity for the athlete who has spent their entire life to get to this moment.

In any case, analgesics for acute pain should normally not be used for longer than 5 days before being revaluated based on the clinical presentation at that point in time.[65-67] This standard principle when prescribing analgesics is not always followed in the games environment. The survey of team physicians conducted at the Rio 2016 Olympic Games indicated that 31% of physicians usually prescribe NSAIDs for 1-2 days duration; 42% prescribe a 3-5-day course; but 21% of physicians prescribe courses of NSAIDs for periods longer than 7 days.[25]

Treatment of severe pain in athletes

Major acute or traumatic injuries with associated severe pain may require immediate emergency pain management on the field of play. A severely injured athlete may require effective analgesia as soon as possible, and certainly before any pre-hospital treatment is attempted.[68]

At all competition venues at the Olympic Games, a strong opioid analgesic such as morphine will be available, as mandated by the IOC.[1] [18] The OPF also recommends examples of inhalation agents including methoxyflurane due to their rapid onset of action and ease of administration to be accessible on the field of play in countries where they are available.[68] Such analgesics for acute emergency must be limited to use immediately post-injury to enable the athlete to be referred to hospital services for ongoing care. In these scenarios, it is highly unlikely that the athlete would be able to return to competition for some days after the incident. If ongoing strong analgesia is warranted, the continued use opioid analgesics should generally be limited to a maximum of five days use.[25]

Treatment of moderate to severe pain in athletes

The OPF contains a broad selection of medicines with various routes of administration for the moderate to severe category of pain intensity, which range from simple analgesics such as paracetamol and NSAIDs to a selection of different potency opioid analgesic drugs. It is conceivable that athletes treated for moderate pain, may still be likely to compete. As such, there are some unique considerations when selecting a suitable analgesic.

For athletes, any cognitive effects produced by the chosen analgesia needs to be carefully considered, such as potential effect on reaction time and alertness, which could result in an ergolytic effect, or in other words negatively impact their performance. As such, opioids such as morphine and tramadol, are often avoided in athletes who may still be able to compete after the injury.[69]

The safety issues relating to the athlete's particular sport should also be considered with analgesics such as tramadol and morphine in light of potential associated cognitive

impairment. This is particularly important for team sports or sports in close contact with other athletes where an accident due to reduced reaction time could affect the safety of both the individual and the other competitors.[70 71] The status of opioid analgesics according to the *WADA List of Prohibited Substances and Methods* also needs to be checked carefully as a number of these drugs are prohibited to be used by athletes during competition.

Injectable local anaesthetics are often used for moderate to severe pain for their immediate analgesic effect to enable fast return to play during competition, although should not be a first-line choice.[72 73] However, local anaesthetics do provide a viable option for some types of localised pain which is impairing performance, but where administration will not present a worsening of the injury.[72 73]

Injectable NSAID medications are frequently used in sports medicine for the short-term management of moderate to severe pain, with the advantage of a more rapid onset of action than oral NSAIDs and thus faster possible return to play for the athlete. Intramuscular ketorolac is one such example specifically listed on the OPF, which is used predominantly for its rapid analgesic effects rather than its anti-inflammatory effects.[74]

Glucocorticoid injections are widely used in sports medicine by local administration, including intraarticular, periarticular and intrabursal routes. Glucocorticoids administered by local injection can be an important and effective option in the treatment plan of a number of musculoskeletal conditions commonly encountered in sports medicine.[75-77] They are effective in rapidly suppressing inflammation within the joints, which leads to pain relief and rapid restoration of function of the joint. Compared with NSAIDs, glucocorticoid drugs are associated with a more pronounced and lasting anti-inflammatory effect, but they have been shown to actually impair the healing response in a number of studies.[25 78-89]

Despite their highly effective therapeutic effect, glucocorticoids have a relatively high potential for triggering adverse effects, and systemic effects have been documented after local injection.[90] The potential for harmful effects ultimately depends on the duration of treatment, dose, route of administration and patient-specific factors.[91] For these reasons,

glucocorticoids have limited use in acute injury of elite athletes, but examples are provided on the OPF, which include injectable triamcinolone and hydrocortisone.[1]

Treatment of mild to moderate pain in athletes

For mild to moderate pain on the day of competition, the most common and effective treatment options are paracetamol, either alone or in combination with NSAIDs.[92 93] Oral paracetamol has a very similar analgesic profile to oral NSAIDs, but when both are combined, an additive analgesic effect has been demonstrated.[92]

In the following days after injury, both oral NSAIDs and paracetamol provide a comparable level of pain relief when treating for mild to moderate pain in athletes. Paracetamol has a much safer side-effect profile than NSAIDs, particularly when prescribed for longer periods of time, but does not have the anti-inflammatory action of NSAIDs, which is often desirable when treating musculoskeletal injuries.[65 92 94] If there is no inflammation present, then paracetamol is preferable to NSAIDs due to less potential for adverse effects.[65]

1.2.5 Prescribing considerations for chronic pain management at major games

Chronic pain is generally defined as the continuation of pain for a period greater than three months. The OPF has a remit of providing options for the treatment of conditions requiring immediate and necessary care in the games environment, and so the focus is primarily on the treatment of acute conditions, and less of focus on longer-term or pre-existing conditions. However, the range of medications for pain and inflammation provided on the formulary is also expected to provide any essential care that is required at the time of the games, and given that chronic pain is something that some athletes experience as a result of their sport, examples of medicines covering the full spectrum of pain treatment are provided.[1]

Most medicines prescribed to athletes for the treatment of acute pain are rarely indicated to be used for longer-term treatment of chronic pain. For example, there is no clinical rationale for use of paracetamol past the acute treatment period, nor the long-term use of NSAIDs for pain management in athletes.[65-67] Similarly, opioid analgesics should be used with extreme

caution for extended periods of time due to the serious risk of addiction and lack of evidence regarding benefits of long-term use. For chronic pain in athletes, the treatment approach usually includes preventative measures and other interventions such as physical therapies to improve function.[95-98]

Adjuvant pain medications are often used for the treatment of chronic pain conditions in athletes, and a number of commonly prescribed examples are provided on the OPF. These medications are not routinely prescribed to directly mask pain but rather may be helpful for its management. Adjuvant pain medications can include sedatives, muscle relaxants, antidepressants and anticonvulsant medications.[99-105] The most commonly used adjuvants for chronic pain are gabapentin, pregabalin, serotonin–noradrenaline reuptake inhibitors, and tricyclic antidepressants. For second line treatment of local pain, medications include lidocaine and capsaicin patches, both of which are provided on the OPF.[1]

1.2.6 OPF categories of medicines for pain and inflammation

For this study, the following OPF pharmacological categories have been determined to have a clinical role in the treatment of pain and/or inflammation in athletes due to sports-related conditions. It is these categories that are the subject of this PhD research to determine the most optimal examples to include on the OPF for the Olympic Games. They are referred to throughout this thesis collectively as "PI medications"

OPF PI medication categories

01.1.1 NSAIDs
01.1.2 COX-2 inhibitor
01.1.3 Non-opioid analgesics
01.2 Opioid analgesics*
01.3 Medicines for neuropathic pain
01.4 Corticosteroids for intra-articular use*
01.5 Local anaesthetics
01.5.1 Local anaesthetics + vasoconstrictor
02.1 Corticosteroids for oral use*
03.1 Benzodiazepines
03.2 Skeletal muscle relaxants
10.9 Massage and physical therapy preparations
23.1.2 General anaesthetics with analgesics

*Categories that contain prohibited medications, which may require a TUE to be applied for if used by athletes.

It is important to recognise that a number of these categories contain medications which are licenced for use for multiple clinical indications, some of which are unrelated to the treatment of pain or inflammation, or used in the context of sports injury. For example, some tricyclic medications used for neuropathic pain are also used for depressive disorders, anxiety, or insomnia; some oral corticosteroids are also used for allergic, asthmatic, autoimmune, or skin conditions; and benzodiazepines are used for insomnia, or anxiety disorders.[106 107] However, they were included in this definition of PI medications as they can potentially have some role either as single agent medications or as adjuvant treatments for painful or inflammatory musculoskeletal conditions in athletes.

Estimating prevalence of PI use

Approaches to estimating the prevalence of PI medication use in athletes vary significantly across the research literature, which complicates the ability to make precise comparisons of prevalence between studies. Some research, relying on doping control data, estimates use based on self-reported athlete consumption within the last week. Other studies survey athletes outside of competition, inquiring about medication use over extended periods of time, such as the past year. Other studies have used pharmacy dispensing records or physician reports of prescriptions to athletes. These methodological variations hinder reliable comparisons of use rates over time, across different sports, or between sub-populations of athletes.

The following sections present a summary of the clinical use of the PI medication classes on the OPF, and what is currently known in terms of their use in the athlete population. The prevalence is reported in accordance with how it is presented in the primary study publication, with numerous sources cited where they exist.

1.2.6.1 *Non-steroidal anti-inflammatory drugs (NSAIDs)*

NSAIDs are one of the most widely used class of drugs to treat soft-tissue, musculoskeletal, and painful inflammatory joint conditions associated with sports injury. They are also used for the treatment of post-exercise delayed onset muscle soreness (DOMS). Their primary use is

for pain reduction and inflammation control, demonstrating advantages over other analgesia used for musculoskeletal problems because of this dual effect. NSAIDs are presented on the OPF in a number of dosage-forms including oral, topical, rectal, intravenous, and intramuscular. The oral and topical routes are the most frequently used for sports injury.[20]

The anti-inflammatory effects of NSAIDs are primarily attributed to the inhibition of prostaglandin synthesis. They inhibit the cyclo-oxygenase enzyme which in turn inhibits the conversion of arachidonic acid to cyclic endoperoxides resulting in reduced production of prostaglandins including PGE_2 and prostacyclin which leads to a reduction in inflammation and pain, decreased swelling, and improved flexibility. Mobility and strength of joint movement also improves when the inflammation is reduced.[108]

The healing of an acute soft-tissue injury with inflammation may be negligible or only slightly faster with the use of NSAIDs than without them. Inflammation is certainly better controlled with their use, but most patients recover from the acute condition irrespective of taking NSAIDs.[109] If the inflammatory symptoms can be reduced in the early stages of recovery, quicker progression into remedial exercise programs can occur.[110] Although effective in the treatment of pain and stiffness of soft-tissue injury, NSAIDs also have the potential to mask the symptoms associated with sports injury and may enable the athlete to continue with a normal training schedule. Athletes should be made aware of the risk of further injury if NSAIDs are used to mask pain for the purpose of performance continuation during the recovery period.[111]

Topical NSAIDs include creams and transdermal patch formulations and are used for the relief of pain and inflammation caused by soft-tissue injury, sprains, strains, and musculoskeletal trauma. Topically NSAIDs penetrate the skin and result in therapeutic concentrations for treatment of inflamed soft-tissues and joints, with similar analgesic effects to oral administration.[112] The lower plasma concentrations that result from the use of topical diclofenac and other topical NSAIDs are unlikely to be sufficient to cause the systemic side-effects generally associated with oral NSAID use. The benefit of topical NSAID agents over oral simple analgesic preparations has not been demonstrated.[113 114]

Studies regarding the prevalence of NSAID use by athletes differ significantly, although differing methodologies and data presented by research at previous games makes direct comparisons difficult. Low use of NSAIDs was observed at the Calgary 1988 Winter Olympics, where only 2.4% of urine samples collected from athletes were found to contain traces of NSAIDs.[43] At the Athens 2004 Paralympic Games, 9.8% of athletes declared use of NSAIDs at the time of the games on the doping control form, with 11.6% of those being declared as administered by injection.[115] But in the year preceding the Athens Olympic and Paralympic Games, 34.8% of Olympic athletes and 48.7% of Paralympic athletes declared their use. [50 116] In another study of professional Italian football players, 93% of the athletes reported NSAID use in the past year,[117] and a similar study reported 50% of American college football players used NSAIDs during the course of a 5-month season.[118]

A systematic review of 49 studies of athletes aged 15-24 years reported that nearly half (48%) of young athletes had been found to use NSAIDs at some point. Another study reported the use in athletes varied greatly, from 7% using them in the past week, to 95% having used them at some point in their lifetime. Elite athletes, or those competing at a very high level, are more likely to use NSAIDs (64%) than non-elite athletes (31%).[119] Reports of prevalence of NSAID use in the general population also vary between demographic groups; one study reported that 15% of college students use NSAIDs continuously, and another study reported that 11% of adults in an Australian population used NSAIDs regularly.[120 121]

Adverse effects of NSAIDs can include upper gastro-intestinal effects including dyspepsia, heartburn, and less commonly nausea. Inhibition of prostaglandin synthesis is partly responsible for the side-effects, although these drugs also directly irritate the gastrointestinal mucosa, further contributing to the risk of peptic erosions and ulcers. Although rare, dizziness and drowsiness are also reported with NSAIDs, which should be considered when prescribing to competing athletes. The risk of adverse effects is reported to be of a greater concern for athletes than the general population due to evidence of higher use of multiple concurrent NSAIDs, multiple routes of administration, and use of higher doses than the manufacturer's licenced doses. There is also limited evidence to describing the positive effects on injury healing in the athlete population.[42 46 47 54-56 59 118]

There is a clear relationship between increasing daily doses and the risk of upper-gastrointestinal bleeding or perforation. In general, patients should be prescribed NSAIDs for the shortest period of time, at the lowest effective dose, to minimise the risk of gastrointestinal, and other adverse effects.[122]

1.2.6.2 *COX-2 inhibitors*

COX-2 inhibitors, also known as cyclooxygenase-2 inhibitors, are widely used in sports medicine due to their ability to reduce inflammation and alleviate pain associated with sports injury and they have been on the medicines formulary at every Olympic Games, since Sydney 2000.[6-9] Where traditional NSAIDs inhibit both COX-1 and COX-2 enzymes, COX-2-specific inhibitors inhibit only the COX-2 enzyme, and thus have a reduced incidence of serious gastrointestinal adverse effects compared with the administration of traditional NSAIDs.[123]

COX-2 inhibitors are most commonly taken orally, although injectable formulations are also currently licenced for use for some drugs. Common examples of COX-2 inhibitors include celecoxib, etoricoxib and parecoxib, with indications relevant to sports medicine including post-operative pain following sports injuries, chronic pain conditions including osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and treatment of pain and inflammation in acute injuries such as sprains and strains.[124-126]

Although COX-2 inhibitors present a more favourable gastrointestinal side-effect profile in comparison to non-selective NSAIDs, concerns remain about their safety, especially for long-term use. Cardiovascular risks, including an increased risk of heart attack and stroke have been associated with some COX-2 inhibitors.[127] This has led to the withdrawal of certain drugs, including rofecoxib and valdecoxib from the market in some countries and heightened surveillance of their use in athletes.[24] As the cardiovascular risks may increase with dose and duration of exposure, the lowest effective dose, with the shortest possible duration of treatment should be prescribed.[124-126]

1.2.6.3 *Other non-opioid analgesics*

Paracetamol (also known as acetaminophen) has long been used as an over-the-counter analgesic medication and remains the most frequently used drug for mild pain not associated with inflammation, and for its antipyretic properties in both athletes and the general population.[128] [119] The mechanism of analgesic action of paracetamol has not been fully determined, but is thought to act predominantly by inhibiting prostaglandin synthesis in the central nervous system and by blocking pain-impulse peripherally.[128]

The prevalence of paracetamol use among athletes has been reported to be 21% for athletes aged 15-24.[119] When looking at usage over specific periods, one study found that 34% of athletes had used paracetamol in the past month, 3% in the past three months, and 19% in the past year.[119] Another study of 141 sub-elite athletes reported that paracetamol was detected in urine samples of 9.5% of the athletes.[129] Similarly, another study reported that in 98 young athletes, paracetamol was detected in 9.2% of the participants during urine anti-doping screening.[130] The prevalence of paracetamol use in the general population is generally reported to be higher than that in the athlete population; one study in Sweden reported that 70.5% of adults, and 75.8% of people aged 18 to 25 years reported use of paracetamol in the last 3 months, and one study in West Bengal reported 47.6% of students between 14 and 18 years routinely self-medicated with paracetamol.[131] [132]

Paracetamol generally has a good safety profile within the recommended dosage ranges and may be prescribed for athletes who are intolerant to other NSAIDs, but can result in acute liver injury when used above therapeutic doses.[133] Paracetamol is always provided as a standard treatment option through the medical services at the Olympic Games for both athletes and non-athletes.[6-9]

1.2.6.4 *Opioid analgesics*

Opioid analgesic drugs are used in the treatment of moderate to severe pain due to sports injuries. They are most frequently used for pain associated with an acute injury, for short-

term analgesia immediately after the injury has occurred.[25] Opioid analgesic drugs are provided through the medical services at the Olympic Games, including for emergency use for athletes on the field of play, and at previous games have included codeine, dihydrocodeine, morphine, oxycodone, tramadol, and fentanyl.[6-9]

Opioid drugs exert their analgesic action by acting mainly on the μ opioid receptors found throughout the brain and spinal cord. This results in inhibition of nociceptive pathways in the brain, spinal cord, and peripheral terminals of nociceptive afferent neurons.[134]

Opioid use in athletes is generally reported as quite low, with most estimates of rates of regular use by elite athletes being under 1%.[53 115 135-138] This rate is somewhat lower than is observed in the general population, for example, the UK prevalence of opioid use is 13% over a period of one year,[139] and lower than what is what is reported in terms of prevalence of non-opioid or NSAID use. This may be explained by the fact that many of the opioid medications are prohibited in sport according to the *WADA List of Prohibited Substances and Methods,* potentially resulting in permitted treatment options to be preferred. However, the prevalence of opioid use differs greatly between sports, with one study in cyclists reporting tramadol use in 3.3% of athletes during the previous 3 months,[140] and another survey stating that 5.6% of Nigerian professional athletes used codeine during their sporting career at some stage.[141] One systematic review reported that the percentage of young athletes aged 15 to 24 years who reported using opioids varied from 3% to 13%.[119] Another systematic review of opioid use in athletes reported that use among professional athletes at any given time ranged from 4.4% to 4.7%, but opioid use over the career of a national-level football athletes was 52%.[142]

Adverse effects of opioid analgesic drugs commonly include nausea, vomiting, constipation and drowsiness, with high doses causing respiratory depression.[143 144] Doses that may have the potential to cause drowsiness or visual disturbance could put the athlete and the other competitors at risk of accidental injury. At higher doses, reaction-time may be impaired and may be detrimental to performance and disadvantageous to competitors in sports where reaction speed is crucial, for example, table tennis, badminton or football.[143]

In some circumstances, athletes taking opioid analgesic drugs may also have a competitive advantage due the reduction in pain, resulting in an increased ability for further exertion over other competitors.[62] For these reasons, the use of many of the strong opioid analgesics such as morphine is prohibited in sport by WADA and tested for during competition time. According to the 2023 *WADA List of Prohibited Substances and Methods*, the use of the following opioid drugs are prohibited during competition: buprenorphine, dextromoramide, diamorphine (heroin), fentanyl, hydromorphone, methadone, morphine, oxycodone, oxymorphone, pentazocine, and pethidine.[63] [145] From 1 January 2024, tramadol is also prohibited during competition.[146]

1.2.6.5 *Medicines for neuropathic pain*

Neuropathic pain may result from damage to nerve tissue, with some sports injuries leading to neuropathic pain through different pathologies and mechanisms.[147] It includes situations commonly found in athletes, such as trauma, compression neuropathies (for example, due to overuse or poorly fitting equipment), and peripheral neuropathies. Central pain might also be seen in athletes, especially after spinal cord injuries or trauma,[148] which might be more commonly seen with Paralympic athletes.[25] Similarly, phantom limb pain might be seen in amputee Paralympic athletes.

Treatment for sports-related neuropathic pain generally includes a tricyclic antidepressant or certain anticonvulsant drugs. Amitriptyline and pregabalin have been found effective first-line treatments for neuropathic pain,[149] [150] and can be used together if the patient does not respond to either medication at the highest tolerated dose.[25] Although nortriptyline is not licensed for use for neuropathic pain,[151] it is used in sports medicine as it is better tolerated than amitriptyline.[148] Gabapentin is another anticonvulsant drug used as a first-line treatment for sports-related peripheral neuropathic pain.[152]

Second-line treatment options for neuropathic pain can include opioid analgesics, such as tramadol. In addition, for athletes with localised pain, topical local anaesthetic preparations

such as lidocaine might be used. Topical capsaicin might also be administered for peripheral neuropathic pain, though its intense burning sensation may limit use.[25 153]

1.2.6.6 *Glucocorticoids*

Glucocorticoids, also referred to as corticosteroids, are the most potent anti-inflammatory drugs available and are often used for the treatment of sports injuries in athletes. They can be administered by intra-articular injection to relieve pain and to increase mobility in inflammatory joint conditions. Smaller amounts can be injected directly into soft tissues to reduce inflammation in conditions such as tennis elbow, or compression neuropathies.[154] Glucocorticoid injections are often combined with a local anaesthetic whereby the local anaesthetic provides immediate analgesia indicating that the precise area has been infiltrated with the glucocorticoid. Systemic side-effects after administration of local glucocorticoid injections in the doses used for sporting injuries are usually minimal, but as with systemic glucocorticoid administration, undesirable effects including adrenal suppression and weakness have been documented.[155 156]

Oral corticosteroids are also reported to be prescribed by sports medicine physicians for musculoskeletal conditions, although there is no licenced indication for this use.[157] One study of primary care sports medicine physicians (n=195) reported that 58.6% prescribed oral corticosteroids for musculoskeletal disorders, with an average of 6.6 prescriptions per month. Prednisone was most frequently administered (82%), for an average of 7 days treatment.[154 158]

Estimates of prevalence of general glucocorticoid use by athletes is varied. In one study reviewing athlete medication declarations on doping control forms, rates of glucocorticoid use in the last three days was estimated at between 1% and 9.2%.[159] Injectable glucocorticoid use was reported in 3.1% of athletes at the 2014 FIFA Football World Cup.[51] It has also been estimated that 13.5% of hamstring injuries in American football athletes are treated with injectable glucocorticoids.[82] In one study of Paralympic athletes, injectable glucocorticoid use was reported in 0.1% of athletes.[115] Given the wide variation in reported prevalence, it is

difficult to compare athlete glucocorticoid use to the general population, but as an example, one study in Denmark reported the annual prevalence of systemic (oral and injectable) glucocorticoid use was 3%, increasing to around 7% in people aged 60 to 79 years.[160]

According to the 2023 *WADA List of Prohibited Substances and Methods*, the use of glucocorticoids are prohibited in athletes when administered orally, rectally, or by any injectable route.[145] Prior to 2023, only intravenous or intramuscular injections were prohibited by WADA.[63] The use of these drugs for legitimate medical use by any other route requires the application and approval of a Therapeutic Use Exemption (TUE) before use.[64]

1.2.6.7 *Local anaesthetics*

Local anaesthetics are used to relieve some forms of pain associated with musculoskeletal injury and often in combination with glucocorticoid injections for the treatment of painful sports injuries.[155] Examples include lidocaine, bupivacaine, levobupivacaine, prilocaine, and ropivacaine. Local anaesthetic drugs act by causing a reversible block to conduction along nerve fibres by impairing the function of the sodium channels in the axon membranes of nerve tissue. They vary widely in their potency, duration of action, and ability to penetrate mucous membranes. These attributes are used when deciding their use, which includes topical, infiltration, peripheral nerve block, intravenous, epidural, or intrathecal administration.[161] The effect of local anaesthetic agents is dose-dependent; an increase in the dose of a local anaesthetic produces a faster onset and a longer duration of pain block.[162]

Lidocaine is the most frequently used injectable local anaesthetic agent as a result of its rapid onset of action, potency, and moderate duration of action. It is the drug of choice for short procedures, due to its duration and safety.[161] Both lidocaine and bupivacaine are provided on the OPF as examples of local anaesthetic agents to be available for use at the Olympic games.[1] Lidocaine is also available as patches and is used as a topical treatment for neuropathic pain.[25] [163]

Vasoconstrictors are sometimes used in combination with local anaesthetics for regional anaesthesia.[164] Since local anaesthetics dilate blood vessels, the co-administration of a vasoconstrictor, such as epinephrine, reduces local blood flow, which slows the rate of absorption, thus extending the anaesthetic effect.[161]

An analysis of medication declarations on 18,000 doping control forms collected between 2002 and 2005, found fewer than 1% of athletes reported the use of local anaesthetics in the previous three days.[165] Similarly, 1.6% of urine samples analysed at the Calgary 1988 Winter Olympics tested positive for lidocaine.[135] During the 2014 Football World Cup, team physicians reported that 2.6% of athletes had been administered injectable anaesthetics.[51] Similarly, it was reported that between 2.2% and 5.7% of male athletes used either injectable anaesthetics or injectable glucocorticoids at each of the Futsal World Cup events between 2002 and 2012.[54] In addition, local anaesthetics accounted for 10.9% (n=40) of injections declared through the *IOC Needle Policy* at the Rio 2016 Olympic Games.[166]

1.2.6.8 *Skeletal muscle relaxants*

The class of medications referred to as skeletal muscle relaxants is broad and includes many different chemically unrelated drugs, with varying uses and pharmacology. Skeletal muscle relaxants are used for the management of acute pain due to muscle spasm, which may be a symptom of musculoskeletal injury and commonly associated with lower-back or neck pain. The choice of muscle relaxant, its dose, and duration of prescribing by physicians varies between global regions, with considerable local differences in preferences in prescribing of one muscle relaxant over another.[167]

There are two main types of muscle relaxants including directly, and centrally acting medications. Centrally acting muscle relaxants selectively act on the central nervous system, with their mechanism of action attributed to their central nervous system depressant effects. They are sometimes prescribed for painful muscle spasms occurring as a result of neuromuscular and musculoskeletal conditions. Examples include baclofen, carisoprodol, methocarbamol, tizanidine, and tolperisone.[34 107 168 169] Directly acting muscle relaxants have

a direct action on skeletal muscle and are used for the treatment of muscle spasticity, with an example being dantrolene.[107 170]

Orphenadrine, thiocolchicoside, mephenoxalone are other drugs with various mechanisms of action reported to be used for their muscle relaxant properties in sports medicine.[171 34 172] Benzodiazepines are also used in sports medicine for their muscle relaxant properties and are covered as a separate category below. Diazepam, baclofen and tizanidine are all provided on the OPF as examples of muscle relaxant and antispasmodic medications.[1]

1.2.6.9 *Benzodiazepines*

Benzodiazepines are used for short-term treatment in sports medicine to relax muscles and relieve acute painful skeletal muscle spasms.[107] Diazepam is one of the most commonly prescribed benzodiazepine drugs for this purpose, with a specific clinical indication for muscle spasm, but all benzodiazepines have muscle-relaxant properties, with the dose of benzodiazepines as muscle relaxants being generally similar to the doses used to treat anxiety.[34] These medications also have significant sedative actions, making them potentially detrimental to sport performance, and with the potential for addiction with longer-term use.[167] A number of cases involving addiction to benzodiazepines have been reported in athletes who started using them for sleep disturbances, to aid recovery after physical training, and to treat musculoskeletal pain.[173]

1.2.6.10 *Massage and physical therapy preparations*

Rubefacients are found in many topical preparations marketed for sports injuries and often used at the Olympic Games in association with sports massage or manual physical therapy or physiotherapy interventions. They exhibit analgesic effects through counter-irritation causing skin irritation, increased blood flow to the skin surface, redness, heat, and a feeling of warmth when applied topically to the skin surrounding soft-tissue injuries. In producing this surface stimulation, relief from superficial pain can be obtained to some extent. They may provide

comfort to injuries involving the muscles, tendons, joints, and non-articular musculoskeletal conditions.[25 34 174]

The effect of rubefacients is understood to be due to the activation of Aβ-fibres which modulate transmission of pain signals by C-fibres to the spinal cord, thereby preventing pain signals reaching the brain. The action of rubbing the skin also results in the activation of Aβ-fibres and may thus enhance the analgesic effect of rubefacients.[34]

Depending on the type of compounds used, either a warm or cold sensation can be produced after topical administration. Menthol and levomenthol are examples of compounds that produce a cold sensation on application by dilating the blood vessels, which is followed by a mild analgesic effect. Other examples include volatile agents such as isopropyl alcohol, N-pentane, isopentane, and ethyl chloride, which are found in over-the-counter aerosol sprays marketed for musculoskeletal injury. As these compounds evaporate from the skin they produce an extreme cold sensation and have a numbing effect on the surface tissue.[34]

In contrast, salicylates are the most common substances used to provide a warming sensation and examples include: methylsalicylate, ethylsalicylate, diethylamine salicylate, glycolsalicylate, and salicylamide. Salicylate compounds can be absorbed through the skin and methylsalicylate is metabolised to salicylic acid in the skin after topical use, however the exact mechanism of action of topical salicylates is unclear.[107]

Capsaicinoids are compounds derived from capsicum are used topically for a range of painful musculoskeletal conditions. These substances give chilli peppers the hot taste and include capsaicin, capsicin and capsaicinoids. Unlike other rubefacients, capsaicinoid compounds do not have a vasodilatory effect, but cause counter-irritation by acting on vanilloid receptors to cause a depletion of the neurotransmitter substance-p, resulting in a reduction of pain-signal transmission from the injured area.[175] Capsaicin has poor to moderate efficacy in the treatment of chronic neuropathic or musculoskeletal pain, but is still used as a topical analgesic product for mild to moderate pain in sports medicine.[25 175] Products containing

capsaicin may be useful as a treatment, or as adjunct therapy in those unresponsive or intolerant to other treatments.[175]

Both methylsalicylate and menthol are provided on the OPF as examples of rubefacients for massage or physical therapy interventions.[1]

CHAPTER 2. RESEARCH OVERVIEW

2.1 AIMS

The overall aims of this research were to:

1. Determine whether the *Olympic and Paralympic Model Formulary* (OPF) met both the clinical needs of the athlete patients, and the prescribing expectations of team physicians relating to the treatment of musculoskeletal sports injury with medicines for pain and/or inflammation (PI) in the athlete population during international games;

2. Present a revised and optimised set of essential PI medications for the Olympic Games based on evidence and prevalence of actual athlete drug use, better matched to the clinical needs of Olympic athletes, to inform future editions of the OPF;

3. To evaluate whether the resulting revised and optimised set of PI medications met the prescribing and stock expectations of team physicians;

4. Establish a quantitative, reproducible approach to the selection of medicines for the OPF which can be implemented for future games to enable continual update the OPF over time to reflect the changing medication needs of athletes.

2.2 OBJECTIVES

In order to investigate the above aims, the objectives of the study were to test the existing OPF published in 2019 in a number of international multi-sport event settings covering both summer and winter sports. The research was conducted at the following games and regions.

Phase	Event	Sports	Location	Year
1	European Games	Summer	Minsk, Belarus	2019
2	Olympic Games	Summer	Tokyo, Japan	2021
		Winter	Beijing China	2022

The first phase of research, which acted as a proof-of-concept pilot study, was undertaken during the Minsk 2019 European Games, and focussed on athletes and their physicians from 50 European countries, competing in summer sports. The second phase of the research was undertaken at the Tokyo 2020 Olympic Games, and the Beijing 2022 Olympic Winter Games and focussed on athletes, and their physicians, from 205 countries covering every winter and summer Olympic sport.

The data collection comprised of five components (shown below), from different sources to comprehensively assess the research question. These sources represented either direct confirmed evidence of medication use by athletes, or indirect evidence of medication use through team stock carried to the games, and the prescribing preferences of team physicians.

Sources of direct evidence of athlete medication use

i. Medications declared by athletes on doping control forms
ii. Pharmacy dispensing reports from athlete village pharmacy
iii. Injection declaration forms (only for Tokyo 2020 and Beijing 2022 Olympic Games)

Sources of indirect evidence: physician prescribing preferences or anticipated stock use

iv. Declarations by team physicians of imported stock medication
v. Cross-sectional survey of team physicians

The specific objectives of each phase of research can be summarised as follows. The full detail for each phase is presented in the sections that follow.

Table 5 Summary of objectives for each phase of research

Objectives	PHASE 1 European Games	PHASE 2 Summer & Winter Olympic Games
Review of medication declared by athletes on doping control forms	✓	✓
Review pharmacy dispensing reports	✓	✓
Review of injection declarations forms		✓
Review team stock importation declarations	✓	✓
Survey of team physicians	✓	✓
Qualitative review of PI medications on the OPF	✓	
Determine prevalence of PI medication use at the Olympic Games		✓
Quantitative approach to develop a revised and optimised set of PI medications		✓
Validate the revised set of PI medications through iv) importation declarations and v) team physician survey		✓

2.2.1 PHASE ONE OBJECTIVES: Minsk 2019 European Games

1. Review of medications declared by athletes on doping control forms

1.1 To review the PI medications declared by athletes on the doping control forms to determine what medications they were taking at the time of the games.

1.2 To evaluate the extent to which the medicines listed on the OPF were matched to those used by athletes.

2. Review of polyclinic pharmacy dispensing reports

2.1 To review the pharmacy dispensing reports from the athlete village pharmacy to evaluate what PI medications were being prescribed from the OPF to athletes at the time of the games.

3. Review of NOC medication importation declarations

3.1 To review the declarations made by NOC teams of the stock medicines imported into the host country, to determine the types of PI medications they carry to the games.

3.2 To evaluate the extent to which the medicines listed on the OPF were matched to the stock medications imported.

4. Survey of team physicians

4.1 To undertake a cross-sectional survey of team physicians to evaluate their prescribing preferences relating to the treatment of pain and inflammation of musculoskeletal sports injury.

4.2 To evaluate the extent to which the medicines listed on the OPF were matched to the prescribing preferences of team physicians.

5. Qualitative assessment of PI medications on the OPF

5.1 To collate the results of all four datasets collected pertaining to each therapeutic class of PI medications on the OPF, and provide a qualitative evaluation and description of potential improvements, to both better meet the needs of athletes, and prescribing preferences of team physicians.

2.2.2 PHASE TWO OBJECTIVES: Tokyo 2020 and Beijing 2022 Olympic Games

6. Determine prevalence of PI medication use at the Olympic Games

6.1 To determine the prevalence of PI medication in Olympic athletes across summer and winter Olympic Games, through the review of the following combined datasets representing direct evidence of medication use:

i) Review of medications declared by athletes on doping control forms

ii) Review of polyclinic pharmacy dispensing reports

iii) Review of administered injectable medications declared by team physicians

7. Quantitative approach to develop a revised and optimised set of PI medications

7.1 To develop a quantitative method and tool to enable a prevalence-based selection process for inclusion of PI medications on the OPF.

7.2 To use the tool to develop a revised and optimised set of PI medications, based on a comparison of the prevalence of PI medication use, with the existing PI medications listed on the OPF.

8. Validate the revised set of PI medications through iv) importation declarations and v) team physician survey

8.1 To review declarations made by NOC team physicians of the stock medicines imported into the host country, to determine the types of PI medications they carry to the games.

8.2 To use the results to determine whether the proposed revised and optimised set of PI medications for the OPF addresses the stock needs of the team physicians.

8.3 To undertake a cross-sectional survey of team physicians at the Tokyo 2020 and Beijing 2022 Olympic and Paralympic Games to evaluate their prescribing preferences relating to the treatment of pain and inflammation of musculoskeletal sports injury.

8.4 To use the survey results to determine whether the proposed revised and optimised set of PI medications for the OPF met the prescribing preferences of team physicians.

2.3 ETHICAL CONSIDERATIONS

The research was conducted as a collaboration between University College London (UCL), the IOC Medical and Scientific Department and European Olympic Committees Medical and Anti-Doping Commission. The research was conducted according to the principles of the Olympic Movement Medical Code and mission of the IOC Medical Commission; the work was expected to develop best medical practices and protect the health of the athlete through selection of safe and effective medicines.

The code of ethics that were adhered to was the Declaration of Helsinki, which provides guidance for clinical research with its focus on the responsibilities of research for the protection of research subjects. This research was reviewed and approved by the UCL Research Ethics Committee (project reference 18955/001).

Permissions

The research was conducted in collaboration with the IOC and EOC, which all data collected for the respective games belong to. Permissions were expressly obtained from both organisations, via the Science and Medical Department of the IOC and the Medical and Anti-Doping Commission of the EOC to undertake the research and to use the information from

the games for this research. Further permission from both organisations were granted to announce the survey and recruit participants at the team physician meetings before the opening ceremony of each games.

In addition, the survey of team physicians was also conducted at the Tokyo 2020 and Beijing 2022 Paralympic Games. The permission to conduct the survey in team physicians at the Paralympic Games was provided by the IPC Medical Committee.

Informed consent

For the European and Olympic Games, all athletes, physicians, and other accredited persons consented to the use of their deidentified personal and health information collected for the purpose of research during and after the Games. This was expressly obtained prior to the start of each games through the official terms of participation provided by the EOC and IOC, and signed by the athlete.[176]

All participating athletes and other accredited people at the Games were officially notified of the processing of their personal data for the Olympic Games. They were informed that their personal data was collected by the IOC and the Organising Committee when they are subjected to anti-doping procedures and healthcare services. And that this information would be processed by the IOC "for various authorised purposes including for the protection of health and wellbeing of the accredited person, the monitoring of athlete injuries, illness, diseases or any other health states at the Olympic Games",[176] as well as for key activities of the anti-doping program. They were also notified that their personal data will be "used for the development of statistics (such as to support future Olympic Games planning needs and optimisation processes), historical studies, scientific and other research projects (such as the prevention of injuries and illnesses in sport) conducted during and after the Olympic Games."[176] This research project is exactly for this defined purpose: to optimise the availability of medications to improve healthcare for athletes at future Olympic Games.

The athlete and non-athlete participants were also informed that the categories of data processed include: "information related to the participation in the Olympic Games such as

accreditation number, sport(s) and discipline(s), team, performances, results, function, National Olympic Committee, International Federation, registration number; health data related to the health status of a person including medical data (doctor referrals and prescriptions, medical examination reports, laboratory tests, radiographs, etc.)".[176]

Lastly, they were informed that the recipients of their personal data would include various categories, including: the IOC, International Testing Agency (ITA), and healthcare and medical service providers who may provide treatment to accredited persons during the games. And that one of the grounds for processing personal data could be for the protection of the interests of the participants when providing healthcare services.

It should be noted that there is an additional consent requested on the doping control forms, which the athlete can tick to also consent to the use of their physical urine or blood sample specifically for anti-doping research purposes by the laboratory or anti-doping agencies, when all analyses have been completed, and the sample would have been discarded anyway.[177] As part of this process, the Doping Control Officer (DCO) informs the athlete that providing consent is optional, and if they decline then this would not compromise their test, or integrity of the sample or process. If they provided no explicit response to consent, then the form was marked that they did not consent to their urine or blood sample being used for research.[178]As this research does not involve testing physical urine or blood samples, this aspect was not applicable to this study.

For the team physician survey, a participant information sheet was provided which explained what they were being asked to consent to. The same participant information sheet was used for the survey conducted at the European, Olympic and Paralympic Games, with minor adaptations to reflect the specific name of the event (see Appendix 2).

All information including source documents and consent forms provided by the IOC and the Organising Committee to athletes and accredited persons at the time of the games were provided for review by the UCL Research Ethics Committee as part of the ethics application for this study.

2.4 DATA STORAGE & SECURITY

All datasets relating to the European Games were owned by the EOC; those relating to the Olympic Games were owned by the IOC; and those relating to the Paralympic Games were owned by the IPC. Consent to use the data was granted by the IOC, IPC and EOC. The data was stored in a password protected format and transferred using secure online protocols and using approved and secure IOC, IPC and EOC data transfer procedures. After transfer from the EOC, IOC, or IPC, data were stored on the UCL OneDrive, as encrypted password protected files, with access provided to the Principal Investigator only.

The survey platform used was *Google Forms*, which had been used before in the Olympic Games context at a recent survey conducted at the Rio 2016 Olympic Games[25] and proved reliable and secure. Both *Opinio* and *Microsoft Forms* were considered as platform options, but for the intended purpose, there was no significant difference between them and *Google Forms,* which was chosen based on previous proven success in this setting.

Doping control form data was stored by the EOC (Rome) and the IOC (Switzerland) for a period of 10 years in accordance with the requirements of the *World Anti-Doping Code*.[5] The subset of information from the doping control forms used for this research will be securely deleted 6 years after the completion of the research (July 2027). The data collected from the team physician survey will also be deleted 6 years after completion of the research (July 2027). This coincides with the Olympic calendar and allows for any retrospective analysis of the data if required after two subsequent editions of the games (winter or summer).

This project was registered as health research with the UCL Data Protection Office under, reference number Z6364106/2020/09/14 in line with UCL's Data Protection Policy.

CHAPTER 3. TESTING THE FORMULARY AT THE EUROPEAN GAMES

A proof-of-concept study.

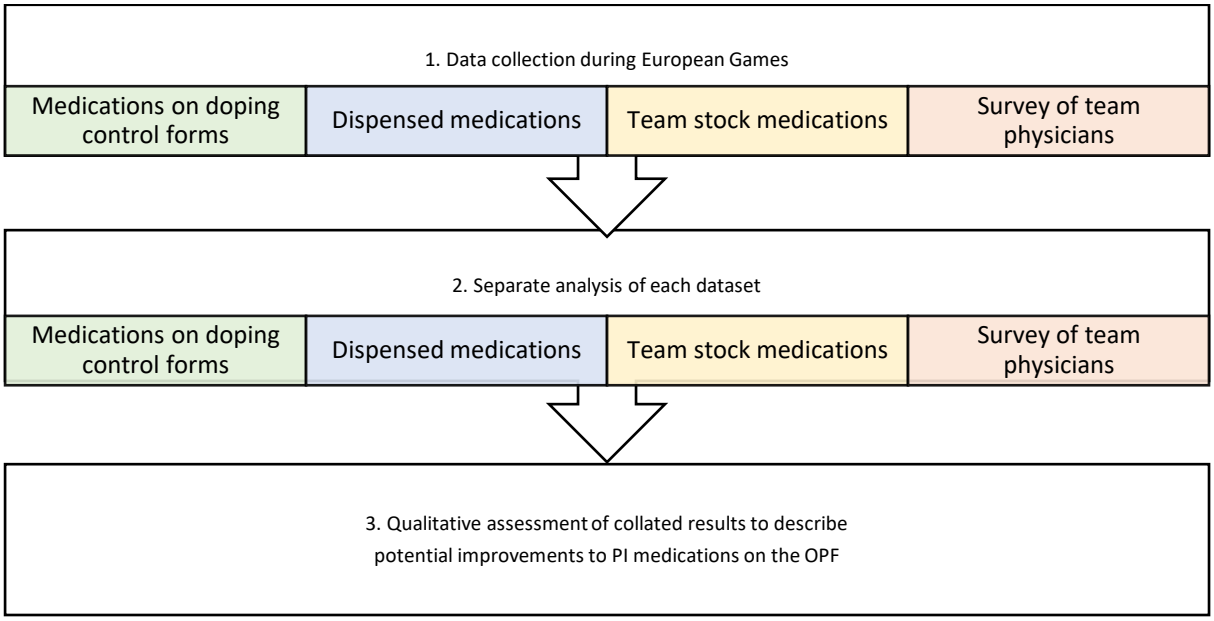
The European Games is a continental multi-sport event delivered in the tradition of the Olympic Games, governed by the EOC, and attended by NOCs from 50 European countries. The games started in 2015 and are staged every 4 years. The third edition of the games was held in Minsk, Belarus from 21-30 June 2019.

Although the OPF was intended to be used at the Olympic and Paralympic Games, it also serves as a general standard of medical care for all international games under the umbrella of the Olympic Movement. The OPF was first published in early 2019, enabling time for it to be implemented for the first time at these European Games. This chapter describes and discusses the results obtained during these games, which enabled a pilot of the data collection methods and analyses prior to starting the main body of research in Phase Two, at the Olympic Games 2 years later.

3.1 STUDY DESIGN

Phase One of the research at the European Games involved a retrospective review of the athlete medication-use data collected during the games through the pharmacy, medical and anti-doping services. In addition, a retrospective review of team drug importation records indicating the stock carried to the games was undertaken. An online cross-sectional survey of team physicians was also conducted to understand what medications they prescribe for musculoskeletal sports injury, to assess whether their prescribing preferences were covered by the OPF. Each dataset was reviewed separately. A qualitative approach was taken in collating, interpreting, and describing the results to present potential recommendations to improve the OPF to better meet the needs of athletes and the prescribing preferences of team physicians.

Figure 1 Overview of Phase One study at European Games



3.2 METHODS

3.2.1 Review of medications declared on doping control forms

At the time of providing a urine or blood sample at a doping control station, all athletes were asked to declare any medications or nutritional supplements taken during the previous 7 days on the doping control form. Completing a doping control form at the time of a doping control test was mandatory for athletes at these Games under the regulations of the *World Anti-Doping Code*.[5] These data provided direct evidence of medication use by athletes at the time of the games.

Data collection and anonymisation

The form used to collect the data was in the format of the standard WADA approved doping control form. The following data was transcribed, with no personal identifiers recorded:

i. Sex
ii. Country of team
iii. Sport competing in
iv. Declared substance
v. Route of administration

A paper version of the form was used for the European Games, and on each day the games the completed forms were returned from the doping control stations to the offices of the EOC Medical and Anti-Doping Commission, where the medication and supplement declarations were manually transcribed onto an Excel spreadsheet. The data from these forms were then provided by the EOC for retrospective analysis for this research after the games, with all personal identifiers removed.

Processing the data

Any declaration made for a product or brand was looked up using online references and translated into the generic substance name in English using International Non-proprietary Names (INN) conventions where they existed. The primary international reference used to do this was *Martindale: The Complete Drug Reference*.[171] *Google Translate* and Internet searches were also used where necessary to identify the generic ingredients of all products declared, and were also used to determine the product name if the declaration was made in a language other than English.

Identification of medicines versus supplements

All declarations were then categorised into two categories: 1) whether they were a licenced medicine, or 2) whether they were a supplement (defined as any nutritional supplement including vitamin and mineral preparations, herbal medicine, homoeopathic preparation, or substance of animal origin). The supplement data was not analysed extensively as part of this

research, but some general observations were presented to provide the basis for potential considerations for future research.

Comparison with the OPF

Total counts of drug types, therapeutic categories, route of administration, country of athlete, sport, and age groups were tabulated. The medication data were categorised into therapeutic class and route of administration using the same drug class naming conventions presented on the original OPF and the subset of PI medications was identified and analysed. For this research, PI medications were defined as any drug in the following 13 therapeutic categories.

01.1.1 NSAID
01.1.2 COX-2 inhibitor
01.1.3 Non-opioid analgesic
01.2 Opioid analgesics*
01.3 Medicines for neuropathic pain
01.4 Corticosteroids for intra-articular use*
01.5 Local anaesthetics
01.5.1 Local anaesthetics + vasoconstrictor
02.1 Corticosteroids for oral use*
03.1 Benzodiazepines
03.2 Skeletal muscle relaxants
10.9 Massage and physical therapy preparations
23.1.2 General anaesthetics with analgesia

*Categories that contain prohibited medications, which may require a TUE to be applied for if used by athletes.

For the European Games data , each PI medication listing was further analysed to establish:

i. If the medication was listed specifically on the OPF;
ii. If an alternative medication was available on the OPF in the same class and route of administration, or;
iii. Whether the medication was not listed, and no alternative in the same class and route was available in the existing OPF

Statistical analysis

All data was coded and analysed using SPSS (v21, USA). Frequencies and percentages were used to describe categorical variables. Mean, standard deviation (SD) and median were used to describe continuous variable relating to the number of medications declared per athlete. When reporting proportions or prevalence estimates, a 95% Confidence Interval (CI) was also reported. A chi-square test of independence was performed to compare the differences in

declarations regarding pain and inflammation drugs between other categorical variables, such as sex, athlete age range, country, route of administration. Non-parametric Fisher's exact test was used instead of chi-square when expected counts per cell was less than 5 in 20% of the cells. A p-value <0.05 was considered cut-off for statistical significance.

3.2.2 Polyclinic pharmacy dispensing reports

This analysis involved reviewing the pharmacy reports of dispensed medications issued to both athletes and non-athletes from the polyclinic pharmacy within the athlete village of the Minsk 2019 European Games. After each event, the end-of-games pharmacy dispensing reports, anonymised with no patient identifiers, were provided by the EOC. The reports contained the following data:

i. Whether the patient was an athlete or non-athlete
ii. Country of team
iii. Age range (<20; 21-30; 31-40; 41-50; 51+)
iv. Sport competing in
v. Drug dispensed
vi. Number of prescriptions dispensed

Total counts of drug types, medication therapeutic categories, country of athletes, sport and age groups were tabulated and analysed. The data were compared against the medication listings on the OPF according to drug name and therapeutic class as listed on the OPF.

Statistical analysis

All data was coded and analysed using SPSS (v21, USA). Frequencies and percentages were used to described categorical variables. A chi-square test of independence was performed to compare the differences in response to categorical variables reported including athlete versus non-athlete, medication types dispensed, patient age range, sport, and the OPF clinical category of dispensed medicines. Fisher's exact test was used instead of chi-square when

expected counts per cell was less than 5 in 20% of the cells. A p-value <0.05 was considered cut-off for statistical significance.

3.2.3 NOC team stock medicines importation declaration review

This analysis involved the review of all declarations of imported medications carried as team stock made by the NOCs prior to each games. At each games, such declarations were required prior to entry into the host country. The declarations were made by the Chief Medical Officer of each NOC to the medical departments of the organising committees the event, and to the customs agencies of the host country as part of the importation declaration requirements outlined in the *Customs and Freight Guide* unique to each games.

Data collection and anonymisation

The medication importation declaration report did not contain any personal or sensitive medical data. It did contain the names of medicines being carried as stock, but they had not been prescribed to any individual athlete at this stage, as they were carried by the teams to be used in the event of a medical situation if needed. Any medicine that had already been prescribed to an individual had to be carried in the personal possession of the athlete on arrival to the host country, and so the declarations reviewed did not contain any personal prescription information.

Processing the data

Every stock medication declaration form was reviewed manually and any declarations for PI medications were recorded on an Excel spreadsheet. Any declaration made for a product or brand was looked up using online references and translated into the generic substance name in English using International Non-proprietary Names (INN) conventions where they existed. The primary international reference used to do this was *Martindale: The Complete Drug Reference*,[171] or the manufacturer's official website.

Total counts of medication types, therapeutic categories, routes of administration and country of the importing teams were tabulated and analysed. The data were compared with the medication listings on the OPF according to the drug name and therapeutic class in the same way described for the doping control form dataset (Section **Error! Reference source not found.**).

Statistical analysis

All data was coded and analysed using SPSS (v21, USA). Frequencies and percentages were used to described categorical variables of: medicines types declared, class, route of administration, country, and specific match to medicine listings on the OPF.

3.2.4 Survey of NOC team physicians

This survey was conducted as an online cross-sectional questionnaire of team physicians attending the Minsk 2019 European Games. It comprised of 25 questions which blended dichotomous, categorical, scaled, and open-ended questions to determine whether the drugs provided by the formulary at each games covered their expected prescribing needs for athletes while at the games. The full questions contained in the survey can be found in Appendix 3.

The questions aimed to evaluate specifically the use of analgesic and anti-inflammatory medicines used for the treatment of musculoskeletal sports injury in athletes. The questions also evaluated whether the formulary as a whole served the broader clinical requirements of athletes and asked what medicines should be included to improve it for future Games.

The survey design was based on a similar survey previously undertaken on behalf of the IOC in the team physician population at the Rio 2016 Olympic Games, which assessed the clinical practices of team physicians when prescribing analgesic and anti-inflammatory medicines for athletes. This survey at Rio 2016 was conducted to inform the *IOC Consensus Statement on Pain Management in Elite Athletes*.[25] The implementation of this survey in Minsk followed the

same methodology used at Rio 2016, using similar communication methods and online survey form. The format for the participant information sheet was based on one successfully used for a study conducted at the London 2012 Olympic and Paralympic Games.[179]

Recruitment

The recruitment for the survey in Phase One at the European Games was done at the team physician meeting held on the day before the opening ceremony of the games in cooperation and with consent of the EOC Medical and Anti-Doping Commission. The Chair of the EOC Medical and Anti-Doping Commission made the announcements and invited participation personally at the meeting. The physicians were then handed the participant information sheet, which contained the link to the online survey. The participant information sheet and consent form used for the survey at both the European Games and the Olympic and Paralympic Games can be found in Appendix 2.

Informed consent

The first question on the survey explicitly asked whether the participant understood the study purpose and consents to participating. The participant had the opportunity to decide whether to or not continue with the survey at that point.

Data anonymisation

The survey did not ask for any personal identifiers, and so the results were anonymised on receipt. Specific consideration was given to whether any combination of responses could be potentially used to disclose any athletes' medical data. However, the survey did not ask any questions relating to the treatment of any individual, with hypothetical questions asking what medicines they would prefer to use for a variety of general clinical scenarios. The questions represented their preferences in the choice of medicine in their clinical practice generally and were not linked to any specific patients.

Participant inclusion and exclusion criteria

Every team physician working as part of a medical team who was eligible to prescribe medicines at the games for athletes of their team was invited to complete the survey before the closing ceremony of each games, but submissions were also accepted up to 7 days later. More than one team physician from each country was able to complete the survey, but the survey could not be completed by a non-prescriber or a representative. Non-prescribing healthcare professionals including physiotherapists, pharmacists and nurses were excluded from this survey, unless they were specifically registered to prescribe at the games.

Languages

For the Minsk 2019 European Games, the survey was in English, which was the official language of the European Games.

Expected sample size

Based on the historical number of team physicians registered to prescribe for the previous European Games in 2015 in Baku 2015 Azerbaijan, it was assumed that each team had on average two team physicians, thus a total of 100 team physicians were expected to attend Minsk for the European Games in 2019. However, it was known that not all teams had a physician accompanying the team, and some of the larger teams had more than two team physicians. It was expected that around 50 physicians would complete the survey, with the aim of one member per participating team.

Statistical analysis

All data was coded and analysed using SPSS (v21, USA). Frequencies and percentages were used to described categorical variables. A chi-square test of independence was performed to compare the differences in declarations between physicians from different countries based on geographical region, between other categorical variables, such as choice of medications, expected polyclinic pharmacy usage, coverage of prescribing needs by formulary and own stock, and expected athlete usage of PI medications.

3.3 RESULTS

3.3.1 Review of medications declared on doping control forms

3.3.1.1 *Sample size and response rate*

During the Minsk 2019 European Games 4082 athletes from 50 countries competed in 15 sports. Of all competing athletes, 24.5% (n=999) were selected for testing through the anti-doping program. Athletes from 96% (n=48) of countries were selected for testing, and athletes were tested across all 15 (100%) sports held at the games.

Table 6 Numbers of athletes tested in each sport

Sport	**n (%)**
Athletics	157 (15.7)
Cycling	152 (15.2)
Judo	97 (9.7)
Canoe	93 (9.3)
Boxing	89 (8.9)
Wrestling	80 (8.0)
Shooting	68 (6.8)
Gymnastics	61 (6.1)
Sambo	37 (3.7)
Basketball	32 (3.2)
Badminton	30 (3.0)
Karate	28 (2.8)
Table tennis	28 (2.8)
Archery	27 (2.7)
Beach soccer	10 (1.0)
Football	10 (1.0)
Total	999 (100.0)

Table 7 Numbers of athletes tested from each country

Country	n(%)	Country	n(%)
Russia	106 (10.6)	Serbia	15 (1.5)
Belarus	89 (8.9)	Slovenia	14 (1.4)
France	61 (6.1)	Armenia	13 (1.3)
Ukraine	57 (5.7)	Slovakia	13 (1.3)
Italy	52 (5.2)	Lithuania	12 (1.2)
Turkey	41 (4.1)	Latvia	11 (1.1)
Czech Republic	36 (3.6)	Estonia	10 (1.0)
Germany	33 (3.3)	Sweden	8 (0.8)
Portugal	31 (3.1)	Israel	7 (0.7)
Spain	29 (2.9)	Moldova	7 (0.7)
Great Britain	28 (2.8)	Norway	7 (0.7)
Netherlands	28 (2.8)	Bosnia and Herzegovina	6 (0.6)
Azerbaijan	26 (2.6)	Kosovo	6 (0.6)
Georgia	25 (2.5)	Luxembourg	6 (0.6)
Hungary	25 (2.5)	Finland	4 (0.4)
Poland	23 (2.3)	Macedonia	4 (0.4)
Bulgaria	21 (2.1)	Albania	3 (0.3)
Austria	19 (1.9)	Cyprus	3 (0.3)
Greece	19 (1.9)	Iceland	3 (0.3)
Switzerland	19 (1.9)	Monaco	3 (0.3)
Denmark	18 (1.8)	Montenegro	3 (0.3)
Romania	18 (1.8)	Belgium	2 (0.2)
Ireland	17 (1.7)	Malta	2 (0.2)
Croatia	15 (1.5)	Andorra	1 (0.1)
		Total	999 (100.0)

3.3.1.2 *Types and numbers of declarations*

Every athlete tested was required to complete the declaration on the doping control form indicating the medications or supplements they had taken in the previous 7 days; there were a total of 703 unique declarations for medications. In terms of medications declared on the doping control forms, 39.4% (95% CI [36.4, 42.5]; n=394) declared taking *at least* one medication in the previous 7 days. Many athletes declared multiple medications, with the highest number of medications declared being 8 by one athlete. The average number of medications declared among all 999 athletes was 0.7 ± SD 1.2 (95% CI [0.6-0.8]) with a median

of zero. The average number of medication use declared among the 394 athletes that used one or more medications was 1.8 ± SD 1.3 (95% CI [1.7-1.9]) with a median of 1.0.

For supplements, 71.6% (95% CI [68.7, 74.4]; n=715) of athletes declared taking at least one, or more in the previous 7 days, and 29% (95% CI [26.2, 31.9]); n=290) of athletes declared taking *both* a supplement and a medication. There were 2492 unique declarations for supplements. A small number of declarations were unidentifiable or illegible (n=31; 1%).

Table 8 Number and proportion (95% CI) of medications and supplement declarations per athlete

	Medication	**Supplement**	**Medication AND Supplement**
	n (%)	n (%)	n (%)
None declared	605 (60.6, 95% CI [57.5, 63.7])	284 (28.4, 95% CI [25.6, 31.3])	709 (71.0, 95% CI [68.1, 73.8])
One or more declared	394 (39.4, 95% CI [36.4, 42.5])	715 (71.6, 95% CI [68.7, 74.4])	290 (29.0, 95% CI [26.2, 31.9])
Total	999 (100.0)	999 (100.0)	999 (100.0)

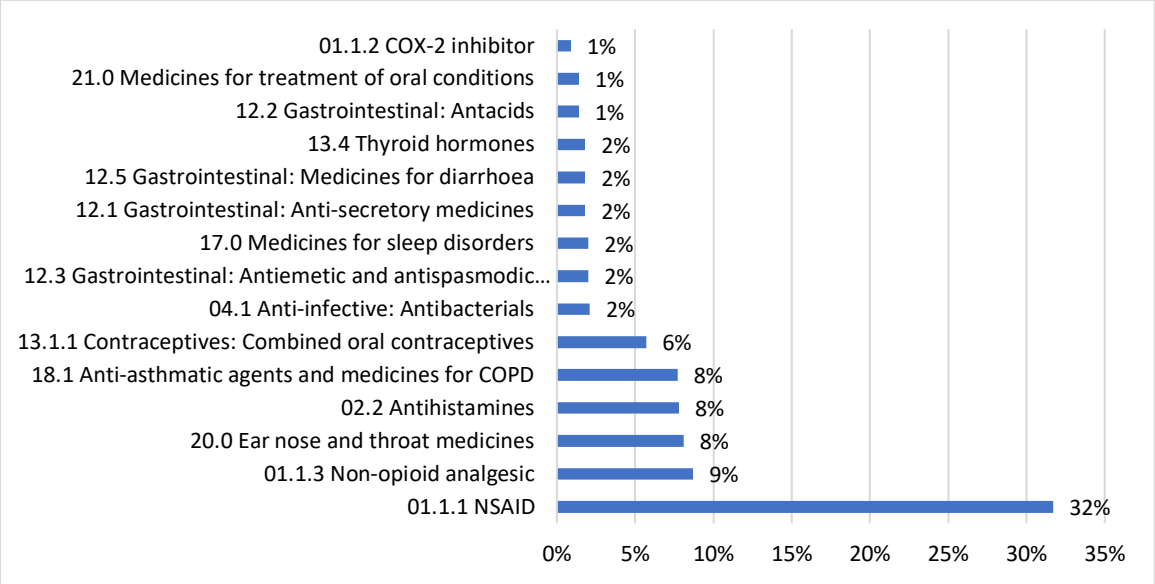
Table 9 Number of different medications declared by the same athlete

Medications	**n (%)**
None declared	605 (60.6)
1	233 (23.3)
2	85 (8.5)
3	36 (3.6)
4	23 (2.3)
5	6 (0.6)
6	8 (0.8)
7	2 (0.2)
8	1 (0.1)
Total	999 (100.0)

3.3.1.3 *Declared medication categories*

Of all 81 therapeutic categories on the OPF, drugs from 54.2% (n=44) of categories were declared by athletes, 45.7% (n=37) of categories were not declared by any athlete at all. Of

all medications declared, NSAIDs were most frequently used (n=223; 31.7%), followed by non-opioid analgesic medications (n=61; 8.7%).



*% values have been rounded to the nearest whole number

Figure 2 Top 15 most commonly declared classes of medications by athletes (%)*

Of all types of medication declarations made by athletes, 74.7% (n=531) were specifically listed on the OPF. For those not specifically listed, 17.0% (n=114) had an equivalent medication in the same therapeutic class and route listed which could be used as an appropriate clinical alternative. Only 8.3% (n=58) of medications declared could not be met by either an exact, or a suitable alternative from the OPF.

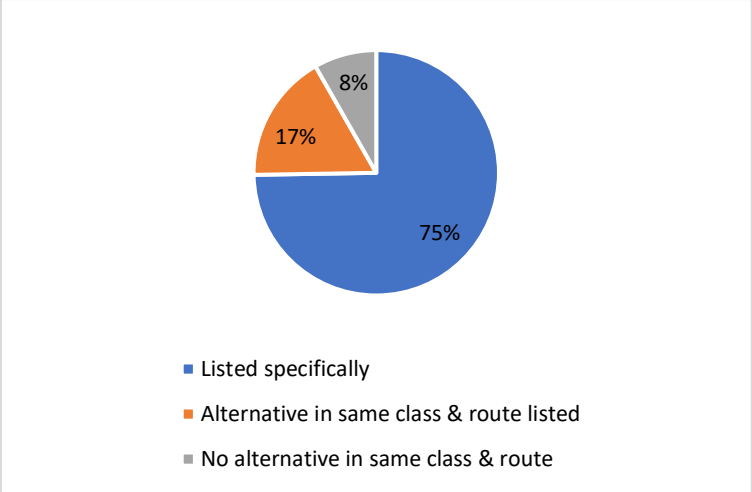


Figure 3 OPF listings of athlete declared drugs on OPF (%)

3.3.1.4 *Declared PI medications*

There were a total of 315 declarations for PI medications from 23% (n=231) of athletes. NSAIDs accounted for most of these declarations (n=223, 70%), followed by non-opioid analgesic medications (n=61, 19.4%). Glucocorticoids for intra-articular use were the least declared medication for pain and inflammation (n=1, 0.3%). There were no medications for neuropathic pain, or single-agent opioid preparations declared by any athlete. NSAIDS had the widest range of individual drug preparations within the class, with 16 unique types of NSAID types declared.

Table 10 Declarations of PI medications by therapeutic class and route of administration

Route	Therapeutic Class / Drug Name	n (%)
	NSAID	**223 (70.8)**
Oral		**216 (68.6)**
	Ibuprofen	79 (25.1)
	Diclofenac	66 (21.0)
	Aspirin	20 (6.3)
	Nimesulide	20 (6.3)
	Ketoprofen	5 (1.6)
	Ketorolac	5 (1.6)
	Aceclofenac	4 (1.3)
	Naproxen	4 (1.3)
	Dexketoprofen	3 (0.95)
	Flurbiprofen	3 (0.95)
	Meloxicam	2 (0.63)
	Aminophenazone	1 (0.3)
	Aspirin + caffeine	1 (0.3)
	Mefenamic acid	1 (0.3)
	Phenylbutazone	1 (0.3)
	Piroxicam	1 (0.3)
	Tiaprofenic acid	1 (0.3)
	Diclofenac + Paracetamol	1 (0.3)
Topical		7 (2.2)
	Diclofenac	5 (1.6)
	Ibuprofen	1 (0.3)
	Ketoprofen	1 (0.3)
	COX-2 inhibitor	**6 (1.9)**

Oral		6 (1.9)
	Etoricoxib	6 (1.9)
	Non-opioid analgesic	**61 (19.4)**
Oral		61 (19.4)
	Paracetamol	53 (16.8)
	Other Paracetamol containing products	4 (1.3)
	Metamizole (dipyrone)	2 (0.63)
	Paracetamol + caffeine	1 (0.3)
	Paracetamol + vitamin C	1 (0.3)
	Opioid + non-opioid combination	**2 (0.63)**
Oral		2 (0.63)
	Codeine + paracetamol	2 (0.63)
	Glucocorticoids for intra-articular use	1 (0.3)
Injection		1 (0.3)
	Triamcinolone	1 (0.3)
	Local anaesthetics for acute pain	**4 (1.3)**
Injection		4 (1.3)
	Lidocaine	4 (1.3)
	Benzodiazepines	**6 (1.9)**
Oral		6 (1.9)
	Diazepam	3 (0.95)
	Alprazolam	1 (0.3)
	Midazolam	1 (0.3)
	Triazolam	1 (0.3)
	Skeletal muscle relaxants	**5 (1.6)**
Oral		5 (1.6)
	Tizanidine	3 (0.95)
	Tolperisone	2 (0.63)
	Massage and physical therapy preparations	**6 (1.9)**
Topical		6 (1.9)
	Methylsalicylate	5 (1.6)
	Menthol	1 (0.3)
Total		315 (100)

There was a significant association between PI medications and the route of administration. The oral route was the most common route (53%) compared to topical (34%) and with injection or any other route (5%; $p<0.001$).

3.3.1.5 *Specific or alternative OPF listings of declared PI drugs*

Of all PI medications declared, 80.0% (95% CI [75.2, 84.2]; n=252) were listed specifically on the current OPF, with 18.7% (95% CI [14.6, 23.5]; n=59) not listed, but which had a suitable alternative in the same therapeutic class and indication available on the OPF.

Table 11 Proportion (95% CI) of specific or alternative OPF listings of declared PI drugs by therapeutic class

	Alternative in same class & route listed	**Listed specifically**	**No alternative**	**Total**
OPF Class	**n (%)**	**n (%)**	**n (%)**	**n (%)**
NSAID	45 (20.2)	178 (79.8)	0 (0.0)	223 (100.0)
NSAID + non-opioid combination	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
COX-2 inhibitor	6 (100.0)	0 (0.0)	0 (0.0)	6 (100.0)
Non-opioid analgesic	6 (9.8)	53 (86.9)	2 (3.3)	61 (100.0)
Opioid + non-opioid combination	0 (0.0)	2 (100.0)	0 (0.0)	2 (100.0)
Glucocorticoids for intra-articular use	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
Local anaesthetics for acute pain	0 (0.0)	4 (100.0)	0 (0.0)	4 (100.0)
Benzodiazepines	2 (33.3)	4 (66.7)	0 (0.0)	6 (100.0)
Skeletal muscle relaxants	0 (0.0)	3 (60.0)	2 (40.0)	5 (100.0)
Massage and physical therapy preparations	0 (0.0)	6 (100.0)	0 (0.0)	6 (100.0)
Total	59 (18.7) 95% CI [14.6, 23.5]	252 (80.0) 95% CI [75.2, 84.2]	4 (1.3) 95% CI [0.4, 3.3]	315 (100.0)

3.3.1.6 *Declarations of PI medications by sex*

Female athletes were more likely to have used PI medications in the last 7 days (29.6%, 95% CI [25.3, 34.2]) compared to male athletes (18.5%, 95% CI [15.4, 21.9]; p<0.001).

Table 12 Prevalence (95% CI) of PI use by sex

Sex	Total athletes (n=999)	Athletes taking PI medications (n=231)	Prevalence	95% CI
Female	416	123	29.6%	25.3, 34.2
Male	583	108	18.5%	15.4, 21.9
Total	999	231	23.1%	20.5, 25.8

p<0.001 (Note: Chi-squared test was used to determine the statistical significance.)

Table 13 Proportion (95% CI) of declarations of PI therapeutic categories by sex

	Female	Male	Total
PI therapeutic category	**n (%)**	**n (%)**	**n (%)**
NSAID	125 (56.1)	98 (43.9)	223 (100.0)
NSAID + non-opioid combination	0 (0.0)	1 (100.0)	1 (100.0)
COX-2 inhibitor	3 (50.0)	3 (50.0)	6 (100.0)
Non-opioid analgesic	39 (63.9)	22 (36.1)	61 (100.0)
Opioid + non-opioid combination	1 (50.0)	1 (50.0)	2 (100.0)
Glucocorticoids for intra-articular use	0 (0.0)	1 (100.0)	1 (100.0)
Local anaesthetics	3 (75.0)	1 (25.0)	4 (100.0)
Benzodiazepines	2 (33.3)	4 (66.7)	6 (100.0)
Skeletal muscle relaxants	1 (20.0)	4 (80.0)	5 (100.0)
Massage and physical therapy preparations	4 (66.7)	2 (33.3)	6 (100.0)
TOTAL	178 (56.5)	137 (43.5)	315 (100.0)
	95% CI [50.8, 62.1]	95% CI [38.0, 49.2]	

3.3.2 Polyclinic pharmacy dispensing reports

The results presented below provide a country-wise comparison of prescription numbers between athletes and non-athletes. Out of the total of 471 prescriptions dispensed by the pharmacy, 65.2% (n=307) were for athletes, while the remaining 34.8% (n=164) were for non-athletes. The highest number of prescriptions were dispensed to Belarussian patients, accounting for 24.4% (n=115) of all prescriptions. Among these, 17.1% (n=28) were non-athletes, and the majority, 28.3% (n=87), were athletes. The Republic of Moldova had the second highest total with 13.2% (n=62) of the prescriptions, with an equal distribution between non-athletes and athletes at 18.9% (n=31) each. This was followed by the Czech Republic with 7.0% (n=33) of prescriptions, 4.3% (n=7) of which were non-athletes and 8.5% (n=26) athletes.

Table 14 Total number of all prescriptions dispensed per country

	Total	Non-Athlete	Athlete
Country	**n (%)**	**n (%)**	**n (%)**
Belarus	115 (24.4)	28 (17.1)	87 (28.3)
Republic of Moldova	62 (13.2)	31 (18.9)	31 (10.1)
Czech Republic	33 (7.0)	7 (4.3)	26 (8.5)
Ukraine	28 (5.9)	18 (11.0)	10 (3.3)
Russian Federation	27 (5.7)	7 (4.3)	20 (6.5)
Azerbaijan	18 (3.8)	13 (7.9)	5 (1.6)
Romania	17 (3.6)	5 (3.0)	12 (3.9)
Germany	14 (3.0)	2 (1.2)	12 (3.9)
Bulgaria	13 (2.8)	7 (4.3)	6 (2.0)
Armenia	12 (2.5)	4 (2.4)	8 (2.6)
Kosovo	11 (2.3)	0 (0.0)	11 (3.6)
Bosnia and Herzegovina	10 (2.1)	2 (1.2)	8 (2.6)
Latvia	10 (2.1)	0 (0.0)	10 (3.3)
Albania	8 (1.7)	2 (1.2)	6 (2.0)
Portugal	8 (1.7)	2 (1.2)	6 (2.0)
Finland	7 (1.5)	3 (1.8)	4 (1.3)
Monaco	7 (1.5)	0 (0.0)	7 (2.3)
Republic of Cyprus	7 (1.5)	2 (1.2)	5 (1.6)
Slovenia	7 (1.5)	0 (0.0)	7 (2.3)
Estonia	6 (1.3)	1 (0.6)	5 (1.6)
Turkey	6 (1.3)	4 (2.4)	2 (0.7)
Denmark	5 (1.1)	4 (2.4)	1 (0.3)
Iceland	5 (1.1)	5 (3.0)	0 (0.0)
Israel	5 (1.1)	4 (2.4)	1 (0.3)
Serbia	4 (0.8)	0 (0.0)	4 (1.3)
Georgia	3 (0.6)	0 (0.0)	3 (1.0)
Italy	3 (0.6)	2 (1.2)	1 (0.3)
North Macedonia	3 (0.6)	3 (1.8)	0 (0.0)
Spain	3 (0.6)	3 (1.8)	0 (0.0)
Austria	2 (0.4)	1 (0.6)	1 (0.3)
Belgium	2 (0.4)	0 (0.0)	2 (0.7)
Greece	2 (0.4)	1 (0.6)	1 (0.3)
Sweden	2 (0.4)	2 (1.2)	0 (0.0)
Hungary	1 (0.2)	0 (0.0)	1 (0.3)
Ireland	1 (0.2)	0 (0.0)	1 (0.3)
Lithuania	1 (0.2)	0 (0.0)	1 (0.3)
Luxembourg	1 (0.2)	0 (0.0)	1 (0.3)
Norway	1 (0.2)	0 (0.0)	1 (0.3)
Switzerland	1 (0.2)	1 (0.6)	0 (0.0)
Total	471 (100.0)	164 (100.0)	307 (100.0)

The table that follows presents the numbers of prescriptions for PI medication categories dispensed to athletes versus non-athletes. Overall, NSAIDs were the most commonly used class of medication in both groups, accounting for 39.5% (n=17) of non-athlete prescriptions and 68.0% (n=104) of athlete prescriptions. Topical applications of NSAIDs were more commonly prescribed to non-athletes, while oral products were more commonly prescribed to athletes. Also notable was the prescribing of massage and physical therapy preparations, which was significantly higher in non-athletes (n=20; 46.5%) compared to athletes (n=41; 26.8%).

Table 15 Numbers of prescriptions for PI medications dispensed to athlete vs. non-athlete

OPF Class			
		Non-Athlete	Athlete
Route	Medication	n (%)	n (%)
01.1.1 NSAID		**17 (39.5)**	**104 (68.0)**
Injection		**1 (5.9)**	**2 (1.9)**
	Ketoprofen	1 (100.0)	2 (100.0)
Oral		**6 (35.3)**	**44 (42.3)**
	Diclofenac	1 (16.7)	12 (27.3)
	Ibuprofen	1 (16.7)	19 (43.2)
	Meloxicam	4 (66.7)	8 (18.2)
	Naproxen	0 (0.0)	4 (9.1)
	Melatonin	0 (0.0)	1 (2.3)
Topical		**10 (58.8)**	**58 (55.8)**
	Diclofenac	5 (50.0)	24 (41.4)
	Ketoprofen	0 (0.0)	22 (37.9)
	Ibuprofen	1 (10.0)	3 (5.2)
	Ibuprofen + Levomenthol	4 (40.0)	9 (15.5)
01.1.2 COX-2 inhibitor		**1 (2.3)**	**3 (2.0)**
Oral		**1 (100.0)**	**3 (100.0)**
	Celecoxib	1 (100.0)	3 (100.0)
01.1.3 Non-opioid analgesics		**3 (7.0)**	**3 (2.0)**
Oral		**3 (100.0)**	**3 (100.0)**
	Paracetamol	1 (33.3)	2 (66.7)
	Metamizole sodium	2 (66.7)	1 (33.3)
01.5.1 Local anaesthetics		**1 (2.3)**	**1 (0.7)**
Injection		**1 (100.0)**	**1 (100.0)**
	Lidocaine	1 (100.0)	1 (100.0)
03.2 Skeletal muscle relaxants		**1 (2.3)**	**1 (0.7)**
Oral		**1 (100.0)**	**1 (100.0)**
	Tizanidine	1 (100.0)	1 (100.0)
10.9 Massage and physical therapy preparations		**20 (46.5)**	**41 (26.8)**
Topical		**20 (100.0)**	**41(100.0)**
	Butane + Isobutane + Propane	6 (30.0)	12 (29.3)
	Menthol + Camphor	3 (15.0)	11 (26.8)
	Dimethyl sulfoxide	3 (15.0)	7 (17.1)
	Heparin	4 (20.0)	4 (9.8)
	Troxerutin	1 (5.0)	3 (7.3)
	Methyl salicylate + Menthol	2 (10.0)	2 (4.9)
	Methylsalicylate + Levomenthol	0 (0.0)	2 (4.9)
	Dimethylsulfoxide + Camphor	1 (5.0)	0 (0.0)

The next table presents an analysis of the number of athletes from different sports prescribed PI medications. The most interesting observation is that athletes competing in boxing were dispensed the most prescriptions with a total of 55 athletes. This was significantly more than any other sport, with athletics being the next most common with 17 athletes receiving prescriptions for PI medications. Sports including sambo, judo, and beach soccer also showed a relatively high number of athletes (13, 9, and 9, respectively) being prescribed PI medications. Conversely, sports such as archery, shooting and wrestling had the fewest athletes receiving such prescriptions, with 3, 2, 2, and 1 athlete, respectively.

Table 16 Number of athletes prescribed PI medications per sport

Sport	Number of Athletes (n (%))
Boxing	55 (35.5)
Athletics	17 (11.0)
Sambo	13 (8.4)
Judo	9 (5.8)
Beach Soccer	9 (5.8)
Basketball 3x3	8 (5.2)
Table Tennis	7 (4.5)
Karate	7 (4.5)
Gymnastics – Artistic	6 (3.9)
Badminton	6 (3.9)
Wrestling – Freestyle	4 (2.6)
Cycling - Road	4 (2.6)
Archery	3 (1.9)
Shooting – Rifle and Pistol	2 (1.3)
Shooting – Shotgun	2 (1.3)
Wrestling – Greco-Roman	1 (0.6)

3.3.3 NOC team stock medication importation declaration review

3.3.3.1 *Sample size of countries declaring medications*

A total of 36 of 50 (72%) participating NOC teams submitted a declaration of imported medicines for use at the Games, with 28% (n=14) of NOCs not declaring any imported

medicines. The total number of athletes who were members of the teams that submitted declarations was 3337 (90.4% of all athletes attending).

Table 17 Countries declaring medications imported for use at the games

Armenia	Germany	Norway
Austria	Great Britain	Poland
Belarus	Greece	Portugal
Belgium	Hungary	Romania
Bulgaria	Ireland	Russia
Croatia	Israel	Serbia
Cyprus	Italy	Slovenia
Czech Republic	Lithuania	Spain
Estonia	Luxembourg	Sweden
Finland	Moldova	Switzerland
France	Montenegro	Turkey
Georgia	Netherlands	Ukraine

3.3.3.2 *Unique PI medications declarations, by class, route and OPF category*

The following table shows the number of declarations for each PI medication imported as stock by the teams attending the Minsk 2019 European Games.

Table 18 Imported PI medications declared, by class, route and OPF category

OPF class and route of administration	n	(%)
01.1.1 NSAID	**260**	**(48.9)**
Injection	**32**	**(12.3)**
Diclofenac	18	(56.3)
Piroxicam	4	(12.5)
Ketoprofen	3	(9.4)
Meloxicam	2	(6.3)
Dexketoprofen	2	(6.3)
Ketorolac	2	(6.3)
Lornoxicam	1	(3.1)
Oral	**150**	**(57.7)**
Diclofenac	35	(23.3)
Ibuprofen	23	(15.3)
Aspirin	23	(15.3)
Nimesulide	12	(8.0)
Naproxen	10	(6.7)
Ketoprofen	9	(6.0)
Piroxicam	8	(5.3)
Meloxicam	5	(3.3)
Aceclofenac	4	(2.7)
Dexketoprofen	4	(2.7)
Lornoxicam	3	(2.0)
Ketorolac	3	(2.0)
Niflumic acid	2	(1.3)
Flurbiprofen	2	(1.3)
Mefenamic acid	2	(1.3)
Etodolac	1	(0.7)
Naproxen + esomeprazole	1	(0.7)
Tenoxicam	1	(90.7)
Dexibuprofen	1	(0.7)
Clonixin	1	(0.7)
Suppository	**3**	**(1.2)**
Diclofenac	2	(66.7)

Piroxicam	1	(33.3)
Topical	**64**	**(24.6)**
Diclofenac	22	(34.4)
Ketoprofen	11	(17.2)
Salicyclic acid	6	(9.4)
Etofenamate	6	(9.4)
Ibuprofen + menthol	5	(7.8)
Ibuprofen	5	(7.8)
Diethylamine salicylate	3	(4.7)
Nimesulide	2	(3.1)
Piketoprofen	1	(1.6)
Indometacin + troxerutin	1	(1.6)
Aceclofenac	1	(1.6)
Flurbiprofen	1	(1.6)
Topical patch	**11**	**(4.2)**
Diclofenac	8	(72.7)
Flurbiprofen	2	(18.2)
Ketorolac	1	(9.1)
01.1.1.1 NSAID + non-opioid combination	**4**	**(0.8)**
Oral	**4**	**(100.0)**
Aspirin + Paracetamol	3	(75.0)
Aspirin + Paracetamol + Caffeine	1	(25.0)
01.1.2 COX-2 inhibitor	**21**	**(3.9)**
Injection	**1**	**(4.8)**
Parecoxib	1	(100.0)
Oral	**20**	**(95.2)**
Etoricoxib	13	(65.0)
Celecoxib	7	(35.0)
01.1.3 Non-opioid analgesic	**54**	**(10.2)**
Injection	**11**	**(20.4)**
Meptazinol	10	(90.9)
Paracetamol	1	(9.1)
Oral	**41**	**(75.9)**
Paracetamol	30	(73.2)
Meptazinol	9	(22.0)
Metamizole + pitofenone + fenpiverinium	2	(4.9)
Suppository	**2**	**(3.7)**
Paracetamol	1	(50.0)
Metamizole + pitofenone suppositories	1	(50.0)
01.2 Opioid analgesics	**19**	**(3.6)**
Injection	**4**	**(21.1)**
Tramadol	3	(75.0)
Morphine injection	1	(25.0)
Nasal spray	**1**	**(5.3)**

Fentanyl	1	(100.0)
Oral	**14**	**(73.7)**
Tramadol	11	(78.6)
Codeine	2	(14.3)
Dihydrocodeine	1	(7.1)
01.2.1 Opioid combination	**13**	**(2.4)**
Oral	**13**	**(100.0)**
Codeine + paracetamol	7	(53.8)
Tramadol + paracetamol	5	(38.5)
Opium + paracetamol	1	(7.7)
01.3 Medicines for neuropathic pain	**1**	**(0.2)**
Oral	**1**	**(100.0)**
Pregabalin	1	(100.0)
01.4 Glucocorticoids for intra-articular use	**43**	**(8.1)**
Injection	**43**	**(100.0)**
Methylprednisolone	14	(32.6)
Betamethasone	10	(23.3)
Triamcinolone	9	(20.9)
Dexamethasone	7	(16.3)
Hydrocortisone	2	(4.7)
Prednisolone	1	(2.3)
01.5.1 Local anaesthetics	**26**	**(4.9)**
Injection	**26**	**(100.0)**
Lidocaine	16	(61.5)
Bupivacaine	6	(23.1)
Mepivacaine injection	2	(7.7)
Procaine	1	(3.8)
Prilocaine	1	(3.8)
02.1 Glucocorticoids for oral use	**11**	**(2.1)**
Oral	**11**	**(100.0)**
Prednisolone	6	(54.5)
Prednisone	2	(18.2)
Deflazacort	1	(9.1)
Dexamethasone	1	(9.1)
Methylprednisolone	1	(9.1)
03.1 Benzodiazepines	**20**	**(3.8)**
Oral	**19**	**(95.0)**
Diazepam	8	(42.1)
Oxazepam	4	(21.1)
Bromazepam	2	(10.5)
Alprazolam	2	(10.5)
Prazepam	1	(5.3)
Triazolam	1	(5.3)

Midazolam	1	(5.3)
Suppository	**1**	**(5.0)**
Diazepam	1	(100.0)
03.2 Skeletal muscle relaxants	**23**	**(4.3)**
Injection	**5**	**(21.7)**
Thiocolchicoside	4	(80.0)
Tolperisone	1	(20.0)
Oral	**17**	**(73.9)**
Tolperisone	7	(41.2)
Thiocolchicoside	5	(29.4)
Tizanidine	2	(11.8)
Mephenoxalone	1	(5.9)
Baclofen	1	(5.9)
Orphenadrine + aspirin + caffeine	1	(5.9)
Topical	**1**	**(4.3)**
Thiocolchicoside	1	(100.0)
10.9 Massage and physical therapy preparations	**35**	**(6.6)**
Topical	**35**	**(100.0)**
Menthol	17	(48.6)
Methylsalycilate + menthol	6	(17.1)
Capsaicin	5	(14.3)
Methylsalycilate	5	(14.3)
Nonivamide + Butoxyethyl Nicotinate	1	(2.9)
Chlorethyl	1	(2.9)
23.3.2.1 Emergency: Gases for analgesia	**2**	**(0.4)**
Inhalation	**2**	**(100.0)**
Methoxyflurane	2	(100.0)
Total	**532**	**(100.0)**

3.3.3.3 *Availability of declared imported PI medications on the OPF*

All imported PI medications declared were mapped to the OPF according to the following groups:

1. Medication was specifically listed on the OPF
2. A suitable alternative medication in the same class, route and indication was listed on the OPF
3. Medication was not listed on the OPF, and no suitable alternative in the same class and route was available

Figure 4 shows the results of this.

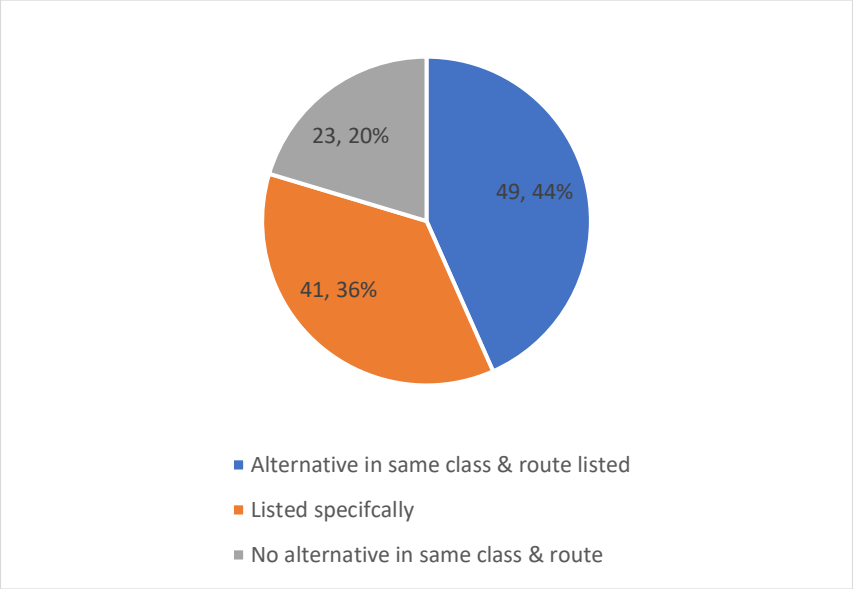


Figure 4 Number of team imported PI medications on the OPF, or alternative medications

3.3.4 Survey of NOC team physicians

The survey was completed by 60 physicians attending the Minsk 2019 European Games, from 33 of 50 (66%) participating countries. The results of the questions from the survey are presented below.

Country of respondents

The distribution of team physician respondents by country is presented below.

Table 19 Number of physician respondents per country

Country	n (%)	Country	n (%)
Germany	7 (11.7)	Belgium	1 (1.7)
Belarus	4 (6.7)	Bulgaria	1 (1.7)
Hungary	4 (6.7)	Denmark	1 (1.7)
Latvia	3 (5.0)	Estonia	1 (1.7)
Lithuania	3 (5.0)	France	1 (1.7)
Armenia	2 (3.3)	Greece	1 (1.7)
Croatia	2 (3.3)	Ireland	1 (1.7)
Czech Republic	2 (3.3)	Netherlands	1 (1.7)
Finland	2 (3.3)	North Macedonia	1 (1.7)
Great Britain	2 (3.3)	Norway	1 (1.7)
Israel	2 (3.3)	Republic of Moldova	1 (1.7)
Italy	2 (3.3)	San Marino	1 (1.7)
Kosovo	2 (3.3)	Serbia	1 (1.7)
Luxembourg	2 (3.3)	Slovenia	1 (1.7)
Spain	2 (3.3)	Switzerland	1 (1.7)
Sweden	2 (3.3)	Ukraine	1 (1.7)
Austria	1 (1.7)	**Total**	**60 (100.0)**

Number of athletes under their care

Physicians were asked about the number of athletes under their care while at the games. Of all respondents, 50.0% (n=30) indicated they cared for fewer than 50 athletes; 20% (n=12) of physicians cared for between 50 and 100 athletes; while 26.6% (n=16), cared for between 101 and 200 athletes. Only a 3.4% of the physicians (n=2) reported caring more than 200 athletes.

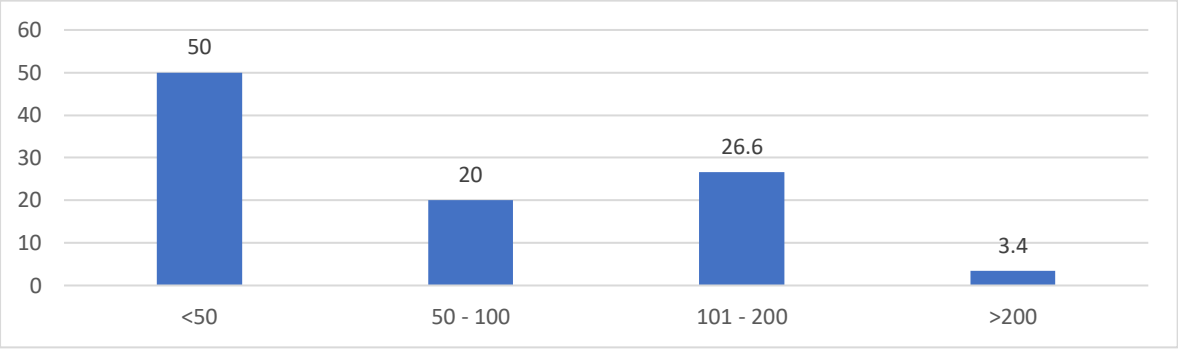


Figure 5 Number of athletes under the care of team physicians (%) at the games

Clinical specialty of team physicians

The majority of respondents, 40.0% (n=24), reported their main clinical specialty as sports medicine (primary care). The second most common was orthopaedics, reported by 21.7% (n=13). The remaining physicians reported their specialties as: other (20.0%, n=12), sports medicine surgery (11.7%, n=7), and less than 2% in other disciplines.

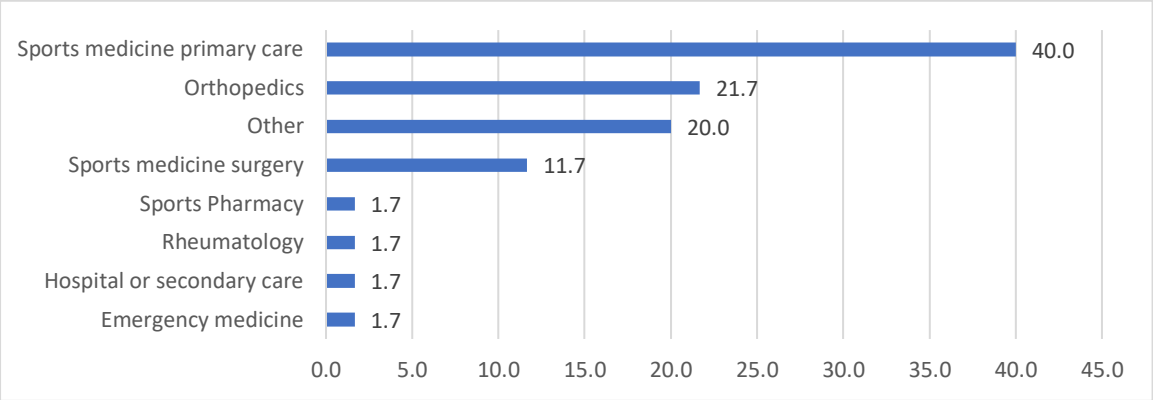


Figure 6 Clinical specialty of team physicians (%) working at the games

Coverage of overall prescribing needs of the OPF

Team physicians were asked approximately what proportion of their overall prescriptions could be covered by the medicines in the games formulary for the athletes under their care. The largest proportion, 46.7% (n=28), reported that the choice covered most (>75%) of their prescriptions, while 26.7% (n=16) stated that all of their prescriptions were covered. Only 15% indicated that less than 25% or none of their prescriptions were covered by the games formulary.

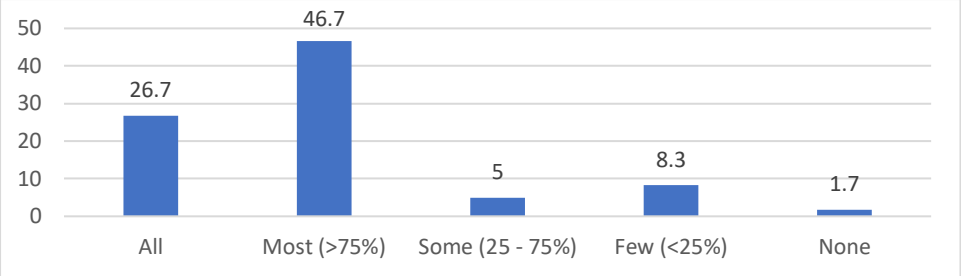


Figure 7 Coverage of overall prescribing needs of NOC team stock versus number of physicians (%)

Coverage of overall prescribing needs from imported team stock

Team physicians were asked what proportion of prescriptions for the athletes under their care could be covered by their team's own stock of medicines. A large majority, 90.0% (n=33), reported that most (>75%) or all of their prescriptions could be covered by their own stock. Only 6.7% (n=4), reported that their stock could cover between 25-50% of their prescriptions, and just 1.7% (n=1) said their stock would cover less than 25% of their prescribing needs.

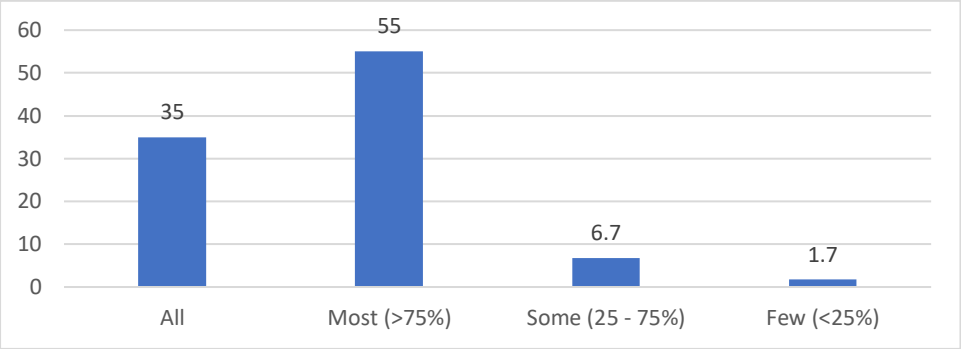


Figure 8 Coverage of overall prescribing needs of NOC team stock per physicians (%)

Expected use of the games pharmacy service

Team physicians were asked what proportion of their prescriptions they anticipate to be obtained from the polyclinic pharmacy. Out of the 60 respondents, 30.0% (n=18) reported that they expect most (>75%) or all of their prescriptions to be sourced from the polyclinic pharmacy. Conversely, 58.3% (n=35), stated that either few (<25%) or no prescriptions would

be expected to be obtained from the polyclinic pharmacy, with 10.0% (n=6) expecting some (25-75%) of their prescriptions to be sourced from the polyclinic pharmacy.

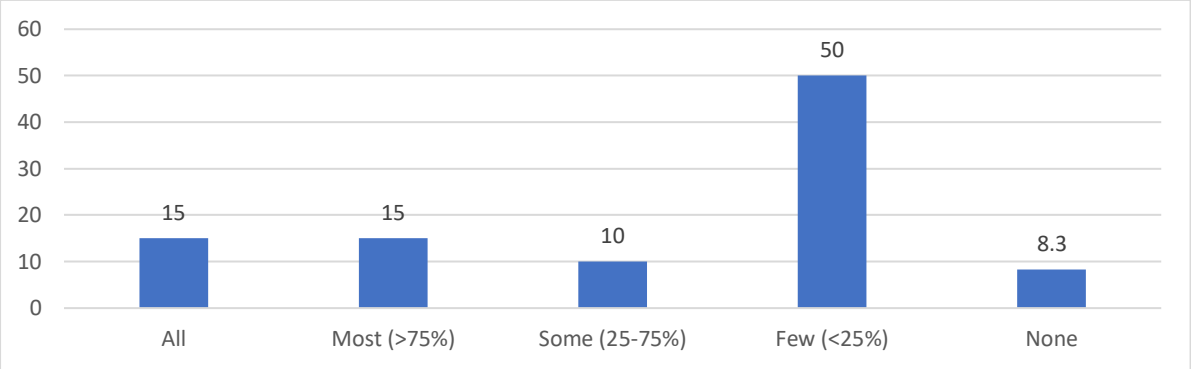


Figure 9 Proportion of medicines expected to be obtained from polyclinic pharmacy per number of physicians (%)

Expected prescribing of PI medications to athletes

Team physicians were asked approximately what percentage of athletes under their care do they expect to require PI medications for sports-related conditions during the course of the games. The majority of team physicians (78.4%, n=47) anticipated less than 25% of athletes to require specific such medications. A smaller proportion (18.3%, n=11) expected 26-50% of individuals to require them. Only one person (1.7%) anticipated that 51-75% of athletes would require these interventions.

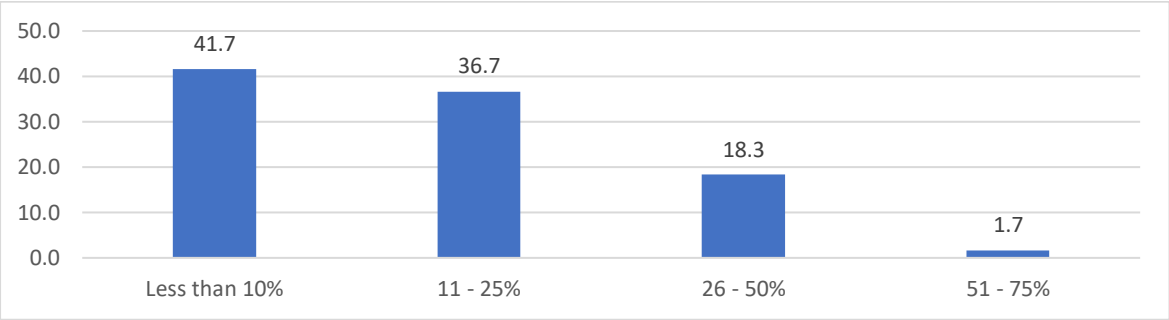


Figure 10 Percentage groupings of athletes in NOC versus athletes (%) expected to require PI medications for sports-related injury during the games

Coverage of PI medications on the OPF

Team physicians were asked what proportion of their expected PI medications for sports-related conditions could be covered by those in the games formulary. Of the 60 respondents, 68.3% (n=41) reported that either most (>75%) or all of their prescriptions could be covered by their existing formulary, with 15.0% (n=9) indicating that fewer than 75% of their prescriptions could be accommodated by the current formulary, and 6.7% (n=4) reporting none.

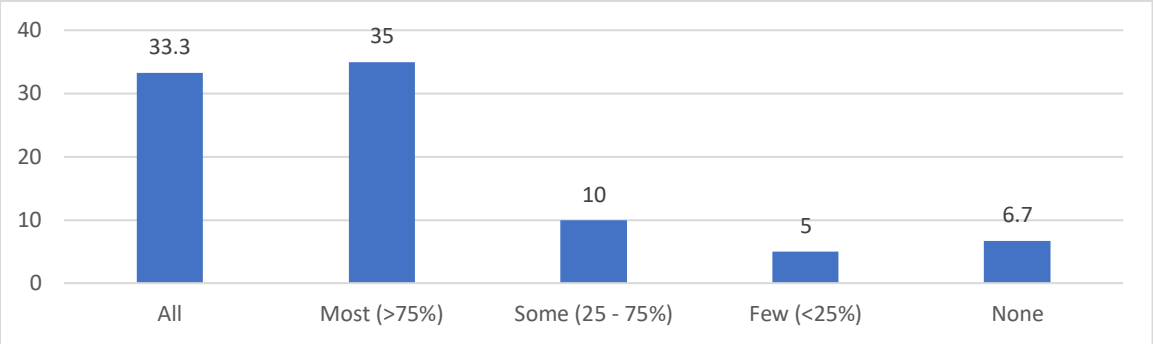


Figure 11 Proportion of prescribing needs of PI medications covered by the OPF per physician (%)

The next section covers the questions in the survey related to specific medication preferences or frequency of use by team physicians. The following colour coding is used to indicate whether the medication was currently listed on the OPF or not, or if an alternative in the same therapeutic class and indication was available on the OPF.

- Medication is specifically listed on the OPF
- An alternative in the same therapeutic class and indication is available on the OPF
- No alternative exists on the OPF

Oral medicines

Use of oral non-opioid or non-steroidal anti-inflammatory drugs (NSAIDs)

Team physicians were asked which oral non-opioid or NSAIDs have they prescribed in the last 12 months for sports-related conditions in athletes. The most frequently used were diclofenac and ibuprofen, prescribed by a large proportion of physicians, 85.0% (n=51) and 83.3% (n=50) respectively. Paracetamol was also a common choice, prescribed by 66.7% (n=40) of physicians. Etoricoxib and naproxen were used by a smaller proportion of respondents, 33.3% (n=20) and 25.0% (n=15) respectively, and meloxicam with 20.0% (n=12). Metamizole and piroxicam were prescribed by 18.3% (n=11) of physicians. Other drugs were used by less than 17% of physicians in the previous 12 months.

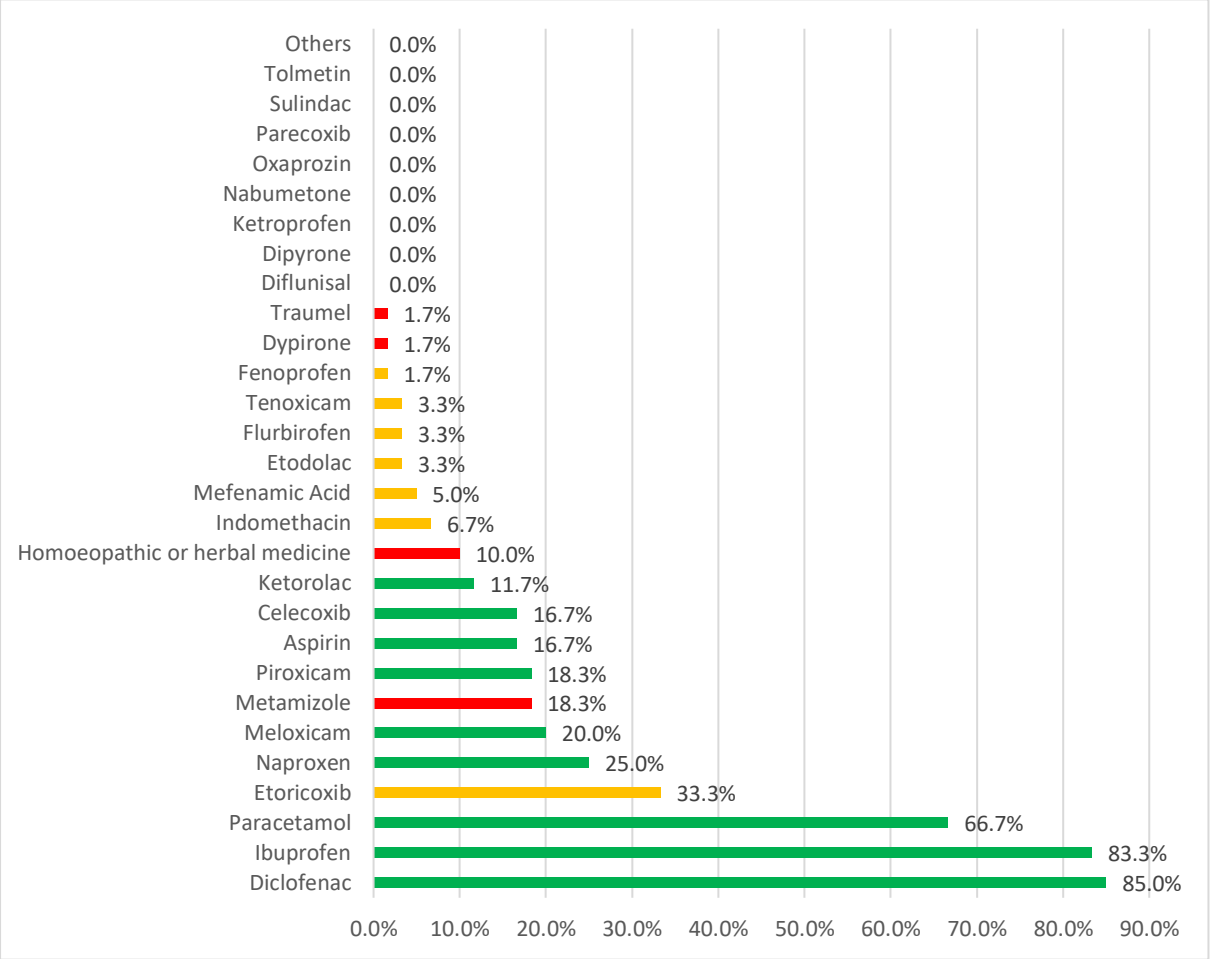


Figure 12 Proportion (%) of team physicians prescribing ORAL non-opioid or NSAIDs in the last 12 months (n=60)

Use of oral opioid analgesic drugs

Team physicians were asked which oral opioid analgesic drugs have they prescribed in the last 12 months to for sports-related conditions in athletes. The most commonly prescribed drugs were oral tramadol (23.3%, n=14) and oral codeine (20.0%, n=20). Other drugs in this class were prescribed by less than 7% of physicians.

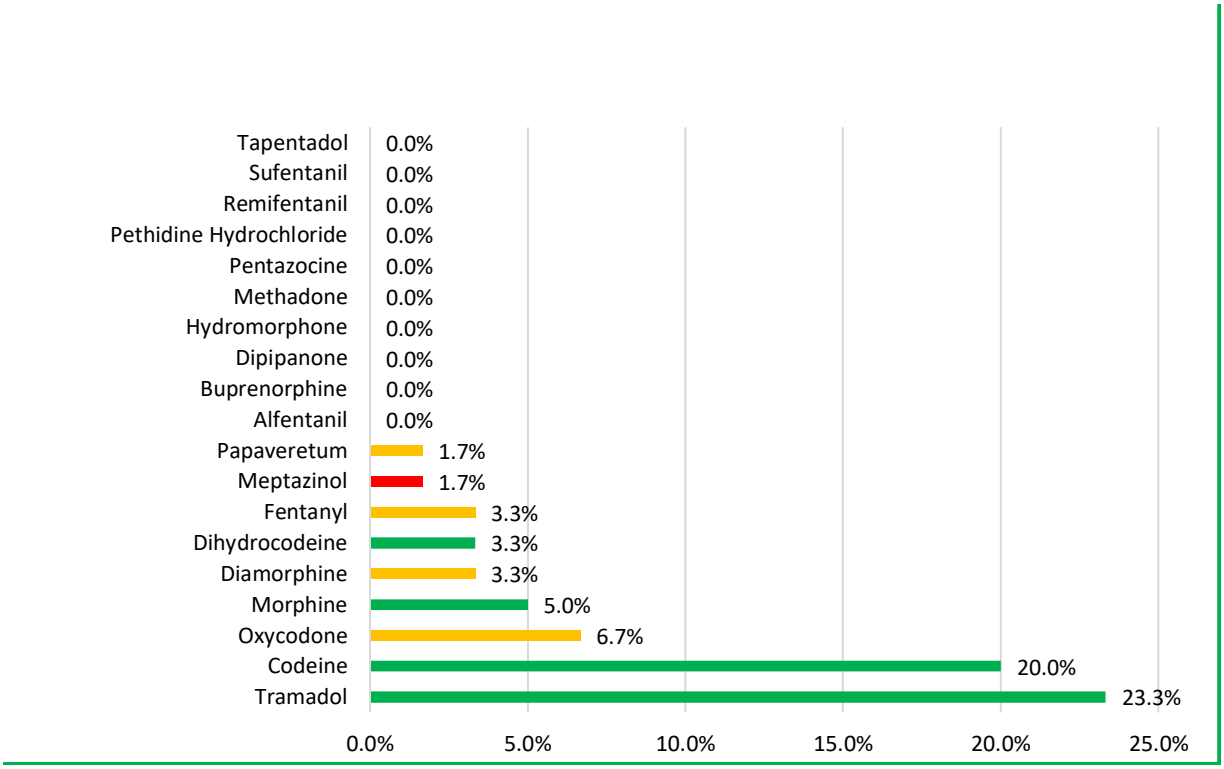


Figure 13 Proportion (%) of team physicians prescribing ORAL opioid analgesic drugs in the last 12 months (n=60)

Oral medicines for mild to moderate pain without inflammation

Team physicians were asked which oral medicine they most frequently prescribe for mild to moderate pain (without inflammation) for sports-related conditions in athletes. The most

commonly prescribed drugs included paracetamol (63.3%, n=38), ibuprofen (13.3%, n=8). Other drugs for this clinical indication were used by less than 6% of physicians.

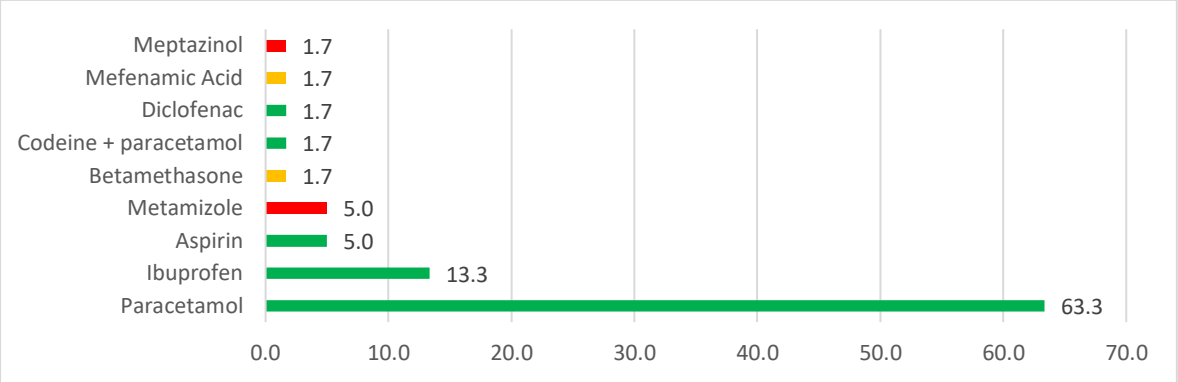


Figure 14 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for mild to moderate pain (without inflammation) for sports-related conditions in athletes (n=60)

Oral medicine for mild to moderate pain with inflammation

Team physicians were asked which oral medicine they most frequently prescribe for mild to moderate pain with inflammation for sports-related conditions in athletes. The most commonly prescribed drugs included ibuprofen (35.0%, n=21) and diclofenac (20.0%, n=12). Other drugs were prescribed by less than 9% of physicians.

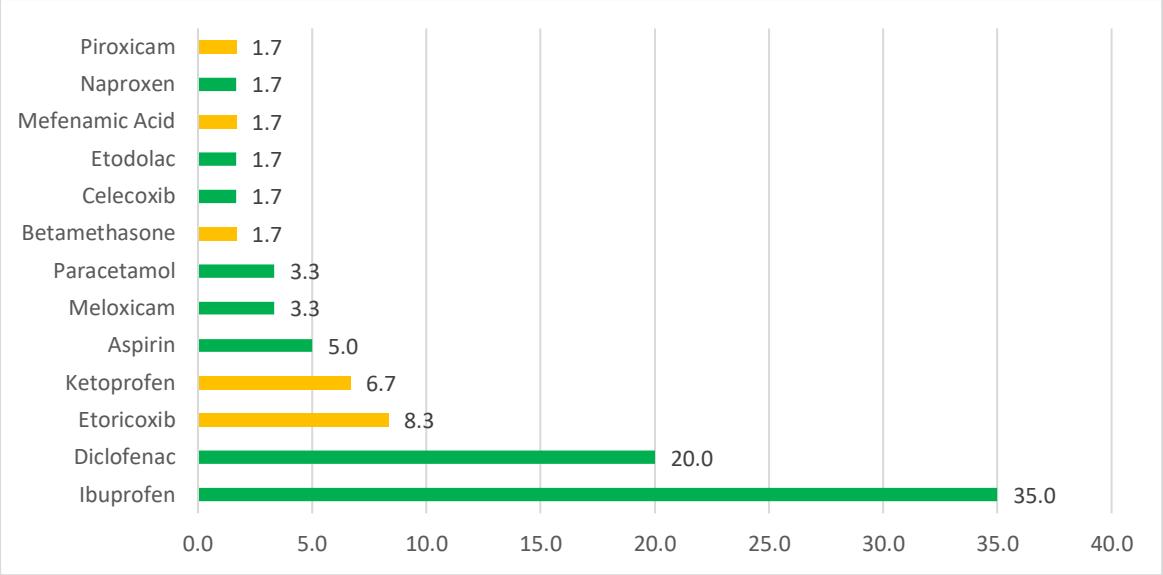


Figure 15 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for mild to moderate pain with inflammation for sports-related conditions in athletes (n=60)

Oral medicine for moderate to severe pain without inflammation

Team physicians were asked which oral medicine they would most frequently prescribe for moderate to severe pain (without inflammation) for sports-related conditions in athletes. The most common prescribed drugs were diclofenac (16.7%, n=10) and ibuprofen (16.7%, n=10). Other drugs were prescribed by 10% or less of physicians for this clinical indication.

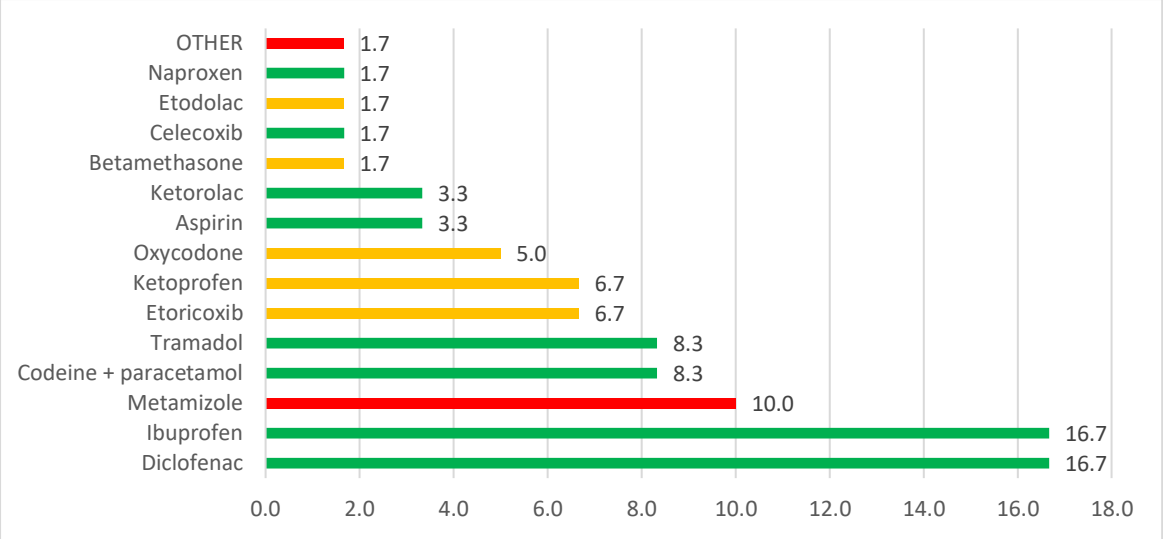


Figure 16 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for moderate to severe pain (without inflammation) for sports-related conditions in athletes (n=60)

Oral medicine for moderate to severe pain with inflammation

Team physicians were asked which oral medicine they most frequently prescribe for moderate to severe pain with inflammation for sports-related conditions in athletes. The most commonly prescribed medicines included diclofenac (26.7%, n=16), ibuprofen (16.7%, n=10) and etoricoxib (13.3%, n=8). Other drugs were prescribed by less than 9% of physicians.

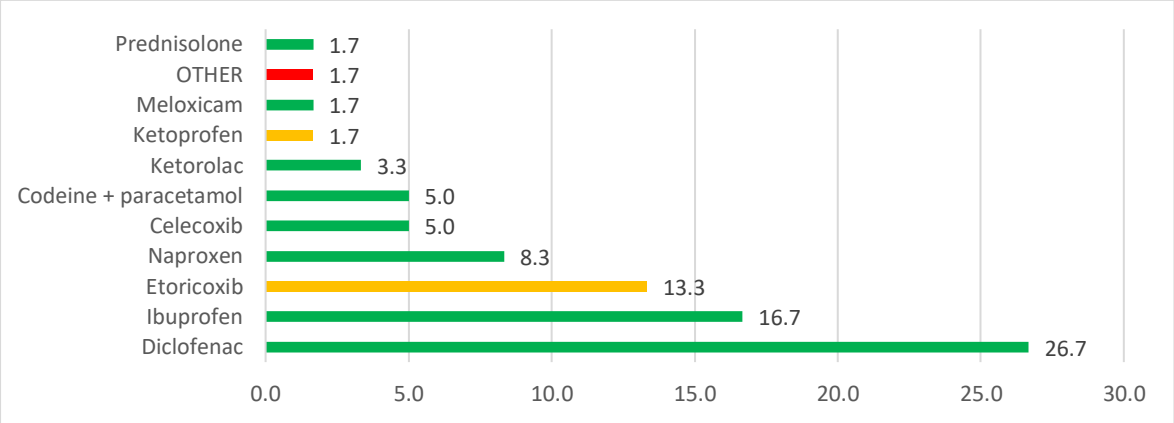


Figure 17 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for moderate to severe pain with inflammation for sports-related conditions in athletes (n=60)

Oral medicines for neuropathic pain

Team physicians were asked which oral medicine they would most frequently prescribe for neuropathic pain in athletes. The most commonly prescribed drugs included gabapentin (35%, n=21) and diclofenac (6.7%, n=4). Other drugs were prescribed by less than 6% of physicians for the treatment of neuropathic pain.

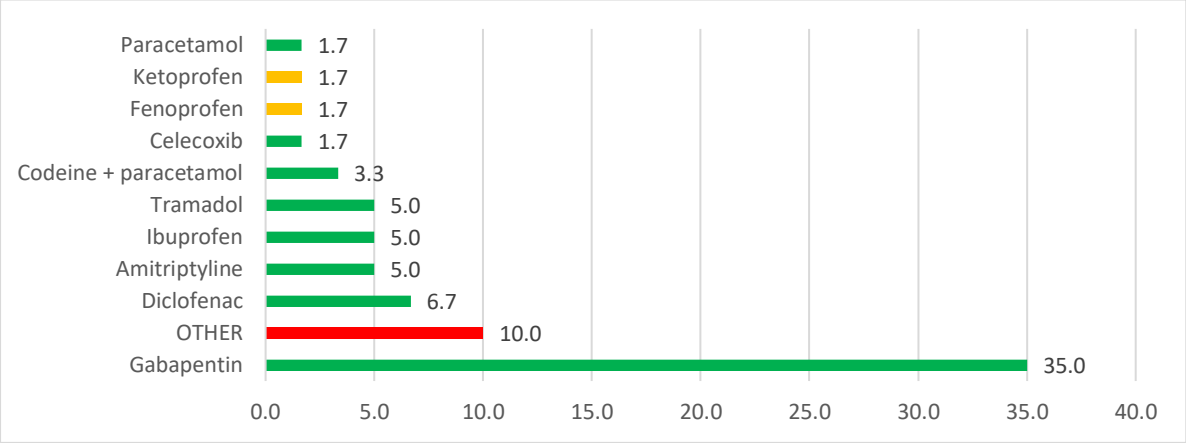


Figure 18 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for neuropathic pain in athletes (n=60)

Injectable medicines

Injectable medicine for moderate to severe pain without inflammation

Team physicians were asked which injectable medicine they most frequently prescribe to athletes for moderate to severe pain without inflammation due to sports-related conditions. The most commonly prescribed drug was by far diclofenac (25.0%, n=15). Other injectable drugs for this clinical indication were prescribed by less than 9% of responding physicians.

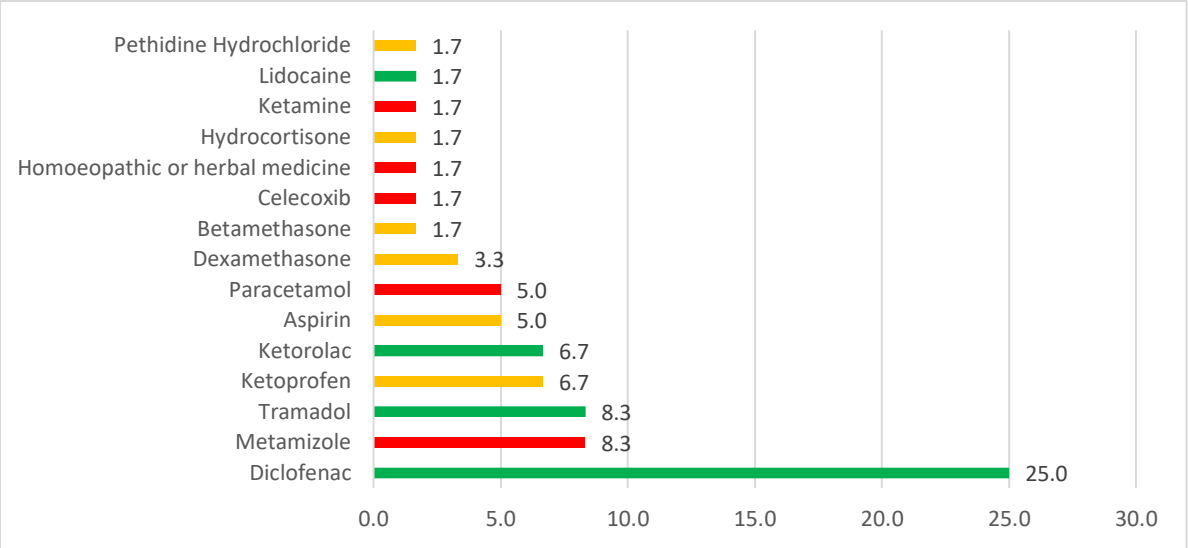


Figure 19 Proportion (%) of team physicians reporting which INJECTABLE medicine they most frequently prescribe to athletes for moderate to severe pain without inflammation due to sports-related conditions (n=60)

Injectable medicine for moderate to severe pain with inflammation

Team physicians were asked which injectable medicine they most frequently prescribe to athletes for moderate to severe pain with inflammation due to sports-related conditions. The most commonly prescribed drug was by far diclofenac (30.0%, n=18). Other injectable drugs for this clinical indication were prescribed by less than 7% of responding physicians.

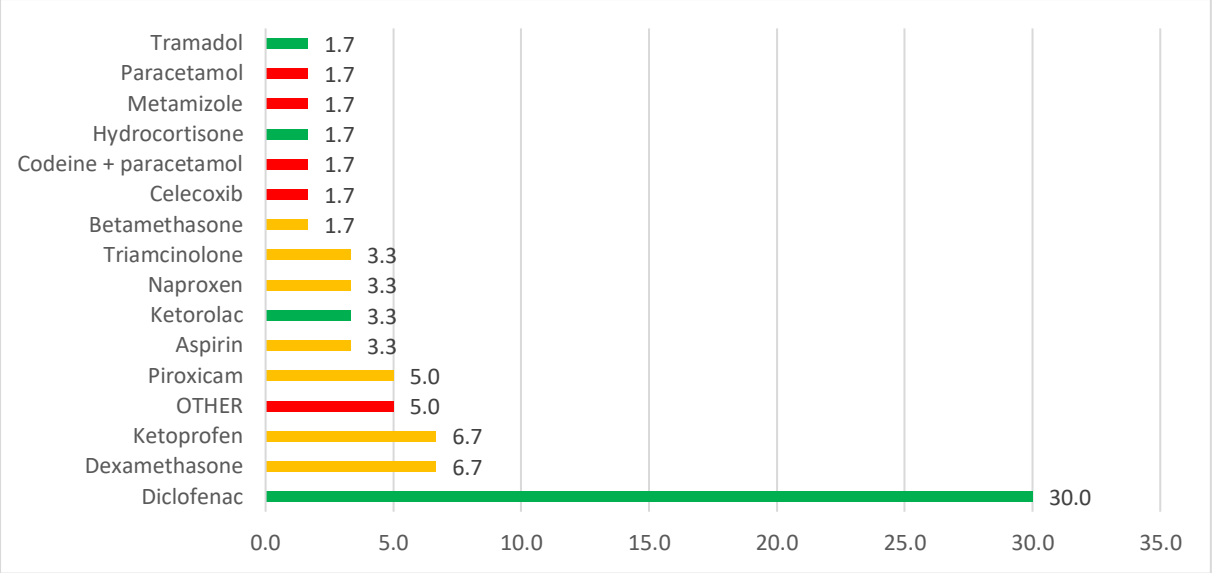


Figure 20 Proportion (%) of team physicians reporting which INJECTABLE medicine they most frequently prescribe to athletes for moderate to severe pain with inflammation due to sports-related conditions (n=60)

Injectable medicines for inflammation of large joints

Team physicians were asked which injectable medications they most frequently administer to athletes for inflammation of large joints due to sports injury. The most commonly prescribed drugs included dexamethasone (18.3%, n=11), diclofenac (13.3%, n=8), and triamcinolone (11.7%, n=7). Others were prescribed by less than 7% of physicians.

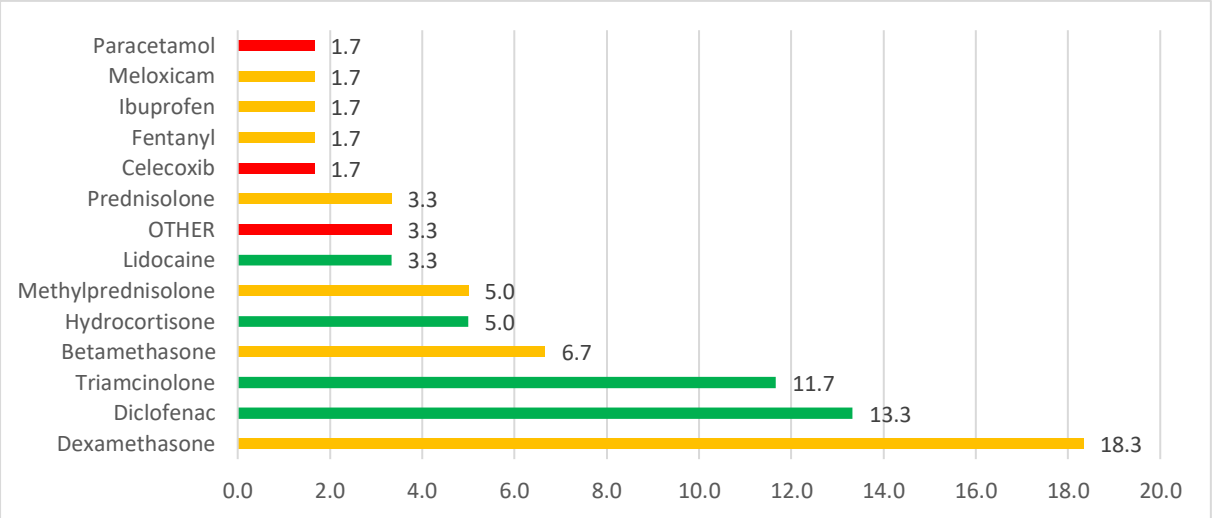


Figure 21 Proportion (%) of team physicians reporting which injectable medications they most frequently administer to athletes for inflammation of large joints due to sports injury (n=60)

Injectable medicines for local pain of large joints

Team physicians were asked which injectable medications they most frequently administer to athletes for local pain of large joints due to sports injury. The most commonly prescribed drugs included lidocaine (25%, n=15), bupivacaine (20.0%, n=12), and dexamethasone (8.3%, n=5). Others were prescribed by less than 7% of physicians.

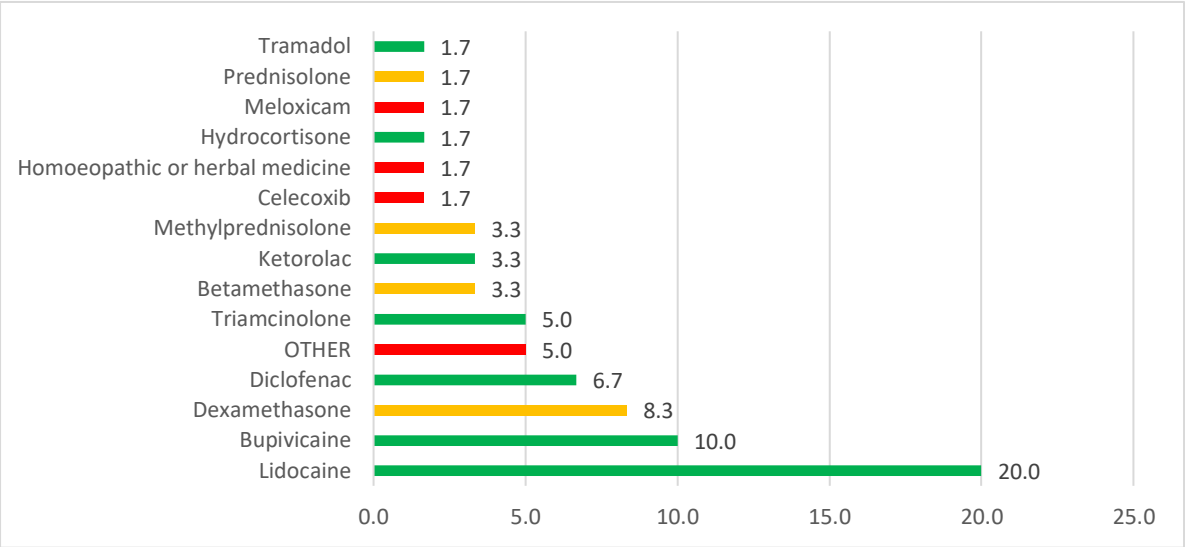


Figure 22 Proportion (%) of team physicians reporting which medication they most frequently administer to athletes for local pain of large joints due to sports injury (n=60)

Urgent or emergency treatment

Emergency analgesia for severe pain on the field of play

Team physicians were asked which injectable medicine they prefer to use for emergency analgesia for severe pain on the field of play due to serious injury. The most commonly preferred drugs were morphine (20.0%, n=12), fentanyl (16.7%, n=10), and tramadol (8.3%, n=5). Other drugs for this use were preferred by less than 4% of physicians.

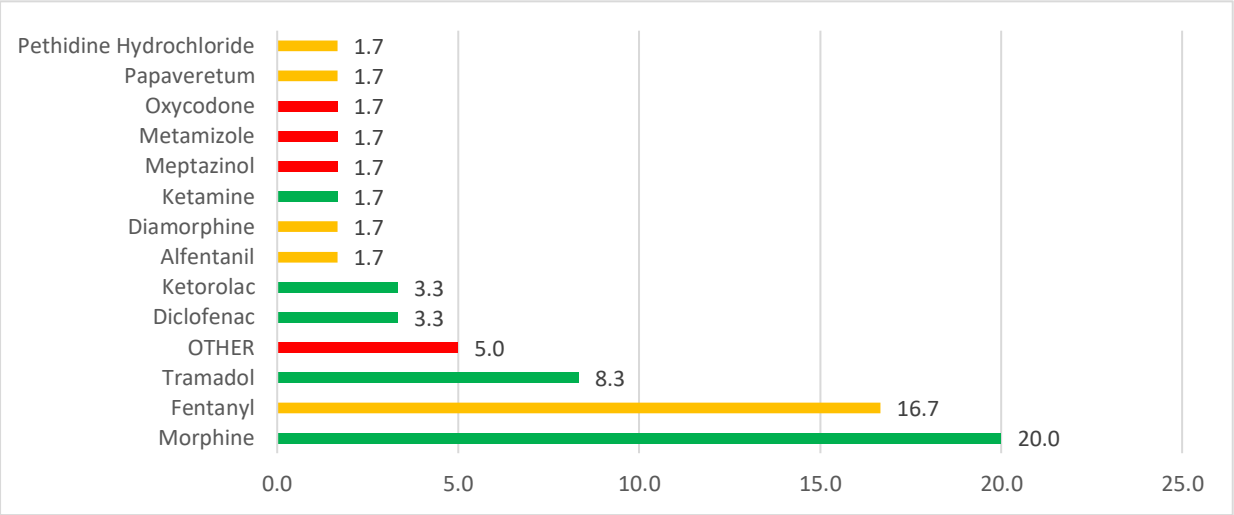


Figure 23 Proportion (%) of team physicians reporting which medicine they prefer to use for emergency analgesia for severe pain on the field of play due to serious injury (n=60)

Analgesia with sedation requiring rapid onset on the field of play

Team physicians were asked which injectable medication they prefer to use for analgesia with sedation requiring rapid onset on the field of play. The most commonly preferred drugs were ketamine (10.0%, n=6), lidocaine (8.3%, n=5), tramadol (6.7%, n=4), and fentanyl (5%, n=3). Other drugs for this use were preferred by less than 5% of physicians, and 13.3% (n=8) reported they would use another drug not listed in the survey.

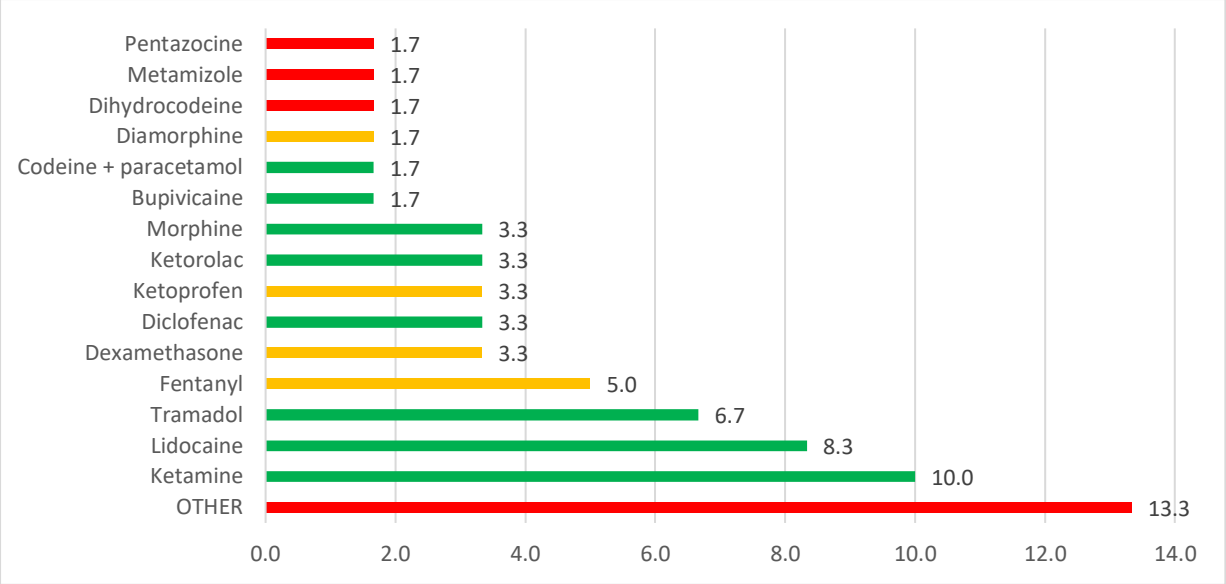


Figure 24 Proportion (%) of team physicians reporting which medication they prefer to use for analgesia with sedation requiring rapid onset on the field of play (n=60)

Topical medicines

Topical medicines for pain and inflammation

Team physicians were asked which topical medicine they most frequently prescribe for pain and inflammation due to sports-related conditions. The three most commonly prescribed drugs were NSAIDs including diclofenac (56.7%, n=34), ketoprofen (8.3%, n=5) and ibuprofen (5.0%, n=3). Other preparations were prescribed by less than 4% of physicians.

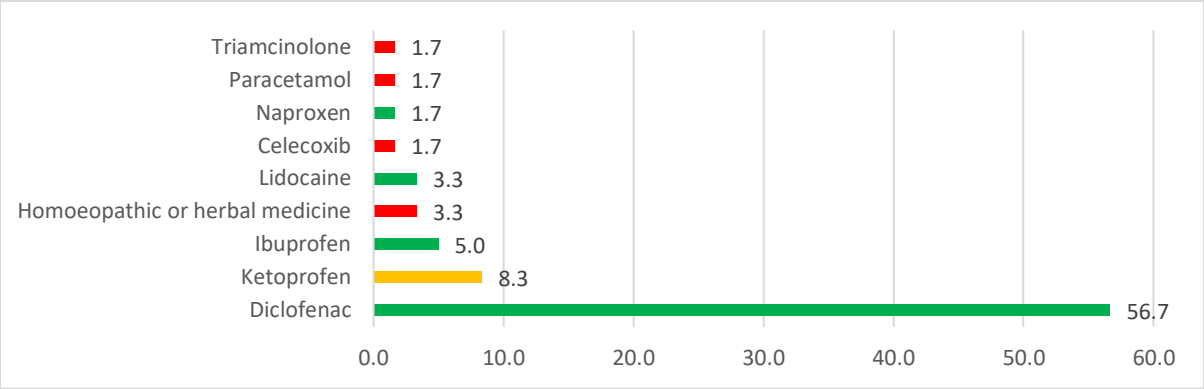


Figure 25 Proportion (%) of team physicians reporting which topical medicine they most frequently prescribe for pain and inflammation due to sports-related conditions (n=380)

3.4 DISCUSSION

The primary aim of Phase One of the research was to evaluate medication use by competing athletes at the European Games to establish which medications for the treatment of pain and inflammation should potentially be available from the pharmacy at future games to better meet their medical requirements. Not only does this study meet the primary aim of providing an understanding of the range of medications that athletes are using for pain and inflammation, and whether they are included on the OPF, but it also illustrates the broader prevalence of both medication and supplement use by athletes between sports and sex.

The medications declared by athletes on the doping control forms, along with the issue of medications from the pharmacy as documented in the pharmacy dispensing reports collectively provides an account of actual use of medications by athletes during the Games, which can be compared to what was listed on the OPF to evaluate whether improvements to the list of medications could be made to enable it to better match the needs of the athletes. In addition, through the responses in both the team physician survey and the declarations of stock medications carried by teams, we can also compare whether the medications currently on the OPF are matched to the to the most common prescribing preferences of the team physicians in this setting.

The first part of this discussion section provides an overview of the general findings from each component of the research. The second part collates the observations from each of the four datasets relating to specific drug categories to qualitatively evaluate and describe the potential improvements which could be made to the OPF to better meet the needs of both athletes and prescribers.

3.4.1 Review of medications declared on doping control forms

General prevalence of medication and supplement use

The results show that 82% of athletes were taking either a medication or supplement of some type in the previous 7 days. This was slightly higher than similar reports of total declared medication or supplement use from other major games; at the Sydney 2000 Olympic Games 78% of athletes were taking either a medication or a supplement, and 75.7% of athletes at the Athens 2004 Olympic Games were taking either a medication or supplement in the 3 days prior to testing.[180]

Of all athletes tested, 39% of were taking medications of some type in the week before they were tested, many taking multiple medications. The average number of medications declared among all 999 athletes was 0.7, with a median of zero. The average number of medication use declared among the 394 athletes that used one or more medications was 1.8, with a median of 1.0. These results are reasonably consistent with other similar studies, including a 2013 survey in Finnish athletes, which reported that 33.3% of Olympic athletes, and 48.9% of Paralympic athletes were taking at least one medication of some type in the last 7 days.[181]

In terms of supplement use, 71.6% of athletes at the Minsk 2019 European Games were taking at least one supplement in the previous 7 days, compared to the Athens Olympics where 42.1% of athletes declared supplement use in the previous 3 days. These lower numbers at other games might be attributed to the shorter length of time (3 days compared to 7 days) required to report use of these substances before the declaration.

A total of 703 unique declarations were made for medications by athletes, and 2492 unique declarations for supplements, with 31 declarations being unidentifiable or illegible. Of all medications declared, 74.7% (n=531) were listed specifically on the current OPF, with 17% (n=114) not listed, but had a suitable alternative in the same therapeutic class and indication available on the OPF. Only 8.3% (n=58) of all medication declarations did not have any suitable

therapeutic alternative on the OPF. These data broadly indicate that the OPF as a whole can meet a high proportion of medication needs either exactly, or with an appropriate alternative. The OPF does not contain any supplement products, and so none of the requirements relating to the use of supplements can be met for athletes. The remit of the OPF is only for medication, and so athletes must continue to find their own sources of supplements, at their own risk. Although given the widespread use of supplements by athletes, the provision of a number of common, and trusted supplements from a doping perspective might be considered in the future. Although comprehensive data has been collected regarding supplement use, this topic will not be covered further in this report as it is outside the scope of this research, however, may form the basis of future postdoctoral studies looking at supplement use in athletes.

Use of PI medications

Athletes may use a variety of medications to treat painful sports injuries and their underlying conditions including NSAIDS, opioids, simple non-opioids such as paracetamol, as well as glucocorticoids, antidepressants, anxiolytics, muscle relaxants and anti-convulsants.[159] Of all declarations for PI medications, NSAIDs accounted for the majority of them (70%, n=223), followed by non-opioid analgesic medications (19.4%, n=61). Glucocorticoids for intra-articular use were the least declared medication for pain and inflammation (0.3%, n=1). There were no declarations for medications for neuropathic pain, or single-agent opioid preparations by any athlete. The high proportion of NSAID use supports the notion of providing a wider selection of this category on the formulary compared to other less-used medications to be able to provide the specific examples athletes are taking or that physicians prefer to prescribe.

There was a significant association between declared PI medications and the route of administration. At these games the oral route of administration was the most common route for PI medications (53%) compared to topical (34%) and with injection or any other route (5%; $p<0.001$). This fact may be useful when selecting formulations of particular medicines for the OPF, providing an oral option where it exists in reference to other routes.

This study also showed that female athletes were significantly more likely to be using any medication, including PI medications than male athletes. Female athletes were more likely to have used PI medications in the last 7 days compared to male athletes (female: 29.6%; male: 18.5%; p<0.001). This may indicate either differences in rates of injury, or differences in approaches to injury treatment in female-dominated versus male-dominated sports and disciplines. Although the OPF does not differentiate use of medicines for female or male athletes, it is important to ensure that the range of medicines most common in both males and females are provided.

Of all PI medications declared, 80.0% (n=252) were listed specifically on the current OPF, with 18.7% (n=59) not listed, but had a suitable alternative in the same therapeutic class and indication available on the OPF. This is a good indication that the current OPF can provide an option for most of the medications the athletes were taking for pain or inflammation at the time of the Games. Only 1.3% (n=4) of all medication declarations did not have any suitable therapeutic alternative on the OPF; these were metamizole (n=2) and tolperisone (n=2).

3.4.2 Polyclinic pharmacy dispensing reports

The Minsk 2019 European Games was the first major games to implement the OPF as the set of medicines to be made available for prescribing by both the physicians working with the organising committee from Belarus, as well as by the visiting team physicians from 50 European countries. The Minsk 2019 pharmacy team adapted the examples on the OPF to match the specific formulations of medicines available in Belarus. The resulting Minsk 2019 medicines formulary was published in the Minsk 2019 Pharmacy Guide[182] and distributed to team physicians a month prior to the start of the Games.

Both Belarusian and visiting European team physicians were able to prescribe medicines from the formulary from the polyclinic pharmacy in the athlete village. An estimated 120 team

physicians attending the games had access to the medicines for prescribing for both athletes and non-athletes residing in the athlete village. A total of 471 prescription items were dispensed, with 65.2% (n=307) of items dispensed for athletes and 34.8% (n=164) for non-athletes.

Most (29.3%, n=87) of the athlete prescriptions were prescribed by physicians of the host country, Belarus. This is understandable due to a dedicated medical polyclinic being operational within the athlete village, with full access for the Belarussian team members. The polyclinic was staffed by Belarussian doctors who were available to treat any athletes and officials attending the games.

The top 5 countries with the most prescriptions dispensed were all from Eastern European countries: Belarus (24.4%, n=115), Moldova (13.2%, n=62), Czech Republic (7%, n=33), Ukraine (5.9%, n=28), Russia (5.7%, n=27). These same countries had the highest numbers of athletes accessing the service. A number of countries had a greater proportion of the total prescription count for non-athletes compared to athletes including: Ukraine (non-athletes: 18%; athletes: 10%); Azerbaijan (non-athletes: 15%; athletes: 5%). These data provide an understanding of how the pharmacy services are accessed during the games. In Minsk, the use of the service by Eastern European teams may reflect a greater trust in the medical services provided, with a greater reliance on the pharmacy compared to their own stock compared to other teams. Whereas the absence of use by some of the larger teams, such as the Great Britain team with 100 athletes,[183] probably indicated a complete reliance on their own comprehensive imported medication stocks.

PI medications represented 49% of all drugs dispensed to athletes. This was similar to the proportion of PI medications declared on the doping control forms (45%, n=315). NSAID drugs were the most commonly dispensed class of drugs to athletes (33.8%, n=104), followed by topical preparations for massage or physical therapies (13.4%, n=41). Very few other medications for pain and inflammation were dispensed for athletes but included: COX-2 inhibitors (1.0%, n=3); non-opioid analgesic (1.0%, n=3); local anaesthetics (0.3%, n=1), and

skeletal muscle relaxants (0.3%, n=1). Similar to the doping control form review, these data indicate that a comprehensive range of PI medications, particularly NSAIDs are warranted on the OPF.

For all types of PI medications, all individual medications were prescribed to athletes more frequently than non-athletes (see Table 15). For all oral PI medications, there was a significantly higher number of prescriptions prescribed to athletes (84%, n=110) compared to those prescribed to non-athletes (16%, n=21; p=0.005).

The numbers of PI medications dispensed to athletes from each sport gives us some insight into the potential differences in occurrence of painful injury between sports. Prescriptions for boxing athletes represented the greatest proportion of all PI medications dispensed (50%, n=55), followed by athletics (15.5%, n=17). Sambo and judo, both combat martial art sports were next highest (sambo: 11.8%, n=13; judo: 8.2%, n=9). But because the actual numbers of athletes competing in each sport was not available, the rates of injuries per sport requiring treatment cannot be determined with this pharmacy data.

Since the OPF was directly used to select the list of medications for the 2019 European Games, all PI medications provided through the pharmacy were either specifically listed on the OPF or represented an acceptable alternative within the same class and route of administration.

3.4.3 NOC stock medicines importation declaration review

This section discusses the results of the stock medicines importation declarations made by the team physicians at the European Games. By comparing what teams choose to carry as stock for potential use with the medications provided on the OPF, we can evaluate how well the OPF meets the anticipated prescribing needs of the team physicians.

Most NOC teams attending the games, had at least one team physician, but often more depending on the size of the team. Each team physician was required to obtain temporary registration to practice as a physician in Belarus through the Ministry of Health. The head physician of the team was the Chief Medical Officer who had the responsibility to arrange and declare the importation of any stock medications being carried into Belarus for use by the team. This process involved a declaration to the Belarus Ministry of Health via the pharmacy services of the Minsk 2019 European Games Organising Committee.[182]

A total of 36 of 50 (72%) participating NOC teams submitted a declaration for imported medicines for use at the games. The declarations reported were from physicians caring for a combined total of 3337 of the 3693 (90.4%) athletes attending the Games. The 14 teams who did not submit a declaration either did not have a dedicated team physician, or did not carry team supplies of medicines, but rather relied fully on the polyclinic pharmacy for accessing any necessary medications during the games.

Of all declared stock PI medications, 80% could be provided by either an exact match or an acceptable clinical alternative in the same class and route from the OPF. Only 20% of PI medications could not be provided at all by the OPF.

3.4.4 Survey of NOC team physicians

The purpose of the survey was to understand how the physicians access medicines during the games and their specific prescribing preferences for various clinical presentations that the OPF provides drug treatment options for.

It was completed by 60 individual team physicians attending the games, from 33 of the 50 (66%) participating countries. Although it was hoped that at least one physician from each team (n=50) would complete the survey, the response rate was deemed to be acceptable for

this pilot study, as overall it represented 60% of the estimated visiting physician population (n=100) of the games, based on historical data from the previous European Games in 2015.[184]

Over half of responding physicians identified as having a specific sports medicine specialty in primary care or surgical fields (52%, n=31). The orthopaedic specialty was the next most common professional field (22%, n=13). The high proportion of these sports and orthopaedic specialist fields affirms the notion that musculoskeletal injury is a primary focus of care at these games, as such highlights the importance of providing a comprehensive medicines formulary that is also focussed on the specialist treatment options pertaining to musculoskeletal injury.

Half (50%, n=30) of physicians cared for less than 50 athletes during the Games; while 20% (n=12) of physicians had 51–100 athletes under their care and 30% (n=18) physicians cared for over 100 athletes during the games. On average, physicians cared for athletes competing in 8 sports within their team. The diversity in the number of athletes each physician cared for and the number of sports they oversaw, highlights the varied responsibilities of team physicians in this setting, and the potentially wide range of treatment options on a medicines formulary that are required to treat a range of unique injuries presented by each sport.

3.4.5 General use of games pharmacy services versus own stock

This survey showed that 91% of all team physicians attending the Minsk 2019 European Games expected to access the medications from the polyclinic pharmacy during the course of the games, highlighting the crucial importance of having an effective formulary to address the medical needs of the athletes they treat during the games. It shows that 45% (n=18) of physicians rely on the medicines available through the polyclinic pharmacy for a large majority (75-100%) all their athlete prescribing, indicating that some teams do not import any medicines to the games. This reliance on local services and drug sources might stem from a variety of reasons including the logistic challenges and costs of importing medicines, and trust

that the medicines provided by the organising committee meets their expected prescribing needs.

In terms of the general range of all medications provided on the formulary, 73% (n=44) physicians stated they would expect them to cover over 75% of all the medicines needed by the athletes in their team, with 27% (n=16) physicians stating that the selection would cover all of their prescribing needs for their athletes. In terms of their own stock drugs, 90% (n=54) of physicians expected their own supplies to cover more than 75% or all of their medication needs while in the host country, with 35% (n=21) expecting their own medications to cover *all* their expected prescribing needs. The finding that 90% of physicians expected their stock to cover more than three-quarters of their medication needs is potentially a reflection of the trust in their sourcing and perhaps concerns about potential gaps or differences in medication availability in the host country.

This information on how physicians plan to use the pharmacy medications versus their own stock is important when developing a formulary for the games. The most successful formulary would be one that met the prescribing need to the greatest extent. In doing so, would mean that teams could carry much less medication to the host country, knowing that the majority of the required medicines would be available onsite. As the formulary is usually published at least 6 months prior to the Games, teams can plan their own stock around this and can reduce their carried stock to just the specialist medications that may be necessary for particular athletes. As the OPF is refined over subsequent editions to better match actual use and prescribers preference, this survey could be repeated to evaluate the impact of the OPF on physician use of pharmacy services and in the stock medicines that they carry.

3.4.6 Use of PI medications

The expected prescribing patterns of PI medications by team physicians, during major sporting events demonstrates the anticipated intensity, physical demands, and potential

injury rates among athletes, but also shows a variation in approaches to treatment between physicians. The survey showed 41.7% of physicians anticipated a relatively low need for PI medications, expecting to prescribe them to fewer than 10% of their athletes. Whereas some team physicians expected a moderate to high use, with 55% of physicians anticipating the need for prescribing PI medications in 11-50% of their athletes. The differences in expected use may be explained by the levels of risk of injury in the different types of sports the athletes under their care compete it, or differences in preventative measures or treatment approach such as the use of conservative or other non-pharmacological pain management strategies.

The physicians were asked to review the list of analgesic and anti-inflammatory drugs provided and asked to state how well the list of drugs in this category met their prescribing needs for the athletes under their care. A total of 68.3% (n=41) physicians said that the selection covered between 75-100% of their requirements, with 33% (n=20) stating that their complete prescribing requirements could be met. These responses suggest that the OPF was overall already reasonably effective at anticipating and meeting the expected prescribing needs of the team physicians in terms of PI medications.

3.4.7 Qualitative assessment of PI medications on the OPF

The next section presents each of the classes of PI medications in the OPF, with a collation and discussion of the results obtained from each of the four datasets relating to each medication category. It presents considerations for improvements for each section of the OPF relating to PI medications.

3.4.7.1 *NSAIDS*

Oral NSAIDs

Of all NSAIDs declared by athletes, 97% were an oral formulation, with ibuprofen and diclofenac the most frequently declared (ibuprofen: 36%, n=79; diclofenac: 30.1%, n=66). This

closely corresponded with the most frequently dispensed oral NSAIDs from the Polyclinic Pharmacy (ibuprofen: 40%, n=20; diclofenac: 26%, n=13). Both of these drugs were specifically listed on the OPF, and these data confirm their widespread use in this setting. Diclofenac was the only oral slow-release preparation declared (n=3). Two combination oral products were declared: diclofenac + paracetamol (n=1) and diclofenac + codeine (n=1), but each of the ingredients of these combinations could be provided from the OPF as single-agent formulations.

In terms of team stock medicines, 53 different formulations of NSAID products were reported across all teams, including 23 different types of oral NSAIDs, indicating the vast differences in preference of these drug types between different European countries. Of the 23 oral formulations, 7 (30.4%) were specifically listed on the OPF, which included the three most frequently stocked of all oral NSAIDS (diclofenac: 23.3%, n=35; ibuprofen: 15.3%, n=23; aspirin: 15.3%, n=23). An alternative within the same class and route could be provided for all other oral NSAIDs stocked. Given loxoprofen use was not reported as used by any athlete, nor was it carried as stock by any teams, this example could be considered for removal from the OPF.

In terms of the survey results, all oral NSAIDs preferred by physicians for the treatment of mild to moderate, and moderate to severe pain could be met by the OPF as the exact medication, with the exception of ketoprofen, mefenamic acid and piroxicam, however suitable alternatives in the same class exist on the OPF for these drugs. Only one physician preferred mefenamic acid as the treatment of choice for mild to moderate pain with inflammation, but its actual use was not declared by any athlete. However, 4 (7%) physicians preferred ketoprofen for treatment of mild to moderate pain with inflammation, and moderate to severe pain. Given this drug was also reported to be used by athletes on the doping control forms, ketoprofen could potentially be considered for addition to the OPF.

Topical NSAIDs

Of all NSAIDs declared by athletes, just 3% (n=7) were for topical use and just included diclofenac, ibuprofen and ketoprofen. Similarly, ketoprofen and diclofenac were the two most frequently dispensed topical NSAIDs from the polyclinic pharmacy (diclofenac: 42.6%, n=29; ketoprofen: 32.4%, n=22). In terms of team stock medicines, diclofenac was the most common topical NSAID carried by 61% (n=22) of teams, followed by ketoprofen carried by 30.6% (n=11) of teams. Through the survey 8% (n=5) of physicians indicated a preference for ketoprofen for topical treatment of musculoskeletal pain.

Topical diclofenac was listed on the OPF, but not topical ketoprofen. The inclusion of topical ketoprofen could be considered to be added for future editions of the OPF, and would be supported by the fact that it has broad global availability; *Martindale* (Pharmaceutical Press, London) lists availability of topical ketoprofen in 39 of 41 (95%) countries it covers.[171]

Topical naproxen was listed as an example on the OPF, but its use was not declared by any athlete, nor was carried by any team as stock, and was noted as being the preferred topical NSAID by just one physician in the survey. The removal of this example from the OPF could be considered.

Although there were no declarations by athletes of use of NSAID transdermal patches, 30% (n=11) of teams carried them as stock, with diclofenac patches the most commonly carried by 22% (n=8) of teams. NSAID transdermal patches were not listed as an essential route of administration on the OPF due to the almost 10-fold higher cost of this formulation compared to oral treatment, and the fact that the clinical use could be met by other formulations.[185]

Injectable NSAIDs

No injectable NSAIDs were declared on the doping control form by athletes, but injectable ketoprofen was dispensed from the polyclinic pharmacy for 3 athletes. Ketoprofen was also the injectable NSAID of choice for 7% (n=4) physicians completing the survey for the

treatment of moderate to severe pain. Ketoprofen injection was not specifically listed on the OPF but given the use and availability of this drug in Europe, this could potentially be considered as a named example for future editions of the OPF.

In terms of team stock medicines, diclofenac was the most common injectable NSAID carried by 50% (n=18) of teams, and which was listed on the OPF. All other injectable NSAIDs were declared by less than 4 teams. Ketorolac was listed on the OPF as the main example in the class and route, however only 2 teams declared carrying it and there were no reports of administration to athletes. As such injectable ketorolac could be considered to be removed from the OPF.

Rectal NSAIDs

No rectal NSAIDs were declared by athletes on the doping control forms, and none were dispensed to athletes from the pharmacy. Only 3 teams carried the rectal formulation as stock (diclofenac: n=2; piroxicam: n=1). Diclofenac was included on the OPF as an option for this route of administration, although given no evidence of actual use was found, this route could be considered for removal from the OPF but left to individual teams to decide whether to carry this for specific athletes if this route was required on a case-by-case basis.

Overall, all reported actual usage of NSAIDs by athletes at the games could have been met exactly by the OPF for 79.8% of medications. A suitable alternative NSAID with the same clinical indication and route of administration was available for the other 20.2% of NSAIDs declared but which were not specifically listed on the OPF. These are listed on the table below.

Table 20 NSAID types declared but not listed on the OPF

NSAID type	Number of declarations
Nimesulide	20
Aceclofenac	4
Dexketoprofen	3
Flurbiprofen	3
Tiaprofenic acid	3
Meloxicam	2
Aminophenazone	1
Mefenamic acid	1

NSAIDs with risks to athlete health

Oral nimesulide use was declared on the doping control forms by 20 athletes as having been used in the last 7 days. In addition, oral nimesulide was carried as team stock by 33% (n=12) countries. In 2011, the European Medicines Agency Committee for Medicinal Products for Human Use (CHMP) completed a review of the safety and effectiveness of this drug, concluding that it should no longer be used for the treatment of painful osteoarthritis due to increased risk of liver toxicity compared to other NSAIDs and stated that it was as effective as other NSAIDs such as diclofenac, ibuprofen, and naproxen. Based on this guidance, nimesulide should not be prescribed to athletes over other safer alternatives.[186]

Although not declared as used by athletes, oral piroxicam was carried by 22% (n=8) of countries and its prescribing in the last 12 months was reported in the team physician survey by 18% (n=11) of physicians. In June 2017 the CHMP recommended restrictions on the use of piroxicam because of the increased risk of gastrointestinal side effects and serious skin reactions, and that it should no longer be used for the treatment of acute painful and inflammatory conditions.[187] [188]

Given the serious potential risks to athletes' health with both nimesulide and piroxicam, a specific warning about their use should be considered on the next edition of the OPF. They should never be included as options in any future games formulary.

3.4.7.2 *COX-2 inhibitors*

There was a total of only 6 declarations for oral etoricoxib by athletes on doping control forms, representing 1% of all declarations made. The polyclinic pharmacy dispensed 3 prescriptions of celecoxib to athletes, similarly, representing 1% of all pharmacy dispensing to athletes.

In terms of team stock, oral etoricoxib was carried by 36% (n=13) of teams and oral celecoxib was carried by 23% (n=7) of teams. In addition, the survey of team physicians asked which COX-2 inhibitors they had prescribed in the last 12 months, with the top responses being etoricoxib (33%, n=20) followed by celecoxib (16.7%, n=10). For the treatment of mild to moderate pain with inflammation, the survey indicated 8% (n=5) of physicians preferred etoricoxib, and 1.7% (n=1) preferred celecoxib; for moderate to severe pain 7% (n=4) of physicians preferred etoricoxib, and 1.7% (n=1) preferred celecoxib.

Only celecoxib is listed as an example of a COX-2 inhibitor on the OPF. But given that etoricoxib is carried and prescribed by a greater number of physicians, and used by more athletes, consideration should be made to listing etoricoxib as the primary example, with celecoxib listed as an acceptable alternative.

It should be noted that parecoxib injection was declared as stock by only one team. However, parecoxib injection is only licensed for the short-term treatment of postoperative pain in adults.[189] The need for this injection in the athlete village setting is therefore not warranted.

3.4.7.3 *Non-opioid analgesics*

For the purpose of this study, the definition of non-opioid analgesics does not include NSAIDs, which have been covered as a separate category.

Non-opioid analgesics represented 19.4% (n=61) of all athlete declarations for PI medications and were the second most used PI medications after NSAIDs (70.8%, n=223). Oral paracetamol-containing products accounted for 96.7% of medications in this class, of which 87% were single-agent paracetamol products; a small number (n=2) of products contained additional ingredients such as vitamin C or caffeine. There were 2 (3.3%) athlete declarations for oral metamizole. With the exception of metamizole, the exact medications could be provided by the OPF for 86.9% (n=53) of declarations, and a suitable clinical alternative in the same class and route could be provided for 9.8% (n=6) of others.

Small numbers of prescriptions were dispensed by the polyclinic pharmacy for this class of drugs (paracetamol: n=3; metamizole: n=3). This may have been since oral paracetamol was readily available at all venues, and also carried by 83% (n=30) of teams as stock. Paracetamol injection was carried by one country.

The survey of team physicians showed that 67% (n=40) of physicians had prescribed paracetamol in the last 12 months, and that it was the most preferred oral medication for the treatment of mild to moderate pain (without inflammation). Given the common prescribing by team physicians and the prevalence of actual declared use by athletes, paracetamol was appropriately listed on the OPF as oral formulations. The listing for rectal paracetamol formulations could potentially be omitted as there was no evidence of athlete use or team stock at these games.

Non-opioid medications with risks to athlete health

Various formulations of metamizole (also known as dipyrone) were carried as stock by teams (injection: 28%, n=10; oral: 31%, n=11; rectal suppositories: 3%, n=1). Metamizole was also reported in the team physician survey to be prescribed by 18% (n=11) physicians in the previous 12 months and was the preferred oral treatment by 5% (n=3) physicians for mild to moderate pain (without inflammation).

Metamizole was not included on the OPF due to its documented risk of serious adverse effects including increased risk of agranulocytosis with shock, and in many countries it is either banned or its use is considered justified only in severe pain or fever where no alternative is available, however it is still licensed for use in Belarus.[171 190] Given the serious potential risks to athletes' health, and the evidence that metamizole is still being prescribed and used by athletes, a specific warning about its use should be considered on the next edition of the OPF.

3.4.7.4 *Opioid analgesics*

There were no single-agent opioid preparations declared by any athlete, but there were two declarations for codeine + paracetamol oral combination products, and one declaration for a codeine + diclofenac oral combination product; all these products were specifically listed on the current OPF. There were no opioid medications dispensed from the polyclinic pharmacy.

In terms of team stock, 75% (n=27) of teams carried some sort of oral opioid with the most popular being tramadol containing preparations (44%, n=16), followed by codeine containing preparations (25%, n=9); both of which were listed on the OPF. Injectable opioids were carried by 8.3% (n=3) of teams and included tramadol and morphine. Controlled drugs such as morphine could not be imported to Belarus without a special importation application, which would explain the low number of importation declarations of this drug. Morphine was however on the OPF and was available from the athletes village pharmacy and at every competition venue for emergency use. One team declared fentanyl nasal spray, which was licensed for breakthrough cancer pain.[171] Its use in the sports setting may have potentially been intended for acute injury with severe pain.

In the team physician survey, the opioids prescribed by most physicians in the last 12 months were: tramadol (23%, n=14) and codeine (20%, n=12); for the oral treatment of moderate to severe pain (without inflammation), the survey indicated that 8% (n=5) of physicians

preferred a codeine plus paracetamol combination product, similarly 8% (n=5) of physicians preferred tramadol for this indication. Both codeine and tramadol were appropriately listed on the OPF.

Oxycodone prescribing in the last 12 months was reported by 7% (n=4) of physicians, and although low, was reported to be prescribed by more physicians than dihydrocodeine and hydromorphone. Consideration of replacing hydromorphone with oxycodone as an example on the OPF should therefore be considered for subsequent editions of the OPF.

3.4.7.5 *Medicines for neuropathic pain*

No medications for neuropathic pain were declared as used by athletes on the doping control forms nor dispensed from the polyclinic pharmacy. However, the need for these medications is likely to be more relevant to the Paralympic Games setting, where some athletes with disability will experience chronic neuropathic pain syndromes which may necessitate the long-term use of this class of analgesic.

The only drug in this class carried as stock by one team only was pregabalin. The OPF does list this drug for use as a second-line neuropathic pain agent as an alternative to gabapentin. In the team physician survey, gabapentin was the preferred drug in this class by 35% (n=21) of physicians, which was already listed on the OPF. Amitriptyline was on the OPF as a first-line treatment option but was not declared by any athlete or as team stock at these games.

3.4.7.6 *Glucocorticoids*

Glucocorticoids for local injection were the least declared PI medication by athletes. Triamcinolone injection was the only glucocorticoid declared as being used by one athlete (1%), which was listed on the OPF. No glucocorticoid medications of any route were dispensed from the polyclinic pharmacy.

In terms of team stock, the most frequently carried injectable glucocorticoids were methylprednisolone by 39% (n=14) of teams, betamethasone by 28% (n=10) of teams, and dexamethasone by 16.3% (n=7) of teams. Triamcinolone and hydrocortisone were examples on the OPF, but triamcinolone was carried by 25% (n=9) teams and hydrocortisone by only 2 (5.6%) teams.

The survey indicated that for injectable treatment of local inflammation of large joints, 18.3% (n=11) of physicians preferred dexamethasone, 12% (n=7) triamcinolone, 7% (n=4) betamethasone, 5% (n=3) hydrocortisone or methylprednisolone, and 3% (n=2) prednisolone.

Consideration should be made to adding methylprednisolone, betamethasone, and dexamethasone as additional examples to the OPF. To also support these additions to the OPF, since January 2022, all local injections were prohibited by WADA during the in-competition period. Washout periods were published by WADA to guide their use to avoid an adverse analytical finding. The washout periods for all local glucocorticoid injections are 3 days, except triamcinolone, prednisone and prednisolone which require a 10-day washout period. In light of this, examples of glucocorticoids on the OPF should be revised to include drugs that require a short washout period; dexamethasone, methylprednisolone and betamethasone are examples that have this short 3-day washout period.[191]

Oral glucocorticoids were carried by only a small number of teams, with the most popular examples being prednisolone carried by 17% (n=6) of teams and prednisone by 5.6% (n=2) of teams. Prednisolone was listed on the OPF, and is clinically interchangeable with prednisone, so the existing OPF oral glucocorticoid option was adequate.

3.4.7.7 *Local anaesthetics*

There was a total of 4 lidocaine injections declared as used by athletes on the doping control forms, representing 0.6% of all medications declared, and were dispensed twice from the polyclinic pharmacy. Lidocaine injections were carried by 44% (n=16) of teams and bupivacaine by 17% (n=6) of teams. A smaller number of other anaesthetic agents were carried by teams including mepivacaine, procaine and prilocaine.

In terms of the survey, the only local anaesthetics preferred by physicians for prescribing for local pain of large joints were lidocaine (25%, n=15) and bupivacaine (10%, n=6). Both lidocaine and bupivacaine injections were listed on the OPF and so no further additions to this category were warranted.

3.4.7.8 *Skeletal muscle relaxants*

There was a total of 5 declarations of oral skeletal muscle relaxants by athletes on the doping control forms representing 0.7% of all medications declared. Two types were declared: tizanidine (n=3) and tolperisone (n=2). Tizanidine was listed specifically on the OPF and was also dispensed twice from the polyclinic pharmacy. However, tolperisone is documented to have less drowsiness and CNS effects than tizanidine, and could be considered as an alternative on the OPF in the future as it may be more favourable for competing athletes due to potentially less ergolytic effects.[192]

A total of 6 declarations of oral benzodiazepine drugs, representing 0.9% of medications were declared by athletes including diazepam (n=3), alprazolam (n=1), midazolam (n=1) and triazolam (n=1). Oral diazepam is listed on the OPF for use in muscle spasm but alprazolam and triazolam are not, however these are more likely to be used for anxiety and sleep disorders than for their muscle relaxant properties in the management of pain, so addition to the OPF as an option for muscle spasm is not warranted.

In terms of team stock, 6 types of muscle relaxant drugs were carried by a small number of teams including tolperisone (oral: n=7; injection: n=1), thiocolchicoside (oral: n=5; injection n=4), oral mephenoxalone (n=1), oral baclofen (n=1) and oral orphenadrine (n=1). In addition, 7 different short-acting benzodiazepine drugs were carried by teams including: diazepam, oxazepam, bromazepam, alprazolam, prazepam, triazolam, and midazolam, with the most common being diazepam by 22% (n=8) of teams. Diazepam was on the OPF and was a suitable alternative for any of the benzodiazepines carried by teams. In the team physician survey, three examples of oral muscle relaxant drugs were suggested for inclusion on the OPF, including: orphenadrine, tolperisone, and tizanidine. Further consideration should be given to the inclusion of an oral centrally acting muscle relaxant on the OPF, such as tolperisone or another alternative.

3.4.7.9 *Massage and physical therapy preparations*

There was a total of 6 declarations of use by athletes of topical preparations used as massage or physical therapies, representing 0.9% of all declarations made for all medications. These included topical preparations containing methylsalicylate (n=5), and menthol (n=1).

A total of 13.4% (n=41) of all medications dispensed from the polyclinic pharmacy were preparations for topical use for massage and physical therapies. Most contained rubefacient ingredients that produce either a cooling or warming effect on the skin such as methylsalicylate, eucalyptus, turpentine oil, menthol, camphor, isobutane, and propane. The OPF specifically lists methylsalicylate which produces a warming sensation, and menthol which produces a cooling sensation, which sufficiently covers the range of effects that these products have on the skin. It would also be expected that the selection of the specific products for use at a games would be guided by local availability of particular products of this type in the host country.

In terms of team stock, 97% (n=35) of teams carried examples of preparations in this class. Most preparations carried had either menthol, methylsalicylate, or a combination of these two ingredients. Five (14%) teams declared topical preparations with capsaicin as an ingredient, which is indicated for localised neuropathic pain and symptomatic relief in osteoarthritis.[187] Although this has the potential to have some benefits in sports injury, the lack of reported use, and the non-specific indications for sports injury does not make a case for including it on the OPF.

3.4.7.10 *Emergency pain medications*

There were no PI medications used in the emergency setting including general anaesthetics with analgesia, opioid injections for severe pain, or gases for analgesia and sedation declared by athletes on the doping control forms or dispensed from the polyclinic pharmacy. These findings were to be expected as if such drugs were prescribed in the last 7 days, it would probably be due to a serious injury and it would be unlikely that the athlete would be fit to compete at this level within the week. In addition, if such medications needed to be administered at the time of the event or immediately after, it would likely be due to a serious medical event and thus would also be unlikely that the athlete would be subjected to doping control and asked to declare the medicines. And in any case, such drugs are likely to be administered directly from ambulance or first-response venue stocks and so would not be expected to be reported on the pharmacy dispensing reports.

In terms of team stock, 5.6% (n=2) teams carried methoxyflurane solution for inhalation. The OPF did list this drug specifically, and its use as an analgesic for acute pain on the field of play is increasing in sports globally, however global availability is still limited to a small number of countries.[107] As an effective non-controlled medication for severe pain in the emergency setting, it is expected that this medication will become more available for use at international games in the future. Morphine injection was carried by a small number of teams as described previously in this chapter.

Physicians completing the survey indicated a wide range of 13 various drugs as preferred treatment for emergency analgesia for serious injury with severe pain. Morphine was the most preferred drug in this class by 20% (n=12) physicians. Fentanyl injection was the next most preferred option by 17% (n=10) of physicians. Fentanyl was not listed on the OPF, but morphine was, and remains the drug of choice for provision of emergency analgesia for serious injury for athletes on the field of play at the Olympic Games.[1 25] Ketamine was the most preferred treatment option for rapid onset of analgesia with sedation and was appropriately listed on the OPF.

3.4.8 Summary of potential PI medication considerations for future editions of the OPF

The following table summarises the observations made from the review of each of the datasets for this phase of study relating to each class of PI medications on the OPF. It describes the potential improvements which might be considered in light of the data.

Table 21 Summary of potential PI medication considerations for future editions of the OPF.

1. Muscle relaxants Inclusion of a new section for skeletal muscle relaxants, with examples such as tolperisone, tizanidine, or orphenadrine. 2. COX-2 inhibitors Inclusion of oral etoricoxib as primary example of COX-2 inhibitor in addition to celecoxib. 3. NSAIDs Inclusion of oral, topical, and injectable ketoprofen as examples. Addition of diclofenac transdermal patch. Removal of naproxen as an example. Removal of injectable ketorolac. Removal of rectal diclofenac. 4. Other non-opioid analgesics Removal of paracetamol suppositories. 5. Opioids Replace hydromorphone with oxycodone as an example of an oral opioid. 6. Glucocorticoid injections Inclusion of methylprednisolone, dexamethasone, and betamethasone as examples of injectable glucocorticoids. 7. Clinical safety warnings Addition of a warning about the use of nimesulide, metamizole and piroxicam and the unsuitability for use in musculoskeletal injury in athletes. Exclusion of these medications from any future edition of the OPF.

3.5 CONCLUSIONS FROM THE PHASE ONE PILOT STUDY

From the four datasets collected over the course of the Minsk 2019 European Games it was evident that the current OPF could provide a reasonable option for most of the PI medications athletes were taking during the games, either through an exact match or a suitable clinical alternative, with the exception of those medications with potential risk to athlete health.

However, the list of PI medications could potentially be improved to either better reflect the medications athletes are known to be taking, or which were stocked and preferred by team physicians. Given that around half (49%) of all medications dispensed to athletes from the pharmacy are for this group of medications, close evaluation and refinement of this category is warranted. The study highlighted the potential need for additional drugs in the classes of NSAIDs, COX-2 inhibitors, opioids, glucocorticoids, and skeletal muscle relaxants to be considered for inclusion of future formularies. The study also indicated several PI medications that could be removed from the OPF due to no evidence of actual or anticipated use.

Athlete safety risks identified

This study has uncovered the use of a number of PI medications documented to have significant safety concerns and which may present a serious risk to athlete health, including metazimole, piroxicam and nimesulide. These drugs continue to be used by athletes and remain the preferred choice in their class by some physicians, despite strong clinical safety warnings issued by European regulatory agencies regarding their use for musculoskeletal injury. The ongoing use of these drugs should be proactively addressed and actively discouraged in future updates of the OPF with specific warnings regarding their inappropriate use in athletes.

Revisions to the approach for the next phase of research

It is important to note that the analysis of the results to date at the European Games has been purely qualitative. As they stand, these observations would be reasonably sufficient to inform opinion to update medications on the OPF for the purposes of the next edition of the

European Games, but do not provide a definitive quantitative measure to determine a clear cut-off for inclusion or exclusion. This limitation in the approach should, and was, addressed in the next phase of the study in Tokyo and Beijing. This pilot study at the European Games has highlighted that a quantitative approach to analysis is needed to inform the definitive list of drugs for pain and inflammation, and which can be repeatedly applied to all future games drug data to enable continual updates of the OPF over time to ensure current medical practice is always represented.

This study at the European Games has also highlighted the vast differences in the stock carried by teams, and the personal prescribing choice by physicians – these two factors, in essence, represent the anticipated use of medications. However, it has shown that much of the stock carried is never used, and the range of physician's personal preference is very wide for some therapeutic categories. To construct a list of medications for the OPF solely based on *anticipated use*, that is, based on carried stock or physician preference, would result in a list of drugs of which many will never be used, or where multiple interchangeable drugs in the same therapeutic class would co-exist. This would inevitably result in over-stocking, higher costs, and significant drug wastage after the games.

Direct evidence of actual medication use by athletes at the games was represented by the athlete declarations on the doping control forms and the pharmacy dispensing reports. *Actual use* accounts for every variable and determinant that contributes to the final outcome to determine whether the athlete takes the medication or not, and encompasses: 1) presenting clinical condition of the athlete; 2) availability of appropriate stock medications and; 3) personal decision of the prescriber. The best selection of medications for the OPF should therefore be based on data indicating documented *actual use* of medications by athletes, through their doping control declarations and pharmacy reports.

In undertaking this proof-of-concept pilot phase, another set of data that could potentially be used to widen the knowledge of actual athlete medication use at the games was identified.

That was the injection declaration data that is submitted according to the games needle policy every time an injection is administered in the athlete village, outside of the polyclinic setting.[28] [29] The next phase of the study conducted in Tokyo and Beijing will be expanded to include this wider dataset.

Lastly, the study was conducted on a solely European population of athletes covering 50 countries and so is limited in terms of its wider generalisability to the Olympic Games context. The next phase of the study was undertaken directly in the summer and winter Olympic environment. The results of Phase Two were therefore directly applicable to athletes from every country of the world and every Olympic sport.

CHAPTER 4. TESTING THE FORMULARY AT SUMMER & WINTER OLYMPIC GAMES

Phase Two of the research takes the lessons and recommendations from the research conducted at the 2019 European Games to establish a quantitative approach based on clear rules for inclusion or exclusion, to inform the selection of a revised and definitive list of PI medications for the OPF.

4.1 STUDY DESIGN

This phase of the research at the Olympic Games focussed only on direct evidence of athlete medication use to test the OPF in the Olympic setting, and to propose a revised and optimised set of PI medications for future editions of the OPF based on prevalence of use in the athlete population. All data representing direct evidence of medication use at both summer and winter Olympics were combined into a single dataset, with an additional dataset covering declarations of injections administered to athletes included. Direct evidence of medication use was obtained through the following three sources:

i. Declared medication use by athletes on doping control forms
ii. Dispensed medication from the athlete village pharmacy
iii. Declared injection administration

The prevalence of actual medication use in athletes attending the Tokyo 2020 and Beijing 2022 Olympic Games was established, and the list of drugs on the existing OPF was then compared with this dataset. The areas of agreement and differences between the existing OPF and the medications being actually used by athletes were identified and systematically analysed.

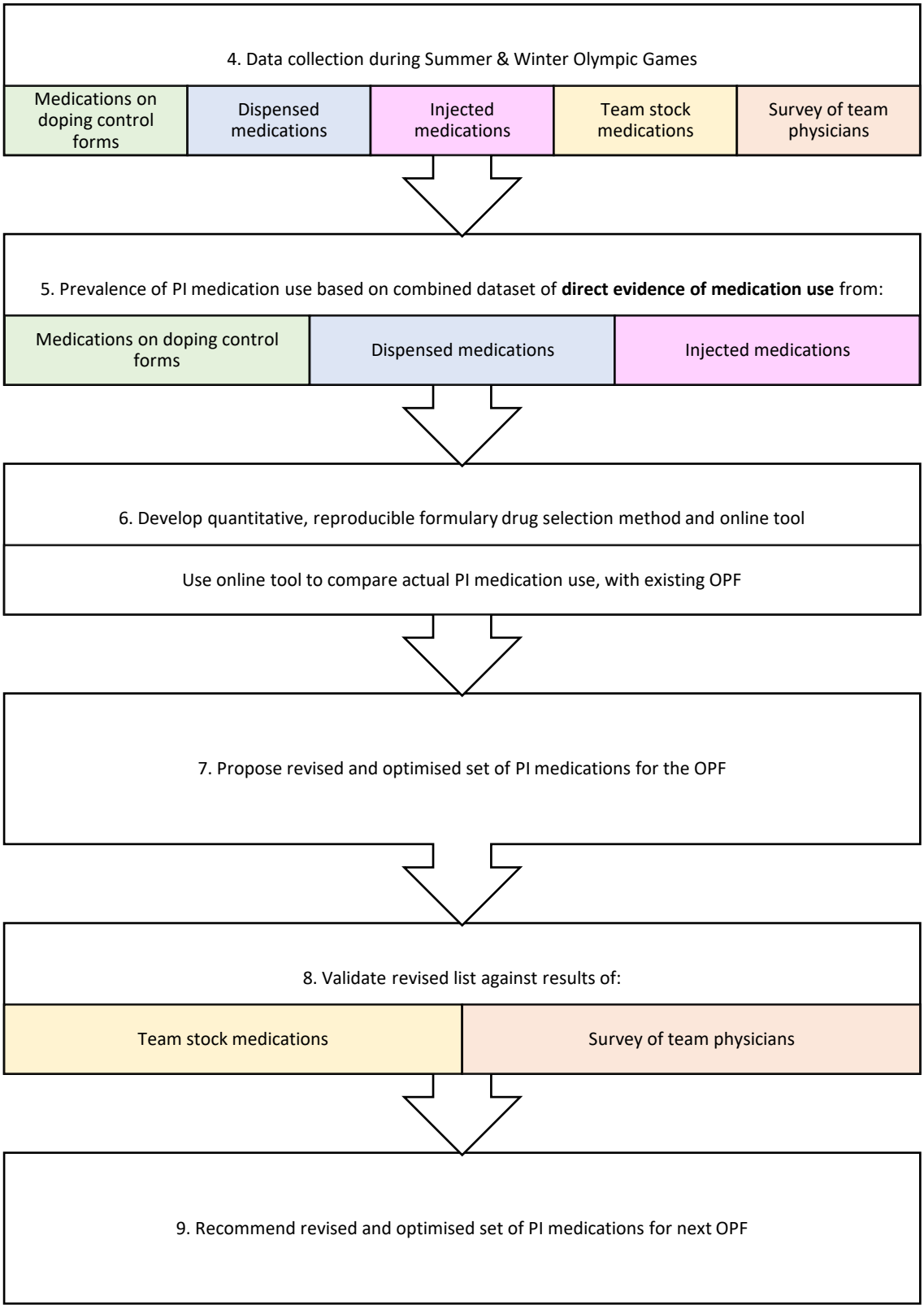
A quantitative approach to the analysis was undertaken through the development of an online data visualisation tool to compare the prevalence of PI medication use by athletes with the existing OPF. Inclusion of a PI medication on a revised OPF was determined using a cut-off threshold set as the cumulative % of top drugs used within each OPF class and route category which maximised the % of agreement with the existing OPF. Using this method, a revised and optimised set of PI medications was subsequently recommended for the next edition of the OPF.

Validation of the revised and optimised set of PI medications

The team physician survey was repeated at the Tokyo 2020 and Beijing 2022 games, with the inclusion of team physicians working at the 2020 and 2022 Paralympic Games that coincided. The retrospective review of imported team stock medications was also conducted. The revised and optimised set of PI medications was compared with the results of these components, to assess to what extent the revised list met the stock and prescribing preferences of team physicians.

The following diagram (**Error! Reference source not found.**) illustrates each phase and s equence of research in Phase Two.

Figure 26 Overview of Phase Two study at Olympic Games



4.2 METHODS

The approach to the research conducted at the Tokyo 2020 and Beijing 2022 Olympic Games differed to that of the European Games study in that it only used data confirming evidence of actual medication use in athletes to determine the selection, rather than use team stock lists or indications of preferred or anticipated prescribing as described by the team physician survey. But rather, it used these team stock importation records and survey results to further validate the resulting revised OPF after a revised and optimised set of PI medications was developed. This approach ensured that the revised OPF reflected evidence of real usage of drugs by athletes, rather than assumed or anticipated need.

4.2.1 Review of medications declared on doping control forms

At the time of providing a urine or blood sample at a doping control station, all athletes were asked to declare any medications or nutritional supplements taken during the previous 7 days on the doping control form. Completing a doping control form at the time of a doping control test was mandatory for athletes at these Games under the regulations of the *World Anti-Doping Code*.[5] These data provided direct evidence of medication use by athletes at the time of the games.

Data collection and anonymisation

The form used to collect the data was in the format of the standard WADA approved doping control form. An electronic version of the doping control form was used for the Tokyo 2020 and Beijing 2022 Olympic Games and the information was completed in the system directly at the time of testing. These electronic forms were provided on a tablet computer through the MODOC® Doping Control Platform, which was managed by the ITA on behalf of the IOC. At the end of each games, the ITA with permission from the IOC (who owned the data) provided the extracted data for this research, after all personal identifiers had been removed and included:

i. Sex
ii. Country of team
iii. Age range (<20; 21-30; 31-40; 41-50; 51+)
iv. Sport competing in
v. Declared substance
vi. Route of administration

Any declaration made for a product or brand was looked up using online references and presented as the generic substance name in English using International Non-proprietary Names (INN) conventions where they existed. The primary international reference used to do this was *Martindale: The Complete Drug Reference*.[171] *Google Translate* and Internet searches were also used where necessary to identify the generic ingredients of all products declared, and were also used to determine the product name if the declaration was made in a language other than English.

Identification of medicines versus supplements

All declarations were then categorised into two categories: 1) whether they were a licenced medicine, or 2) whether they were a supplement (defined as any nutritional supplement including vitamin and mineral preparations, herbal medicine, homoeopathic preparation, or substance of animal origin). The supplement data was not analysed as part of this research.

Total counts of drug types, therapeutic categories, route of administration, sex, country of athlete, sport, and age groups were tabulated.

4.2.2 Polyclinic pharmacy dispensing reports

This analysis involved reviewing the pharmacy reports of dispensed medications issued only to athletes from the polyclinic pharmacy within the athlete villages of the Tokyo 2020 and Beijing 2022 Olympic Games. For each event, the end-of-games pharmacy dispensing reports,

anonymised with no patient identifiers, were provided by the IOC. The reports contained the following data:

i. Whether the patient was an athlete or non-athlete
ii. Sex
iii. Country of team
iv. Age range (<20; 21-30; 31-40; 41-50; 51+)
v. Sport competing in
vi. Drug dispensed
vii. Number of prescriptions dispensed

Total counts of drug types, medication therapeutic categories, country of athletes, sport and age groups were tabulated.

4.2.3 Needle use declarations at the Olympic Games

At both the Tokyo 2020 and Beijing 2022 Olympic Games, the *IOC Needle Policy*[28 29] required any team physician to declare the administration of any injection and provide a clinical justification of its use through an online reporting platform managed by the IOC, with all declarations reviewed daily by the IOC Medical Commission. An anonymised post-games report of all injection declarations for both the Tokyo 2020 and Beijing 2022 Olympic Games was provided by the IOC containing the following data:

i. Whether the patient was an athlete or non-athlete
ii. Sex
iii. Country of team
iv. Age range (<20; 21-30; 31-40; 41-50; 51+)
v. Sport competing in
vi. Injectable drug administered

Total counts of drug types, route of administration, medication therapeutic categories, country, sport and age groups were tabulated.

4.2.4 Processing the data

The three actual-use data sources were processed to enable them to be combined into a single dataset representing prevalence of all documented use of medications by athletes through these sources. The medication data were categorised into therapeutic class and route of administration using the same drug class naming conventions presented on the original OPF and the subset of PI medications was identified and analysed.

Duplicate records of drug use for individual athletes were deleted. The reason duplicate records existed was that if athletes were selected for doping control, they would be required to declare medications that were dispensed by the pharmacy or administered by injection by a team physician. As such, the record of actual use could be presented in multiple records.

4.2.5 Selecting OPF medicines based on direct evidence of actual medication use

The following two datasets were used for the analysis.

Dataset 1. (Baseline) List of PI medications on the 2019 OPF

The set of medications listed in the first edition of the OPF were used as the baseline list for comparison. For the purpose of this study, PI medications were described using the same naming convention used in the OPF, and included the following 13 therapeutic categories:

01.1.1 NSAIDs	01.5.1 Local anaesthetics + vasoconstrictor
01.1.2 COX-2 inhibitors	02.1 Corticosteroids for oral use*
01.1.3 Non-opioid analgesics	03.1 Benzodiazepines
01.2 Opioid analgesics*	03.2 Skeletal muscle relaxants
01.3 Medicines for neuropathic pain	10.9 Massage and physical therapy
01.4 Corticosteroids for intra-articular use*	preparations
01.5 Local anaesthetics	23.1.2 General anaesthetics with analgesia

*Categories that contain prohibited medications, which may require a TUE to be applied for if used by athletes.

Dataset 2. Direct evidence of actual PI medication use

For this study, the term "actual use" refers to PI medication that was confirmed to be taken by athletes during the period of the games. This evidence was obtained through 3 data sources including:

i. Athlete declarations of medicines used in the 7 days prior to testing, as provided on the doping control forms
ii. Records of prescriptions dispensed to athletes from the athlete village pharmacy
iii. Team physician declarations of injectable drug administration to athletes through the IOC needle-use declaration process, as required by the *IOC Needle Policy*.[28 29]

Statistics

All data were coded and analysed using SPSS (v21, USA). Frequencies and percentages were used to described categorical variables. When reporting proportions or prevalence estimates, a 95% Confidence Interval (CI) was also reported. A chi-square test of independence was performed to compare the differences in declarations of PI medications between other categorical variables, such as route of administration, OPF drug classes, age range, sex, and country. Non-parametric Fisher's exact test was used instead of chi-square when expected counts per cell was less than 5 in 20% of the cells. A p-value <0.05 was considered cut-off for statistical significance.

Setting a cut-off threshold for inclusion

The PI medications used by athletes across the two Olympic Games were tabulated by OPF class and route of administration, against frequency, prevalence of use and cumulative percentage of use within each OPF class and route category. Cumulative percentage of use ranged from 0% to 100% and using this variable, the list of drugs was sorted in order of most frequently used.

A cut-off threshold for inclusion of a drug for the revised OPF was set as the cumulative percentage of top drugs within each OPF class and route category used across both the Tokyo 2020 and Beijing 2022 Olympic Games which maximised the percentage of agreement with the existing set of drugs on the OPF within the corresponding class and route category, ideally up to 100%, or otherwise at the highest percentage of agreement reached.

Recommending drugs for inclusion on the revised OPF

The cut-off threshold for inclusion was systematically applied to each separate OPF class and route subset to select the PI medications to be recommended for inclusion on the revised OPF. Medications within the inclusion range were recommended for the revised list of PI medications for the OPF. Drugs not used by athletes were recommended to be deleted from the OPF.

Multiple drugs with the same clinical indication and route of administration were generally deemed acceptable to recommend, to ensure that the revised OPF was representative of the most frequently prescribed treatment options in the Olympic athlete population. However, if the cut-off threshold resulted in the inclusion of multiple drugs within the same class and route, then further evaluation of prevalence data was undertaken to determine whether the list could be further rationalised. This evaluation was based on the following rules and exceptions.

Exception 1. Multiple drugs within the same class and route

If any medication was used by less than 0.2%* of all athletes in the study population, then it was not recommended to be included on the revised OPF, providing there was an acceptable alternative with the same clinical indication in the same class and route. But if there was no acceptable alternative, then one example, with the greatest prevalence of athlete use was recommended for inclusion. For cases where the prevalence was equal, the data from the team drug importation data (Table 85) was used to decide which medication should be recommended, based on the highest rate of importation by countries across both the Tokyo and Beijing Olympics.

*The value of 0.2% was selected based on an assessment of the resulting potential numbers of athletes who would be taking those medicines. At the Tokyo Olympics (n=11,420), 0.2% represented 23 athletes, and at the Beijing Olympics (n=2,834), 0.2% represented 6 athletes. These numbers of athletes were considered acceptable in terms of not being able to provide an exact match of their current medications on the revised OPF, as a many of these medications were also available via team stock. Or if they were not, then access to non-formulary medicines is always possible through the medical services at the Olympic Games, if required. For such low numbers, the burden on pharmacy services to access such drugs if absolutely required would be minimal, and would be acceptable based on the historical level of access for non-formulary drug at previous games; at London 2012, 8% of all drugs required were not on the formulary, which was not problematic.[14]

Exception 2. Drugs for emergency use

If a drug had no documented athlete usage, or rarely used, but was essential for immediate treatment of a clinical condition which represented an emergency or life-threatening condition, then these medications were not recommended for deletion from the existing OPF.

Exception 3. Drugs with known safety risks

If the cut-off threshold resulted in the inclusion of drugs with known patient safety risks, or potential harm, then these drugs were not included in the revised OPF.

4.2.6 NOC team stock medicines importation declaration review

This analysis involved the review of all declarations of imported medications carried as team stock made by the NOCs prior to each games. At each games, such declarations were required prior to entry into the host country. The declarations were made by the Chief Medical Officer of each NOC to the medical departments of the organising committees of each event, and to the customs agencies of the host country as part of the importation declaration requirements outlined in the *Customs and Freight Guide* unique to each games.

Data collection and anonymisation

The medication importation declaration report did not contain any personal or sensitive medical data. It did contain the names of medicines being carried as stock, but they had not been prescribed to any individual athlete at this stage, as they were carried by the teams to be used in the event of a medical situation if needed. Any medicine that had already been prescribed to an individual had to be carried in the personal possession of the athlete on arrival to the host country, and so the declarations reviewed did not contain any personal prescription information.

Processing the data

Every stock medication declaration form was reviewed manually and any declarations for PI medications were recorded on an Excel spreadsheet. Any declaration made for a product or brand was looked up using online references and translated into the generic substance name in English using International Non-proprietary Names (INN) conventions where they existed. The primary international reference used to do this was *Martindale: The Complete Drug Reference*,[171] or the manufacturer's official website.

Total counts of medication types, therapeutic categories, routes of administration and country of the importing teams were tabulated and analysed. The data were compared with the medication listings on the OPF according to the drug name and therapeutic class.

Statistical analysis

All data was coded and analysed using SPSS (v21, USA). Frequencies and percentages were used to described categorical variables of: medicine types declared, class, route of administration, country, and specific match to medicine listings on the OPF.

4.2.7 Survey of NOC team physicians

This survey was conducted as an online cross-sectional questionnaire of team physicians attending the Tokyo 2020 Olympic and Paralympic Games and the Beijing 2022 Olympic and Paralympic Games. It comprised of 25 questions which blended dichotomous, categorical, scaled, and open-ended questions to determine whether the drugs provided by the formulary at each games covered their expected prescribing needs for athletes while at the games. The full questions contained in the survey can be found in Appendix 3.

The questions aimed to evaluate specifically the use of analgesic and anti-inflammatory medicines used for the treatment of musculoskeletal sports injury in athletes. The questions also evaluated whether the formulary as a whole served the broader clinical requirements of athletes and asked what medicines should be included to improve it for future Games.

The survey design was based on a similar survey previously undertaken on behalf of the IOC in the team physician population at the Rio 2016 Olympic Games, which assessed the clinical practices of team physicians when prescribing analgesic and anti-inflammatory medicines for athletes. This survey at Rio 2016 was conducted to inform the *IOC Consensus Statement on Pain Management in Elite Athletes*.[25] The implementation of this survey followed the same methodology used at Rio 2016, using similar communication methods and online survey form. The format for the participant information sheet was based on one successfully used for a study conducted at the London 2012 Olympic and Paralympic Games.[179]

Recruitment

For recruitment of participants for the survey at the Olympic Games, an initial announcement about the intended research was made at the 'pre-Tokyo 2020 IOC Team Physician Meeting'

held in Monte Carlo, Monaco in February 2020. All Chief Medical Officers of the participating NOCs were personally in attendance or joined virtually. The aims of the survey to improve medicines selection at future games were presented, and it was announced that all team physicians were invited to participate.

During the Tokyo 2020 Olympic and Paralympic Games (which were eventually held in 2021 after they were postponed due to the Covid-19 pandemic), team physicians were again invited to participate in the survey at the time of the official team physicians meeting which was held the day before the opening ceremony of both the Olympic Games and Paralympic Games. They received a short verbal presentation delivered by the Chair of the IOC Medical Commission at the Olympic Games, and the IPC Medical Committee at the Paralympic Games, and then handed the participant information sheet, which contained the link to the online survey. The same recruitment method as was used at the Beijing 2022 Olympic and Paralympic Games. The participant information sheet and consent form used for the survey at both the European Games and the Olympic and Paralympic Games can be found in Appendix 2.

Informed consent

The first question on the survey explicitly asked whether the participant understood the study purpose and consents to participating. The participant had the opportunity to decide whether to or not continue with the survey at that point.

Data anonymisation

The survey did not ask for any personal identifiers, and so the results were anonymised on receipt. Specific consideration was given to whether any combination of responses could be potentially used to disclose any athletes' medical data. However, the survey did not ask any questions relating to the treatment of any individual, with hypothetical questions asking what medicines they would prefer to use for a variety of general clinical scenarios. The questions represented their preferences in the choice of medicine in their clinical practice generally and were not linked to any specific patients.

Participant inclusion and exclusion criteria

Every team physician working as part of a medical team who was eligible to prescribe medicines at the games for athletes of their team was invited to complete the survey before the closing ceremony of each games, but submissions were also accepted up to 7 days later. More than one team physician from each country was able to complete the survey, but the survey could not be completed by a non-prescriber or a representative. Non-prescribing healthcare professionals including physiotherapists, pharmacists and nurses were excluded from this survey, unless they were specifically registered to prescribe at the games.

Languages

For the Tokyo 2020 and Beijing 2022 Olympic and Paralympic Games both the survey and the participant information sheet were provided in multiple translations including: English, French, Spanish, Russian and Japanese.

Expected sample size

For the Tokyo 2020 and Beijing 2022 Olympic and Paralympic Games, 415 team physicians were invited to participate in the study. This was based on those attending the team physician meetings prior to each games, and who provided contact details to either the IOC Medical and Scientific Commission or IPC Medical Committee. The study sought completion of the survey from at least one team physician from each participating team who had a physician accompanying them. More than one survey per team could be completed if more than one physician was travelling with them.

Statistical analysis

All data was coded and analysed using SPSS (v21, USA). Frequencies and percentages were used to described categorical variables. A chi-square test of independence was performed to compare the differences in declarations between physicians from different countries based on geographical region, between other categorical variables, such as choice of medications, expected polyclinic pharmacy usage, coverage of prescribing needs by formulary and own stock, and expected athlete usage of PI medications.

4.3 RESULTS

4.3.1 Use of PI medications by athletes

Sample size and response rate

This study spans both the Tokyo 2020 Olympic Games and the Beijing 2022 Olympic Winter Games and includes athletes representing every summer and winter Olympic sport. A total of 14,254 athletes competed across both games (summer: n=11,420; winter: n=2,834).[193]

A total of 6,155 of 14,254 (43.2%) athletes across both games met the inclusion criteria for the study (summer: n=4,492 (39.3%); winter: n=1,663 (58.7%)). This is shown in Table 22 below.

Table 22 Athletes in study population

Games	Total athletes registered	Sample met inclusion criteria	%
Tokyo	11,420	4,492	39.3
Beijing	2,834	1,663	58.7
Tokyo + Beijing	14,254	6,155	43.2

The study population included athletes from 197 of 205 (96%) NOCs (including the Refugee Olympic Team), and all 40 Olympic winter and summer sports.[193] This sample size provides a highly representative cross-section of the athlete population competing across both games.

Prevalence of PI medication use between games

The prevalence of PI medication use by athletes varied between the summer and winter games as shown in Table 23. In Beijing, 487 of 1663 athletes (29.3%, 95% CI [27.1, 32.0]) reported using PI medications. In Tokyo, the prevalence was significantly higher, with 1771 of 4492 athletes (39.4%, 95% CI [38.0, 41.0]) reporting PI medication use ($p<0.001$). Of the study population of 6155 athletes across both games, the overall prevalence of PI medication use was 36.7% (95% CI [35.5, 37.9]).

Table 23 Overall prevalence (95% CI) of PI medication use by games

Games	Total athletes	Athletes taking PI medications	Prevalence	95% CI
Tokyo	4492	1771	39.4%	38.0, 41.0
Beijing	1663	487	29.3%	27.1, 32.0
Tokyo + Beijing	6155	2258	36.7%	35.5, 37.9

p<0.001 (Note: Chi-square test was used to determine the statistical significance.)

Prevalence of use of PI medications by OPF class, and route of administration

The prevalence of PI medication use varied greatly across different OPF classes and routes of administration, as presented in Table 24. Oral NSAIDs were the most used medication, with 25.6% of athletes reporting use, followed by oral non-opioid analgesics with a prevalence of 9.8%. Oral COX-2 inhibitors and injectable local anaesthetics were next commonly used, but with a much lower prevalence of 2.8% and 2.3%, respectively.

In contrast, some of the least prevalent medication categories included injectable or inhaled general anaesthetics, injectable non-opioids and COX-2 inhibitors, and rectal non-opioids, with a prevalence of only 0.02%.

The oral route of administration was the most common for NSAIDs, COX-2 inhibitors, opioid and non-opioid analgesics, medicines for neuropathic pain, benzodiazepines, and skeletal muscle relaxants. Injection was the most common route for local anaesthetics and corticosteroids. Table 24 presents a comprehensive overview of the prevalence of PI medication use across different OPF classes and routes of administration.

Table 24 Prevalence of PI medication use by athletes per OPF class and route

OPF Class	Route of Administration	Number of Athletes (n=6155)	Prevalence
01.1.1 NSAID	Injection	62	1.01%
	Oral	1578	25.64%
	Rectal	5	0.08%
	Topical	121	1.97%
	Transdermal	49	0.80%
01.1.2 COX-2 inhibitor	Injection	1	0.02%
	Oral	172	2.79%
01.1.3 Non-opioid analgesic	Injection	1	0.02%
	Oral	603	9.80%
	Rectal	1	0.02%
01.2 Opioid analgesics	Injection	7	0.11%
	Intranasal	1	0.02%
	Oral	59	0.96%
	Transdermal	1	0.02%
01.3 Medicines for neuropathic pain	Oral	16	0.26%
01.4 Corticosteroids for intra-articular use	Injection	103	1.67%
01.5 Local anaesthetics	Injection	144	2.34%
	Topical	23	0.37%
	Transdermal	5	0.08%
01.5.1 Local anaesthetics + vasoconstrictor	Injection	7	0.11%
02.1 Corticosteroids for oral use	Oral	7	0.11%
03.1 Benzodiazepines	Injection	2	0.03%
	Oral	101	1.64%
03.2 Skeletal muscle relaxants	Injection	6	0.10%
	Oral	76	1.23%
	Topical	1	0.02%
10.9 Massage and physical therapy preparations	Topical	10	0.16%
	Transdermal	1	0.02%
23.1.2 General anaesthetics with analgesia	Inhalation	1	0.02%
	Injection	1	0.02%

Prevalence of PI use by sex

The prevalence of PI medication use varied between male and female athletes as shown in Table 25. Among the athletes in the sample population, female athletes had a higher prevalence of PI medication use (44.1%, 95% CI [42.3, 46.0]), compared to male athletes (30.0%, 95% CI [28.4, 31.6]). The difference in prevalence between sex was statistically significant ($p<0.001$) and indicates that female athletes were more likely to use PI medications than male athletes.

Table 25 Prevalence (95% CI) of PI use by sex

Sex	Total athletes (n=6,155)	Athletes taking PI medications (n=2,258)	Prevalence	95% CI
Female	2,842	1,254	44.1%	42.3, 46.0
Male	3,255	976	30.0%	28.4, 31.6

p<0.001 (Note: Chi-square test was used to determine the statistical significance.)

There were notable differences between male and female athletes in terms of prevalence of PI medication use for some pharmacological classes, with the largest differences observed for NSAIDs and the non-opioid classes. Female athletes had a higher prevalence of NSAID use than male athletes, with 33.4% (95% CI [30.4, 36.5]) of female athletes reporting use compared to 26% (95% CI [24.5, 27.5]) of male athletes (p<0.001). The use of non-opioid analgesics was also more prevalent among female athletes, with 13.3% (95% CI [12.1, 14.6]) of female athletes reporting use compared to 7.8% (95% CI [6.9, 8.8]) of male athletes (p<0.001).

Table 26 Prevalence of PI medication use per OPF class and sex

OPF Class	All (n=6155)	Overall Prevalence	Female (n=2842)	Female Prevalence	Male (n=3255)	Male Prevalence
01.1.1 NSAID	1681	27%	950	33.4%	731	26%
01.1.2 COX-2 inhibitor	169	3%	101	3.6%	68	2.4%
01.1.3 Non-opioid analgesic	600	10%	377	13.3%	223	7.8%
01.2 Opioid analgesics	61	1%	28	1.0%	33	1.2%
01.3 Medicines for neuropathic pain	14	0%	10	0.4%	4	0.1%
01.4 Corticosteroids for intra-articular use	102	2%	43	1.5%	59	2.1%
01.5 Local anaesthetics	162	3%	81	2.9%	81	2.9%
01.5.1 Local anaesthetics + vasoconstrictor	6	0%	2	0.1%	4	0.1%
02.1 Corticosteroids for oral use	5	0%	5	0.2%	0	0.0%
03.1 Benzodiazepines	99	2%	61	2.1%	38	1.3%
03.2 Skeletal muscle relaxants	80	1%	38	1.3%	42	1.5%
10.9 Massage and physical therapy preparations	9	0%	6	0.2%	3	0.1%
23.1.2 General anaesthetics with analgesia	0	0%	0	0.0%	0	0.0%

Prevalence of PI medication use by age group

The ages of athletes were provided on prescriptions, doping control forms, and injection declarations, and so the prevalence of PI medication could be determined for different athlete age groups, presented in Table 27. This information is unique to this phase of the overall research as age data was not collected in Phase One of the study at the European Games.

The highest prevalence of PI medication use was found among older athletes aged 30-34 (42.0%, 95% CI [39.4, 44.6]), followed by those aged 35-39 (41.8%, 95% CI [36.5, 47.3]) and 40 and over (39.8%, 95% CI [29.5, 50.8]). Younger athletes generally had a slightly lower prevalence of PI use with the lowest rates among athletes aged 19 and under (27.4%, 95% CI [21.8, 33.6]) and those aged 20-24 (31.7%).

The difference in PI medication use between age groups was statistically significant ($p<0.001$), indicating that older athletes are generally more likely to use PI medications than younger athletes.

Table 27 Prevalence (95% CI) of PI medication use per age group

Age group	Athletes taking PI (n=2258)	Total athletes (n=6155)	PI Prevalence	95% CI
19 and under	65	237	27.4%	21.8, 33.6
20-24	528	1664	31.7%	29.5, 34.0
25-29	898	2423	37.1%	35.2, 39.1
30-34	592	1408	42.0%	39.4, 44.6
35-39	140	335	41.8%	36.5, 47.3
40 and over	35	88	39.8%	29.5, 50.8

$p<0.001$ (Note: Chi-square test was used to determine the statistical significance.)

Prevalence of PI medication use by sport

The prevalence of PI medication use was determined for athletes competing in various sports, with the rates varying widely, as presented in Table 28. Sports with the highest prevalence of PI use (over 50%) included: weightlifting (65.6%, 95% CI [58.2, 72.5]), gymnastics (58.1%, 95% CI [48.9, 66.9]), handball (55.0%, 95% CI [45.7, 64.1]) and volleyball/beach volleyball (54.4%,

95% CI [44.8, 63.8]). The sports with the lowest prevalence of PI use were canoe/kayak (19.4%, 95% CI [13.7, 26.2]).

Table 28 Prevalence (95% CI) of PI medication use by sport

Sport	Athletes using PI drugs	Total athletes	Prevalence	95% CI
Weightlifting	118	180	65.6%	58.2, 72.5
Unknown	11	17	64.7%	38.3, 85.8
Gymnastics	72	124	58.1%	48.9, 66.9
Handball	66	120	55.0%	45.7, 64.1
Volleyball/beach volleyball	62	114	54.4%	44.8, 63.8
Rugby	63	132	47.7%	38.9, 56.6
Field Hockey	67	141	47.5%	39.0, 56.1
Football	61	144	42.4%	34.2, 50.9
Modern Pentathlon	11	26	42.3%	23.4, 63.1
Athletics	364	881	41.3%	38.0, 44.6
Judo	62	156	39.7%	32.0, 48.0
Rowing	83	216	38.4%	31.9, 45.2
Fencing	23	60	38.3%	26.0, 51.9
Baseball/softball	47	124	37.9%	29.3, 47.1
Cycling	99	264	37.5%	31.6, 43.6
Table Tennis	14	38	36.8%	21.8, 54.0
Aquatics	182	499	36.5%	32.3, 40.9
Wrestling	65	183	35.5%	28.6, 42.9
Curling	15	43	34.9%	21.0, 50.9
Badminton	18	53	34.0%	21.6, 48.3
Karate	22	65	33.8%	22.5, 46.6
Sport Climbing	8	24	33.3%	15.6, 55.3
Tennis	16	49	32.7%	20.0, 47.6
Equestrian	10	31	32.3%	16.7, 51.4
Bobsleigh/luge	76	236	32.2%	26.3, 38.6
Sailing	23	74	31.1%	20.8, 42.9
Triathlon	21	68	30.9%	20.3, 43.3
Taekwondo	25	81	30.9%	21.1, 42.2
Shooting	24	79	30.4%	20.6, 41.8
Basketball	37	122	30.3%	22.3, 39.3
Biathlon	42	140	30.0%	22.6, 38.3
Ice Hockey	82	282	29.1%	23.9, 34.8
Skiing/snowboard	187	651	28.7%	25.3, 32.3
Surfing	5	18	27.8%	9.7, 53.5
Skating	81	306	26.5%	21.6, 31.8
Boxing	45	171	26.3%	19.9, 33.6
Rollersports/skateboard	7	27	25.9%	11.1, 46.3
Archery	6	25	24.0%	9.4, 45.1
Golf	5	21	23.8%	8.2, 47.2
Canoe/kayak	33	170	19.4%	13.7, 26.2
Total	**2258**	**6155**	**36.7%**	**35.5, 37.9**

Prevalence of PI medication use by athletes by global region

The prevalence PI medication use among athletes varied across global regions, as shown in Table 29. The highest prevalence of PI use was in athletes from the Pacific region, where over half (52.2%, 95% CI [46.7, 57.6]) of athletes reported using PI medications. South America had the second-highest prevalence rate at 43.4% (95% CI [37.7, 49.3]). The lowest prevalence was in the Asia region, where 28.0% (95% CI [25.1, 31.0]) reported using PI medications. There was a statistically significant difference in the prevalence of PI medication use between these global regions ($p<0.001$).

Among the refugee athletes, 50.0% (95% CI [15.7, 84.3]) reported using PI medications, although the numbers of athletes included in the sample population was small (n=8).

Table 29 Prevalence (95% CI) of PI medication use per global region

Region	Athletes using PI medications	Total athletes	Prevalence (%)	95% CI
North America	400	955	41.9	38.8, 45.1
South America	128	295	43.4	37.7, 49.3
Asia	259	925	28.0	25.1, 31.0
Europe	1106	3116	35.5	33.8, 37.2
Middle East and North Africa	88	220	40.0	33.5, 46.8
Pacific	177	339	52.2	46.7, 57.6
Refugee	4	8	50.0	15.7, 84.3
Sub-Saharan Africa	96	232	41.4	35.0, 48.0

$p<0.001$ (Note: Fisher's exact test was used to determine the statistical significance.)

Comparison between games of actual use of PI medications by athletes

Table 30 shows the actual use of PI medications in each OPF class as a proportion of the total number of unique records for PI medication use. This table was analysed using pairwise comparisons, but any category with a column proportion of zero or one was not used in the comparisons. The tests were adjusted for all pairwise comparisons using the Bonferroni correction to reduce the likelihood of false-positive results.

For all OPF classes (with the exception of corticosteroids for intra-articular use), the comparison shows no significant difference between the actual use of PI medications between Tokyo and Beijing. This supports the generalisability of the results across both games to be able to inform the best selection of a single set of medications that will be relevant to both the Summer and Winter Olympic Games setting.

However, for the corticosteroids for intra-articular use category, the comparison showed a significant difference between their use by athletes at Tokyo compared with Beijing, with a higher proportion of use in Tokyo (3.5%) compared to Beijing (1.4%) ($p < 0.05$).

Table 30 Unique records of actual use of PI medications by OPF class in Beijing and Tokyo

OPF Class	**Beijing unique PI records**	**Tokyo unique PI records**
01.1.1 NSAID	440 (63.1%)	1630 (59.8%)
01.1.2 COX-2 inhibitor	27 (3.9%)	144 (5.3%)
01.1.3 Non-opioid analgesic	129 (18.5%)	475 (17.4%)
01.2 Opioid analgesics	14 (2.0%)	53 (1.9%)
01.3 Medicines for neuropathic pain	3 (0.4%)	12 (0.4%)
01.4 Corticosteroids for intra-articular use	10 (1.4%)	95 (3.5%)*
01.5 Local anaesthetics	32 (4.6%)	153 (5.6%)
01.5.1 Local anaesthetics + vasoconstrictor	3 (0.4%)	3 (0.1%)
02.1 Corticosteroids for oral use	1 (0.1%)	5 (0.2%)
03.1 Benzodiazepines	24 (3.4%)	81 (3.0%)
03.2 Skeletal muscle relaxants	12 (1.7%)	68 (2.5%)
10.9 Massage and physical therapy preparations	2 (0.3%)	7 (0.3%)
23.1.2 General anaesthetics with analgesia	0 (0.0%)[a]	0 (0.0%)[a]
Total unique records	**697 (100.0%)**	**2726 (100.0%)**

*P<0.05; [a] Not used in the comparisons (Note: Fisher's exact test was used to determine the statistical significance.)

4.3.2 Selecting drugs for the revised OPF

The results that follow present the analysis for each separate OPF drug class and route category by considering the relationship between the cumulative percentage of actual drug use by athletes, with the percentage of agreement with the drugs on the existing OPF. Using this approach, a set of drugs that better reflects the actual use of drugs by athletes was recommended for a revised and optimised version of PI medications for the OPF (see Section 4.4 for the final revised list).

The Formulary Medication Match Website was developed and used for this analysis (see Appendix 4).

NSAID: Injections

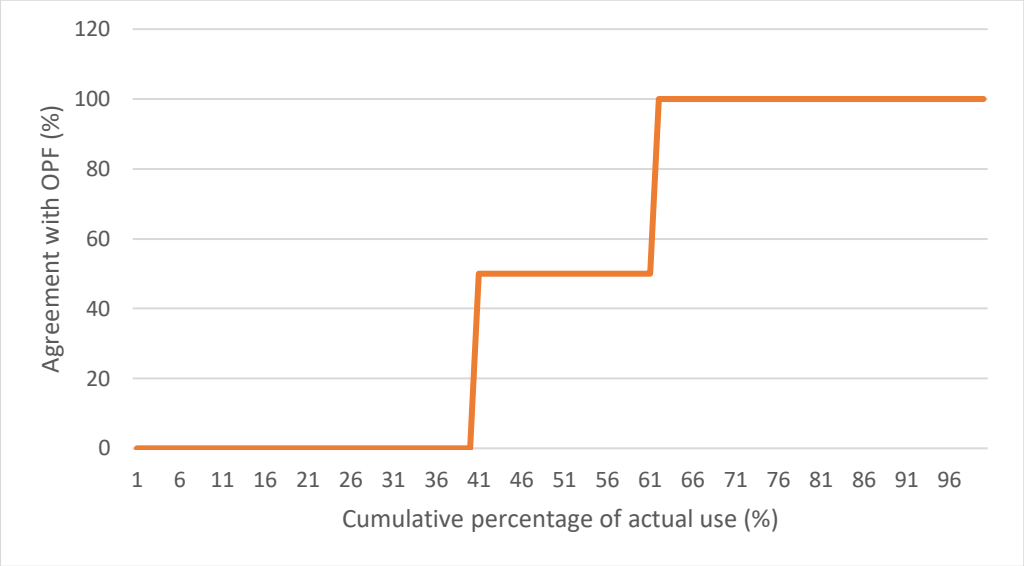


Figure 27 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral opioid analgesics

By examining Figure 27 above, we see that by considering the top 62% of actual-use drugs maximises the percentage of agreement with the OPF up to 100% and hence selected as a cut off threshold. The 62% threshold of actual-use drugs included 2 drugs already listed on the OPF (Table 31).

Table 31 Report from the Formulary Medication Match Website for 62% top actual use for NSAID injections

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Diclofenac Ketorolac		

Of all injectable NSAIDs reported to be used by athletes, 2 drugs were recommended for inclusion on the revised OPF, and 4 drugs were not recommended for inclusion, based on the cut-off criteria and rules for inclusion (Table 32).

Table 32 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for NSAID injections

NSAID: Injections				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Diclofenac	26	0.42	41%
Included	Ketorolac	13	0.21	62%
Excluded	Meloxicam	11	0.18	79%
Excluded	Piroxicam	11	0.18	97%
Excluded	Ketoprofen	1	0.02	98%
Excluded	Loxoprofen	1	0.02	100%

NSAID Oral

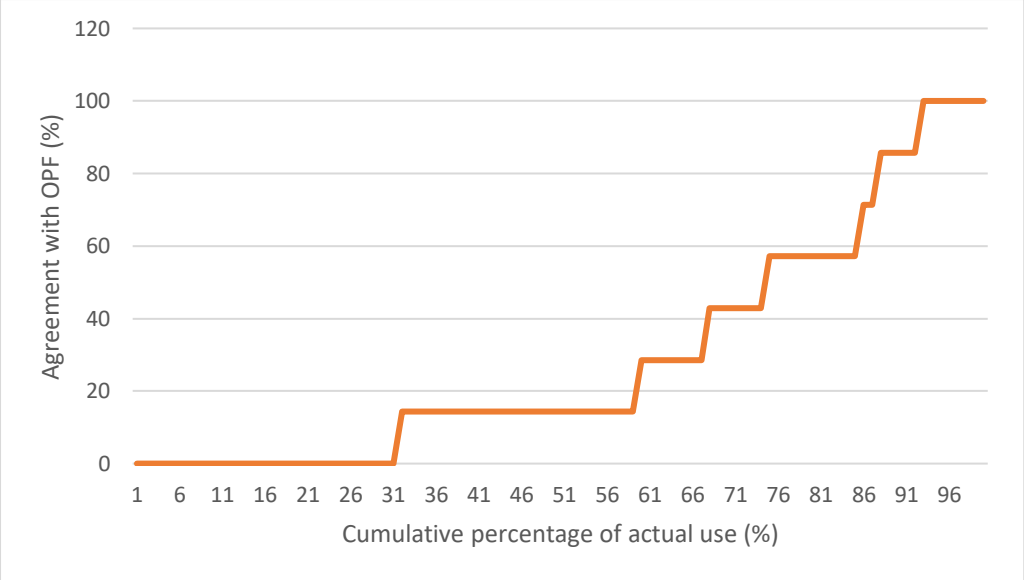


Figure 28 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral NSAIDs

By examining Figure 28 above, we see that by considering the top 93% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 93% of actual-use drugs included 7 drugs already currently listed on the OPF, and 3 drugs that are not currently listed in formulary (Table 33). However, nimesulide and piroxicam cannot be recommended for inclusion due to the risks and safety profile of these drugs. [186] [187] [188]

Table 33 Report from the Formulary Medication Match Website for 93% top actual use for oral NSAIDs

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
Ibuprofen Diclofenac Naproxen Loxoprofen Aspirin Meloxicam Ketorolac	Ketoprofen Nimesulide Piroxicam	

Of all oral NSAIDs reported to be used by athletes, 25 drugs were excluded based on the cut-off criteria and rules for inclusion (see Table 34).

Table 34 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for oral NSAIDs

NSAID: Oral				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Ibuprofen	586	9.52%	32%
Included	Diclofenac	509	8.27%	60%
Included	Naproxen	155	2.52%	68%
Included	Loxoprofen	132	2.14%	75%
Included	Ketoprofen	94	1.53%	80%
Included	Aspirin	93	1.51%	86%
Included	Meloxicam	49	0.80%	88%
Excluded: safety	Nimesulide	42	0.68%	91%
Included	Ketorolac	37	0.60%	93%

Excluded: safety	Piroxicam	17	0.28%	93%
Excluded	Analgesic (non-descript)	15	0.24%	94%
Excluded	Dexketoprofen	15	0.24%	95%
Excluded	Antiinflammatory (non-descript)	12	0.19%	96%
Excluded	Aceclofenac	9	0.15%	96%
Excluded	Indomethacin	9	0.15%	97%
Excluded	NSAID (non-descript)	9	0.15%	97%
Excluded	Flurbiprofen	8	0.13%	98%
Excluded	Naproxen + Esomeprazole	8	0.13%	98%
Excluded	Aspirin + Paracetamol	6	0.10%	98%
Excluded	Mefenamic acid	6	0.10%	99%
Excluded	Aceclofenac + Paracetamol	3	0.05%	99%
Excluded	Acemetacin	3	0.05%	99%
Excluded	Dexibuprofen	3	0.05%	99%
Excluded	Ibuprofen + Paracetamol	3	0.05%	99%
Excluded	Diclofenac + Misoprostol	2	0.03%	100%
Excluded	Etodolac	2	0.03%	100%
Excluded	Aminophenazone	1	0.02%	100%
Excluded	Diclofenac + Carisoprodol	1	0.02%	100%
Excluded	Diclofenac + Paracetamol	1	0.02%	100%
Excluded	Diclofenac + Paracetamol + Carisoprodol	1	0.02%	100%
Excluded	Nabumatone	1	0.02%	100%
Excluded	Propyphenazone + Paracetamol	1	0.02%	100%
Excluded	Tiaprofenic acid	1	0.02%	100%

NSAID: Rectal

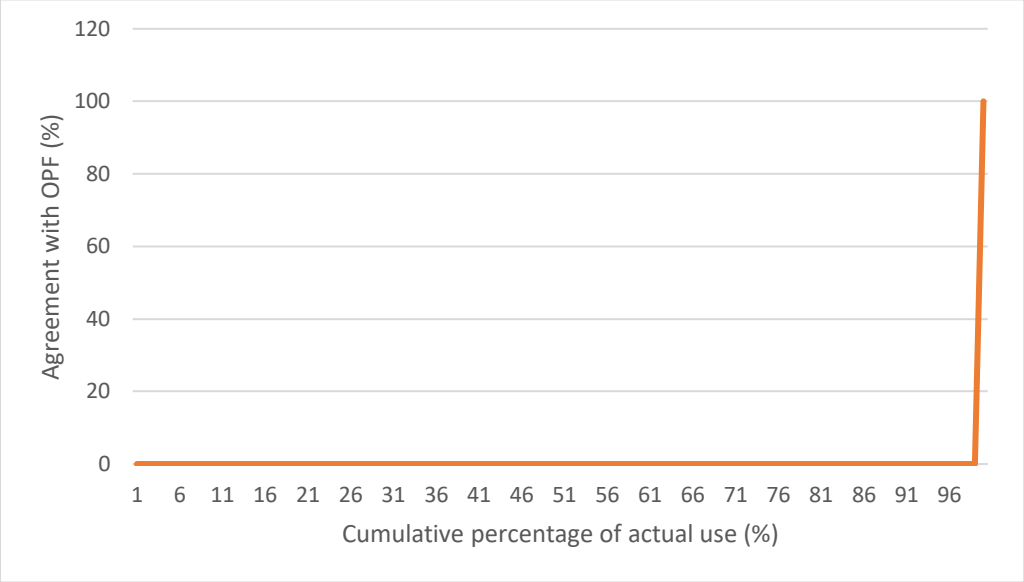


Figure 29 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for rectal NSAIDs

By examining Figure 29 above, we see that by considering the top 100% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 100% of actual-use drugs included 1 drug already currently listed on the OPF (Table 35).

Table 35 Report from the Formulary Medication Match Website for 100% top actual use for rectal NSAIDs

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Diclofenac		

There was only 1 rectal NSAID used by athletes, which is recommended for inclusion.

Table 36 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for Rectal NSAIDs used by athletes, identified for inclusion or exclusion on the revised OPF

NSAID: Rectal				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Diclofenac	4	0.06%	100%

NSAID: Topical

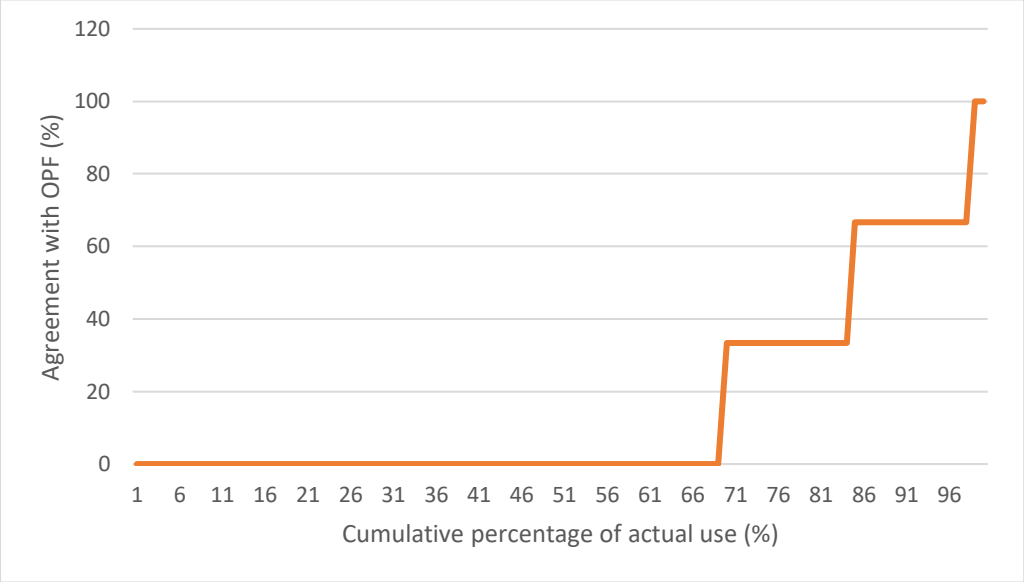


Figure 30 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for topical NSAIDs

By examining Figure 30 above, we see that by considering the top 99% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 99% of actual-use drugs included 3 drugs already currently listed on the OPF, and 6 drugs that are not currently listed in formulary (Table 37). Based on prevalence of actual use, 7 drugs cannot be recommended to be included on the revised OPF since the actual use was both <0.2%, and an alternative in the same clinical class and route category is recommended for inclusion.

Table 37 Report from the Formulary Medication Match Website for 99% top actual use for topical NSAIDs

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Diclofenac Ibuprofen Naproxen	Flurbiprofen Ketoprofen Loxoprofen Piroxicam Dexketoprofen Etofenamate	

Of all 10 topical NSAIDs reported to be used by athletes, 2 drugs were recommended for inclusion on the revised OPF.

Table 38 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for topical NSAIDs

NSAID: Topical				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Diclofenac	85	1.38%	70
Included	Ibuprofen	18	0.29%	85
Excluded	Flurbiprofen	5	0.08%	89
Excluded	Ketoprofen	5	0.08%	93
Excluded	Loxoprofen	2	0.03%	95
Excluded	Piroxicam	2	0.03%	97
Excluded	Dexketoprofen	1	0.02%	98
Excluded	Etofenamate	1	0.02%	98
Excluded	Naproxen	1	0.02%	99
Excluded	Phenylbutazone	1	0.02%	100

NSAID: Transdermal

None of the drugs used by athletes are currently listed on the OPF (Table 39).

Transdermal NSAID preparations were used by 0.78% of athletes (Table 40). Given that this prevalence is <0.2%, and there is no existing alternative in this class and route of administration, one example of a transdermal NSAID is recommended for inclusion. Given the equal prevalence of athlete use, and similar clinical indication, the selection for this category was based on the rate of countries importing these products as stock across the Beijing and Tokyo Olympics. Of all 35 countries importing transdermal NSAIDS, 68%

imported diclofenac patches, compared with 11.4% importing flurbiprofen patches (see Table 85). As such, diclofenac is recommended for inclusion on the revised OPF.

Table 39 Report from the Formulary Medication Match Website for 100% top actual use for transdermal NSAIDs

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
	Diclofenac Flurbiprofen	

Of all 2 transdermal NSAIDs reported to be used by athletes, 1 preparation is recommended for inclusion on the revised OPF (see Table 40).

Table 40 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for transdermal NSAIDs

NSAID: Transdermal				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Diclofenac	24	0.39%	50%
Excluded	Flurbiprofen	24	0.39%	50%

COX-2 Inhibitors: Injection

There were no injectable COX-2 inhibitors used by athletes, and as such they are not recommended for inclusion. These drugs are not currently listed on the OPF.

COX-2 Inhibitors: Oral

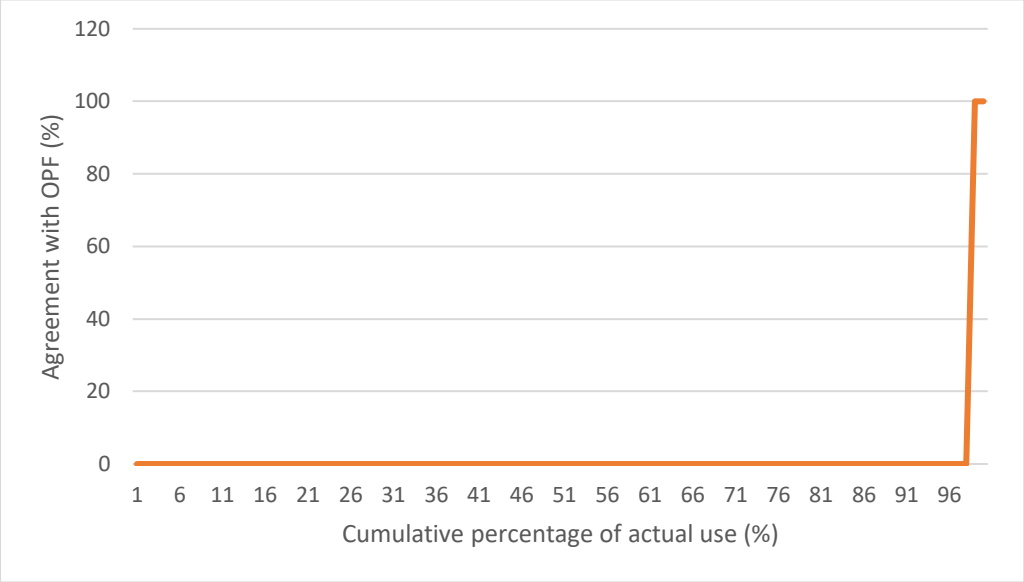


Figure 31 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral COX-2 inhibitors

By examining Figure 31 above, we see that by considering the top 99% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 99% of actual-use drugs included 1 drug already currently listed on the OPF, and 1 drug that is not currently listed in formulary (Table 41).

Table 41 Report from the Formulary Medication Match Website for 99% top actual use for oral COX-2 inhibitors

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Celecoxib	Etoricoxib	

Of all 3 drugs in this class reported to be used by athletes, only 1 drug (parecoxib) was excluded based on the cut-off criteria and rules for inclusion (Table 42).

Table 42 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for oral COX-2 inhibitors

COX-2 Inhibitors: Oral				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Etoricoxib	95	1.54%	56%
Included	Celecoxib	75	1.22%	99%
Excluded	Parecoxib	1	0.02%	100%

Non-opioid analgesics: Injection

There were no non-opioid analgesic injections used by athletes, and as such they are not recommended for inclusion. These drugs are not currently listed on the OPF.

Non-opioid analgesics: Oral

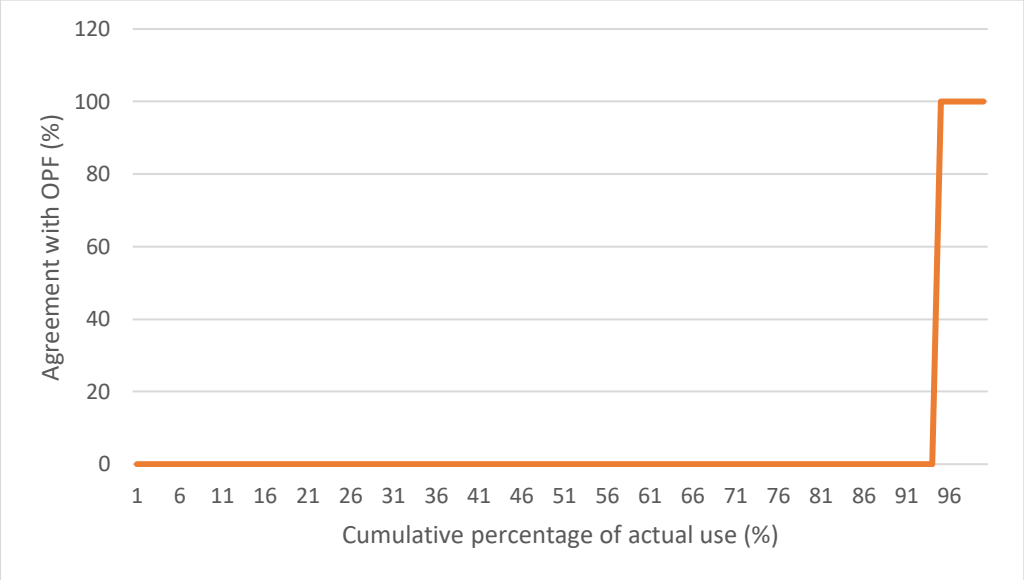


Figure 32 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral non-opioid analgesics

By examining Figure 32 above, we see that by considering the top 95% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 95% of actual-use drugs included 1 drug already currently listed on the OPF (Table 43).

Table 43 Report from the Formulary Medication Match Website for 95% top actual use for oral non-opioid analgesics

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Paracetamol		

Of all oral non-opioids reported to be used by athletes, 1 drug was excluded based on both the cut-off criteria and also safety concerns (see Table 44). It should be noted that though metamizole was not recommended for inclusion, it should be excluded at all times, and never used as an alternative, due to the safety profile of this drug.[188 190 194] Given the fact that 0.54% (n=33) athletes were documented to be using this drug, a special warning in the revised formulary is warranted to actively advise against its use at all times.

Table 44 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for oral non-opioid analgesic drugs

Non-opioid analgesics: Oral				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Paracetamol	571	9.28%	95%
Excluded	Metamizole	33	0.54%	100%

Non-opioid analgesics: Rectal

There were no rectal non-opioid analgesics reported to be used by athletes. There is 1 example of these drugs (paracetamol) currently listed on the OPF (Table 45).

Table 45 Report from the Formulary Medication Match Website for 1% top actual use for rectal non-opioid analgesics

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
		Paracetamol

Rectal paracetamol is therefore not recommended for inclusion on the revised OPF based on lack of actual use (Table 46).

Table 46 Rectal non-opioid analgesics used by athletes, identified for inclusion or exclusion on the revised OPF

Non-opioid analgesics: Rectal				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Excluded	Paracetamol	0	0.00%	0.00%

Opioid analgesics: Injection

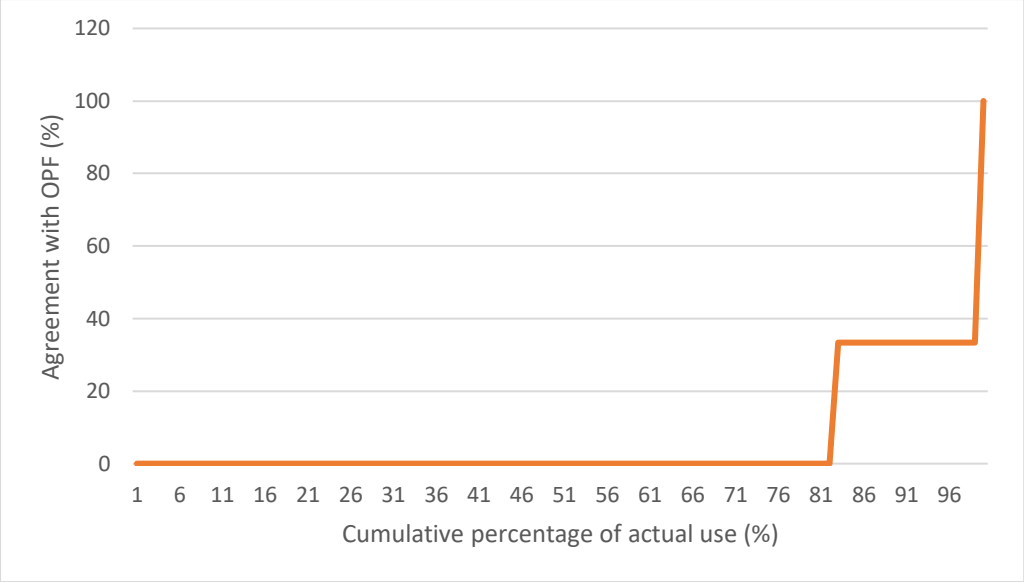


Figure 33 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for injectable opioid analgesics

By examining Figure 33 above, we see that by considering the top 100% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 100% of actual-use drugs included 2 drugs already listed on the OPF, and 1 drug that was listed, but not used by athletes (Table 47).

Table 47 Report from the Formulary Medication Match Website for 100% top actual use for injectable opioid analgesics

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Tramadol Fentanyl		Morphine

If a drug was rarely used or has no documented usage, but it essential for immediate treatment for certain clinical conditions that may present in the games setting, including life-threatening conditions, then these are warranted for inclusion. Morphine is a drug that meets this requirement, and is routinely kept at sporting venues, in emergency rooms and ambulance for use in emergencies. In addition, the data used for this analysis does not include the drug usage reports from emergency services in Tokyo and Beijing, so does not provide a comprehensive account of drugs used in emergency settings. As such, clinical guidelines for use of drugs for emergency care must prevail in terms of selection of emergency drugs for the formulary, therefore morphine injection should be recommended for continued inclusion on the formulary. Three injectable opioid analgesic drugs are recommended for inclusion on the revised OPF (Table 48).

Table 48 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for injectable opioid analgesics drugs

Opioid analgesics: Injection				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Tramadol	5	0.08%	83%
Included	Fentanyl	1	0.02%	100%
Included	Morphine	0	0.00%	100%

Opioid analgesics: Intranasal

There were no intranasal opioid analgesic drugs used by athletes, and as such they are not recommended for inclusion. These drugs are not currently listed on the OPF.

Opioid analgesics: Oral

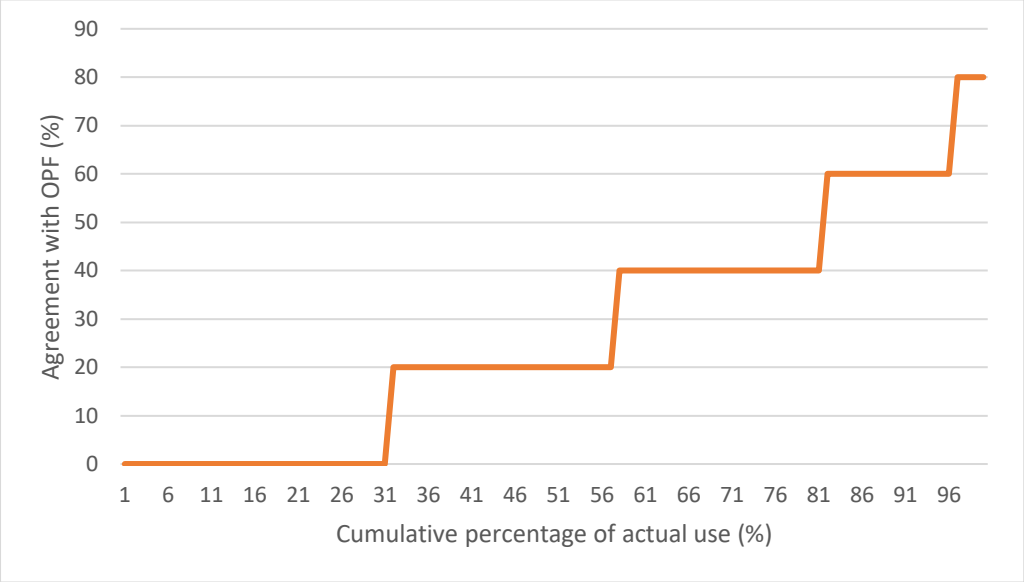


Figure 34 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral opioid analgesics

By examining Figure 34 above, we see that by considering the top 97% of actual-use drugs maximises the percentage of agreement with the OPF up to 80%. The top 97% of actual-use drugs included 4 drugs already currently listed on the OPF, and 3 drugs that are not currently listed in formulary (Table 49). Based on prevalence of actual use, 4 drugs cannot be recommended to be included on the revised OPF since the actual use was both <0.2%, and an alternative in the same clinical class and route category is recommended for inclusion.

Table 49 Report from the Formulary Medication Match Website for 97% top actual use for oral opioid analgesics

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
Codeine + Paracetamol Codeine Tramadol Dihydrocodeine	Tramadol + Paracetamol Codeine + Paracetamol + Aspirin Codeine + Paracetamol + Ibuprofen	Hydromorphone

Of all 9 preparations in this class reported to be used by athletes, 3 were recommended for inclusion on the revised OPF (see Table 50). It is important to note that for 3 combination products not included, the drugs (codeine and tramadol) will still be available as single-agent preparations on the revised OPF.

Table 50 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for oral opioid analgesic drugs

Opioid analgesics: Oral				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Codeine + Paracetamol	19	0.31%	32%
Included	Codeine	16	0.26%	58%
Included	Tramadol	14	0.23%	82%
Excluded	Tramadol + Paracetamol	6	0.10%	92%
Excluded	Codeine + Paracetamol + Aspirin	1	0.02%	93%
Excluded	Codeine + Paracetamol + Ibuprofen	1	0.02%	95%
Excluded	Dihydrocodeine	1	0.02%	97%
Excluded	Dihydrocodeine + Paracetamol	1	0.02%	98%
Excluded	Tramadol + Dexketoprofen	1	0.02%	100%
Excluded	Hydromorphone	0	0.00%	

Opioid analgesics: Transdermal

There were no transdermal opioid analgesics used by athletes, and as such they are not recommended for inclusion. These drugs are not currently listed on the OPF.

Medicines for neuropathic pain: Oral

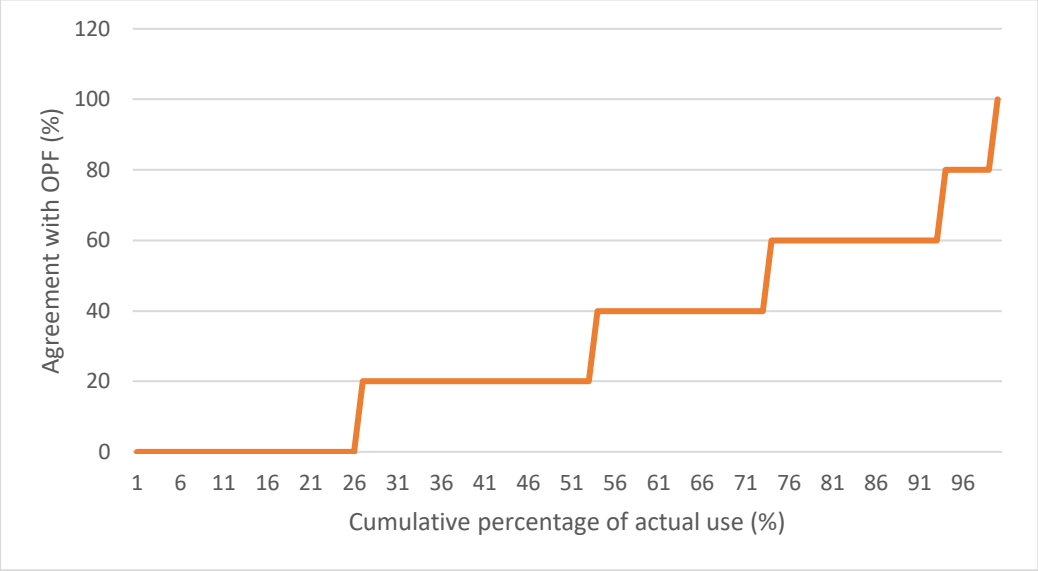


Figure 35 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral medicines for neuropathic pain

By examining Figure 35 above, we see that by considering the top 100% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 100% of actual-use drugs included 5 drugs already currently listed on the OPF.

Table 51 Report from the Formulary Medication Match Website for 100% top actual use for oral medicines for neuropathic pain

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Amitriptyline Nortriptyline Duloxetine Gabapentin Pregabalin		

There were two examples of tricyclic antidepressant drugs (amitriptyline and nortriptyline), and two examples of anticonvulsant drugs (gabapentin and pregabalin). Based on prevalence of actual use, one of each group can be excluded since the actual use was both <0.2%, and an alternative in the same clinical class and route category is recommended for inclusion.

For the anticonvulsant drugs, gabapentin had the highest prevalence of use in athletes so is recommended as the representative anticonvulsant drug in this category.

For the tricyclic drugs, given the equal prevalence of athlete use, and similar clinical indication, the selection for this category was based on the rate of countries importing these products as stock across the Beijing and Tokyo Olympics. Of all 5 countries importing medications for neuropathic pain, 2 (40%) imported amitriptyline, compared with no countries importing nortriptyline (see Table 85). As such, amitriptyline is recommended as the representative example for inclusion on the revised OPF.

Duloxetine is the only example of a serotonin-norepinephrine reuptake inhibitor (SNRI) drug, and so can be recommended for inclusion without further consideration.
Of the 5 medicines for on the OPF category of treatment for neuropathic pain, 3 drugs were recommended for inclusion based on the cut-off criteria and rules for inclusion (see Table 52).

Table 52 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for medicines for neuropathic pain

Medicines for neuropathic pain: Oral				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Amitriptyline	4	0.06%	27%
Excluded	Nortriptyline	4	0.06%	54%
Included	Duloxetine	3	0.05%	74%
Included	Gabapentin	3	0.05%	94%
Excluded	Pregabalin	1	0.02%	100%

Corticosteroids for intra-articular use: Injection

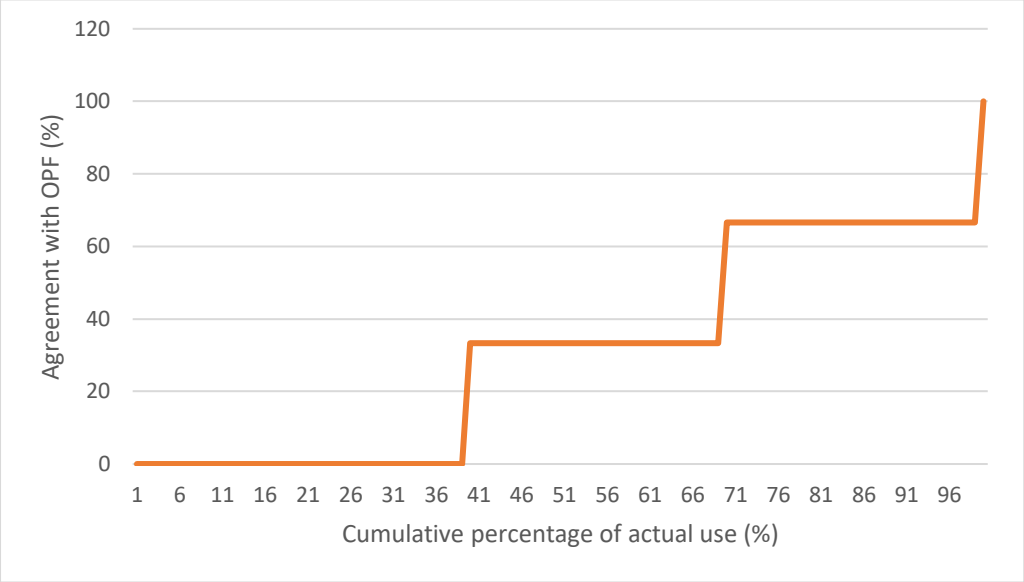


Figure 36 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for injectable corticosteroids

By examining Figure 36 above, we see that by considering the top 100% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 100% of actual-use drugs included 3 drugs already currently listed on the OPF, and 4 drugs that are not currently listed in formulary (Table 53).

Table 53 Report from the Formulary Medication Match Website for 100% top actual use for injectable corticosteroids

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Triamcinolone Dexamethasone Hydrocortisone	Betamethasone Methylprednisolone Prednisolone Cortisone	

Based on prevalence of actual use, 4 drugs cannot be recommended to be included on the revised OPF since the actual use was both <0.2%, and an alternative in the same clinical class and route category is recommended for inclusion.

Of all 7 injectable corticosteroid drugs reported to be used by athletes, 3 drugs were recommended for inclusion on the revised OPF based on the cut-off criteria and rules for inclusion (see Table 54).

Table 54 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for injectable corticosteroids

Corticosteroids for intra-articular use: Injection				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Triamcinolone	42	0.68%	40%
Included	Dexamethasone	32	0.52%	70%
Included	Betamethasone	16	0.26%	86%
Excluded	Methylprednisolone	6	0.10%	91%
Excluded	Prednisolone	4	0.06%	95%
Excluded	Cortisone	3	0.05%	98%
Excluded	Hydrocortisone	2	0.03%	100%

Local anaesthetics: Injection

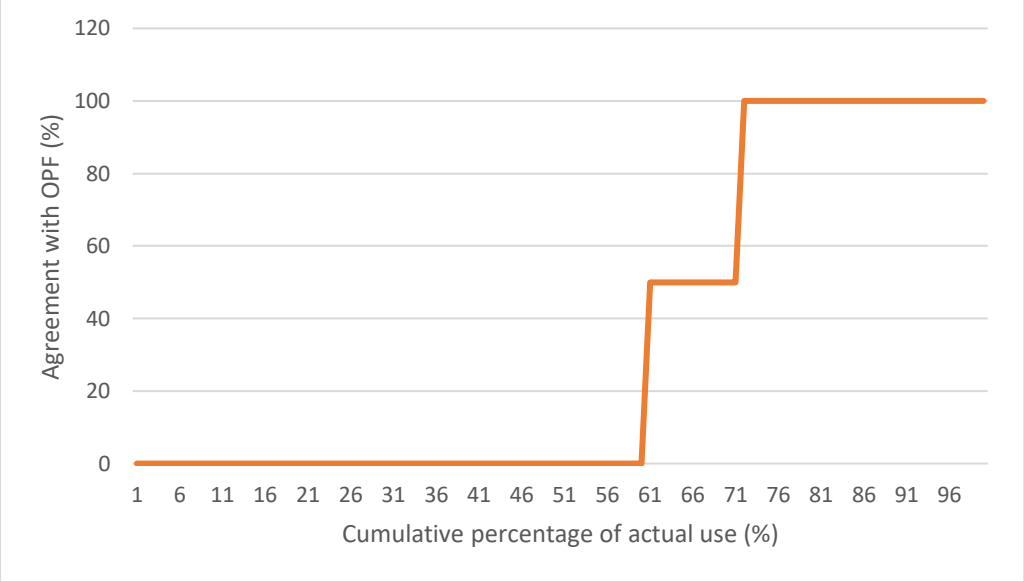


Figure 37 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for injectable local anaesthetics

By examining Figure 37 above, we see that by considering the top 72% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 72% of actual-use drugs included 2 drugs already currently listed on the OPF (Table 55).

Table 55 Report from the Formulary Medication Match Website for 72% top actual use for injectable local anaesthetics

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
Lidocaine Bupivacaine		

Of all 8 injectable anaesthetic drugs reported to be used by athletes, 2 drugs were included based on the cut-off criteria and rules for inclusion (see Table 56).

Table 56 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for injectable local anaesthetics

Local anaesthetics: Injection				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Lidocaine	96	1.56%	61%
Included	Bupivacaine	17	0.28%	72%
Excluded	Procaine	17	0.28%	82%
Excluded	Mepivacaine	12	0.19%	90%
Excluded	Ropivacaine	10	0.16%	96%
Excluded	Anaesthetic (non-descript)	2	0.03%	97%
Excluded	Mesocaine	2	0.03%	99%
Excluded	Prilocaine	1	0.02%	99%
Excluded	Trimecaine	1	0.02%	100%

Local anaesthetics: Topical

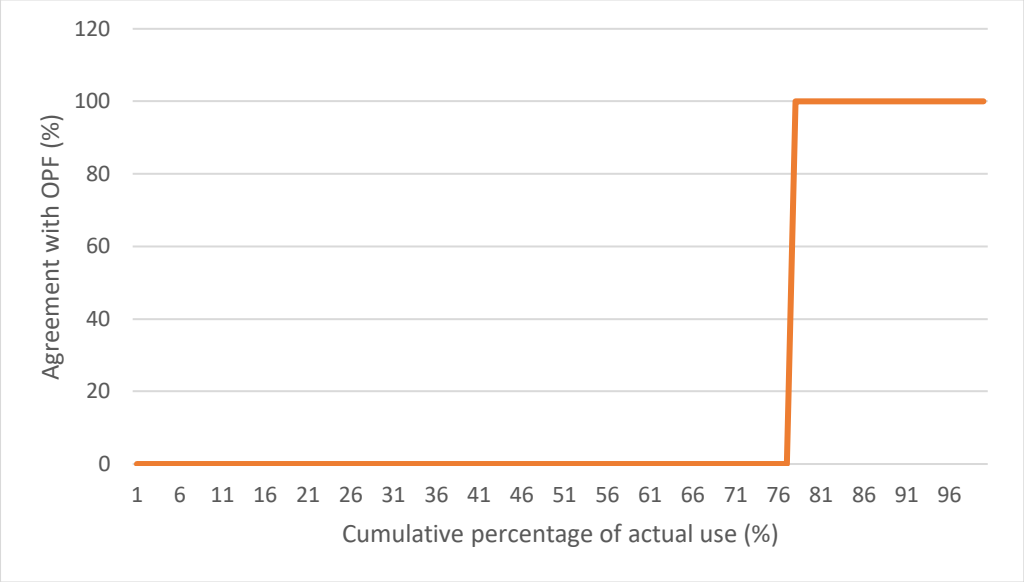


Figure 38 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for topical local anaesthetics

By examining Figure 38 above, we see that by considering the top 78% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 78% of actual-use drugs included 1 drug already currently listed on the OPF (Table 57).

Table 57 Report from the Formulary Medication Match Website for 78% top actual use for topical local anaesthetics

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Lidocaine		

Of all 4 topical anaesthetic preparations reported to be used by athletes, 1 preparation was recommended for inclusion based on the cut-off criteria and rules for inclusion (see Table 58).

Table 58 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for topical local anaesthetics

Local anaesthetics: Topical				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Lidocaine	18	0.29%	78%
Excluded	Articaine	3	0.05%	91%
Excluded	Lidocaine + Chlorhexidine	1	0.02%	96%
Excluded	Lidocaine + Prilocaine	1	0.02%	100%

Local anaesthetics: Transdermal

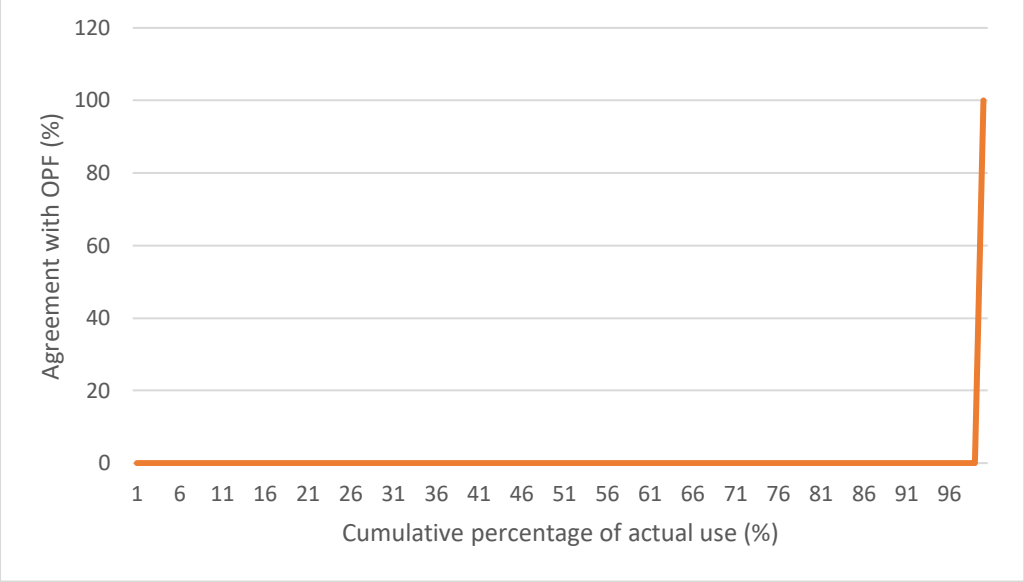


Figure 39 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for transdermal local anaesthetics

By examining Figure 39 above, we see that by considering the top 100% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 100% of actual-use drugs included 1 drug already currently listed on the OPF (Table 59).

Table 59 Report from the Formulary Medication Match Website for 100% top actual use for transdermal local anaesthetics

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Lidocaine		

Lidocaine patches were the only preparation of transdermal anaesthetics reported to be used by athletes and are recommended for continued inclusion on the OPF based on the cut-off criteria and rules for inclusion (see Table 60).

Table 60 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for transdermal local anaesthetics

Local anaesthetics: Transdermal				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Lidocaine	4	0.06%	100%

Local anaesthetics + vasoconstrictor: Injection

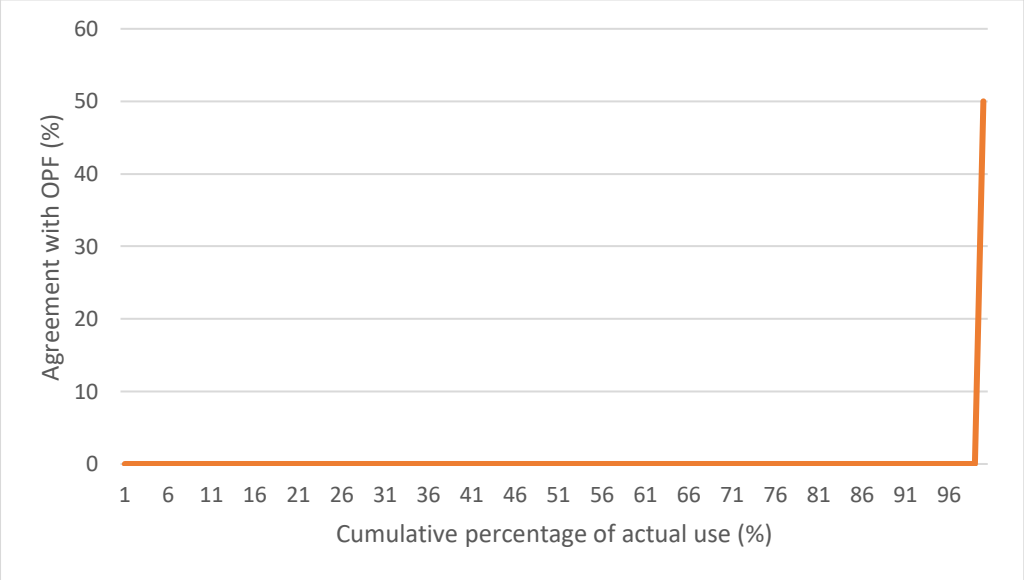


Figure 40 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for injectable local anaesthetics + vasoconstrictor

By examining Figure 40 above, we see that by considering the top 100% of actual-use drugs maximises the percentage of agreement with the OPF up to 50%. The top 100% of actual-use drugs included 1 preparation already currently listed on the OPF, and 1 preparation that was listed but not used by athletes (Table 61).

Table 61 Report from the Formulary Medication Match Website for 100% top actual use for injectable local anaesthetics + vasoconstrictor

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
Lidocaine + Epinephrine		Bupivacaine + Epinephrine

Only lidocaine + epinephrine was reported to be used by athletes, and is the only preparation recommended for continued inclusion on the OPF based on the cut-off criteria and rules for inclusion (see Table 62).

Table 62 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for injectable local anaesthetics + vasoconstrictor preparations

Local anaesthetics + vasoconstrictor: Injection				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Lidocaine + Epinephrine	6	0.10%	100%
Exclude	Bupivacaine + Epinephrine	0	0.00%	

Corticosteroids: Oral

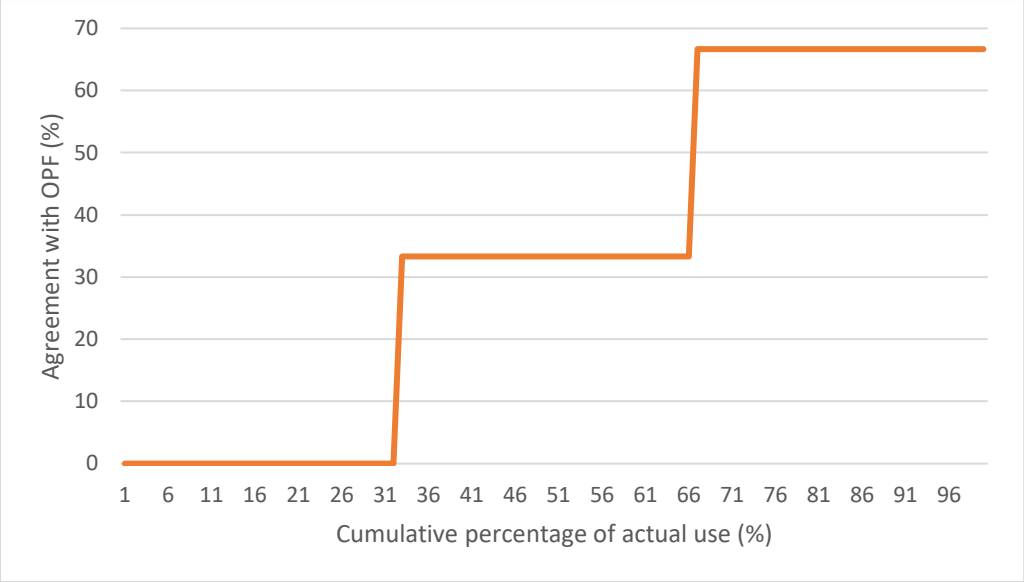


Figure 41 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral corticosteroids

By examining Figure 41 above, we see that by considering the top 67% of actual-use drugs maximises the percentage of agreement with the OPF up to 66%. The top 67% of actual-use drugs included 1 drug already currently listed on the OPF, 3 drugs that are not currently listed in formulary, and 2 that are currently listed but not used by athletes (Table 63).

Table 63 Report from the Formulary Medication Match Website for 67% top actual use for oral corticosteroids

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
Prednisolone	Prednisone Fludrocortisone Triamcinolone	Beclometasone Dexamethasone

There were 4 examples of oral corticosteroid drugs recommended for inclusion, however based on prevalence of actual use, 3 can be excluded since the actual use was both <0.2%, and an alternative in the same clinical class and route category is recommended for inclusion.

Given the equal prevalence of athlete use for prednisolone and prednisone, and similar clinical indication, the selection for this category was based on the rate of countries

importing these products as stock across the Beijing and Tokyo Olympics. Of all 50 countries importing oral corticosteroids, 28 (56%) imported prednisolone, compared with 3 (6%) importing prednisone (see Table 85). As such, prednisolone is recommended as the representative example for inclusion on the revised OPF.

Of all 4 oral corticosteroid drugs reported to be used by athletes, 1 was recommended for inclusion on the revised OPF based on the cut-off criteria and rules for inclusion (see Table 64).

Table 64 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for oral corticosteroids

Corticosteroids: Oral				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Prednisolone	2	0.03%	33%
Excluded	Prednisone	2	0.03%	66%
Excluded	Fludrocortisone	1	0.02%	83%
Excluded	Triamcinolone	1	0.02%	100%
Excluded	Beclometasone	0	0.00%	
Excluded	Dexamethasone	0	0.00%	

Benzodiazepines: Injection

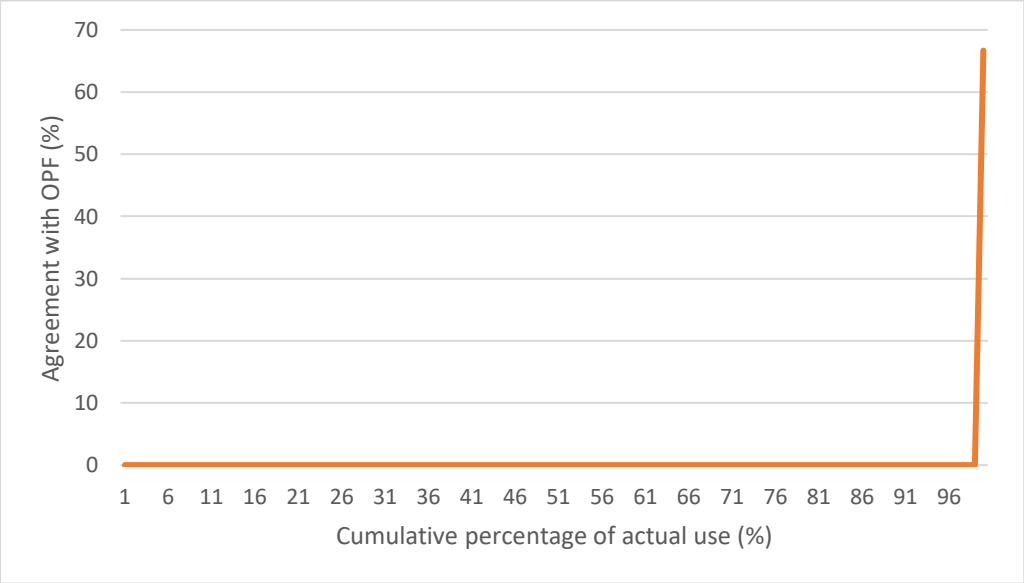


Figure 42 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for injectable benzodiazepines

By examining Figure 42 above, we see that by considering the top 100% of actual-use drugs maximises the percentage of agreement with the OPF up to 66.6%. The top 100% of actual-use drugs included 1 drug already currently listed on the OPF, and 2 drugs that are currently listed but not used by athletes (Table 65).

Table 65 Report from the Formulary Medication Match Website for 100% top actual use for injectable benzodiazepines

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
Midazolam		Diazepam Lorazepam

Of all injectable benzodiazepines reported to be used by athletes, 1 drug was recommended for inclusion based on the cut-off criteria and rules for inclusion (see Table 66).

Table 66 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for injectable benzodiazepines

Benzodiazepines: Injection				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Midazolam	1	0.02%	100%
Excluded	Diazepam	0	0.00%	
Excluded	Lorazepam	0	0.00%	

Benzodiazepines: Oral

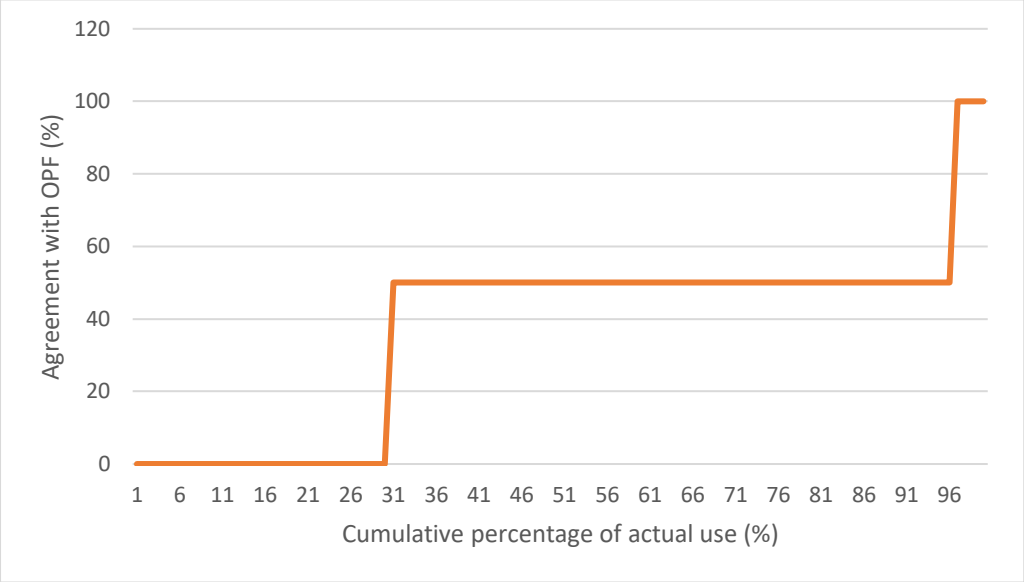


Figure 43 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral benzodiazepines

By examining Figure 43 above, we see that by considering the top 97% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 97% of actual-use drugs included 2 drugs already currently listed on the OPF, and 9 drugs that are not currently listed in formulary (Table 67).

Table 67 Report from the Formulary Medication Match Website for 97% top actual use for oral benzodiazepines

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Diazepam Midazolam	Lorazepam Brotizolam Alprazolam Triazolam Bromazepam Clonazepam Oxazepam Lormetazepam Estazolam	

Based on prevalence of actual use, 7 drugs cannot be recommended to be included on the revised OPF since the actual use was both <0.2%, and an alternative in the same clinical class and route category is recommended for inclusion. Of all 14 oral benzodiazepines reported to be used by athletes, 3 drugs were recommended for inclusion based on the cut-off criteria and rules for inclusion (see Table 68).

Table 68 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for oral benzodiazepines

Benzodiazepines: Oral				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Diazepam	32	0.52%	31%
Included	Lorazepam	17	0.28%	47%
Included	Brotizolam	15	0.24%	62%
Included	Alprazolam	10	0.16%	71%
Excluded	Triazolam	8	0.13%	79%
Excluded	Bromazepam	4	0.06%	83%
Excluded	Clonazepam	4	0.06%	87%
Excluded	Oxazepam	4	0.06%	90%
Excluded	Lormetazepam	3	0.05%	93%
Excluded	Estazolam	2	0.03%	95%
Excluded	Midazolam	2	0.03%	97%
Excluded	Cinolazepam	1	0.02%	98%
Excluded	Etizolam	1	0.02%	99%
Excluded	Phenazepam	1	0.02%	100%

Benzodiazepines: Rectal

There were no rectal benzodiazepines reported to be used by athletes. However, these drugs are currently listed on the OPF (Table 69).

Table 69 Report from the Formulary Medication Match Website for 100% top actual use for rectal benzodiazepines

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
		Diazepam

If a drug is rarely used or has no documented usage, but it essential for immediate treatment for certain clinical conditions that may present in the games setting, including life-threatening conditions, then these are warranted for inclusion. Rectal benzodiazepines are a class of drug that meets this requirement for the treatment of epilepsy and seizures.[187] As such, clinical guidelines for use of drugs for emergency care must prevail in terms of selection of emergency drugs for the formulary, therefore rectal diazepam should remain on the formulary. Rectal diazepam is already listed on the OPF and recommended for continued inclusion due to its role in emergency treatment of epilepsy and seizures.

Table 70 Rectal benzodiazepines used by athletes, identified for inclusion or exclusion on the revised OPF

Benzodiazepines: Rectal				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Diazepam	0	0.00%	

Skeletal muscle relaxants: Injection

There were two injectable skeletal muscle relaxants reported to be used by athletes, but these drugs are not currently listed on the OPF (Table 71).

Table 71 Report from the Formulary Medication Match Website for 100% top actual use for injectable skeletal muscle

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
	Thiocolchicoside Baclofen	

Based on prevalence of actual use, 2 drugs cannot be recommended to be included on the revised OPF since the actual use was both <0.2%, and an alternative in the same clinical class and route category is recommended for inclusion. The alternative drug skeletal muscle relaxant drug is midazolam (described in the injectable benzodiazepine section above). In addition, oral skeletal muscle alternatives are also included (see below).

Of all 2 (non-benzodiazepine) skeletal muscle relaxants reported to be used by athletes, none were recommended for inclusion on the revised OPF based on the cut-off criteria and rules for inclusion (see Table 72).

Table 72 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for injectable skeletal muscle relaxants

Skeletal muscle relaxants: Injection				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Excluded	Thiocolchicoside	3	0.05%	60%
Excluded	Baclofen	2	0.03%	100%

Skeletal muscle relaxants: Oral

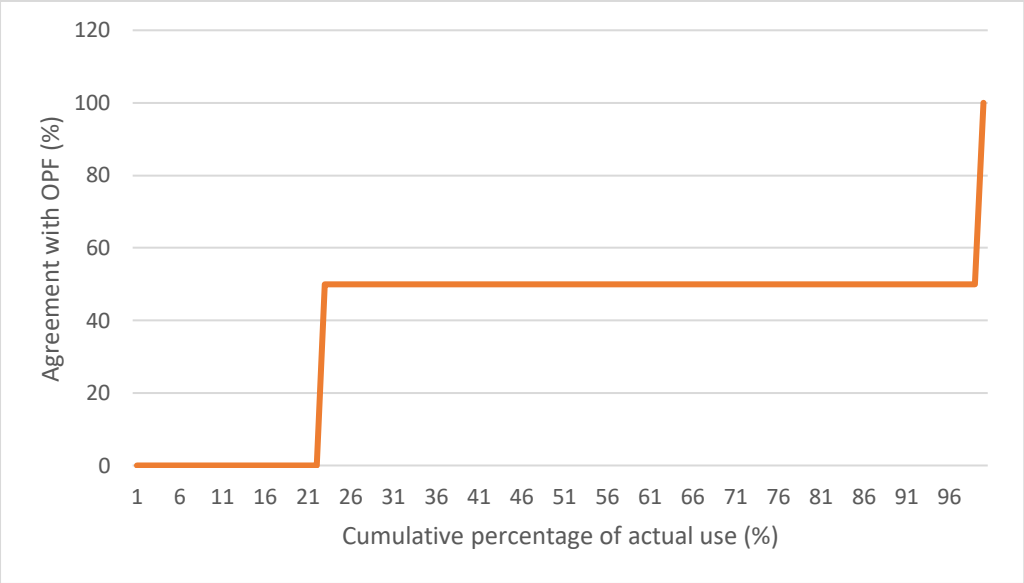


Figure 44 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for oral skeletal muscle relaxants

By examining Figure 44 above, we see that by considering the top 100% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 100% of actual-use drugs included 1 drug already currently listed on the OPF, and 14 preparations that are not currently listed in formulary (Table 73).

Table 73 Report from the Formulary Medication Match Website for 100% top actual use for oral skeletal muscle relaxants

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
Tizanidine	Chlorzoxazone Cyclobenzaprine Thiocolchicoside Methocarbamol + Paracetamol Muscle relaxant (non-descript) Tolperisone Methocarbamol Orphenadrine Metaxalone Pridinol Sirdalud Chlorzoxazone + Paracetamol Chlorzoxazone + Paracetamol + Aceclofenac Chlorzoxazone + Paracetamol + Diclofenac Chlorzoxazone + Paracetamol + Ibuprofen Eperisone Hexafluronium	Baclofen

Based on prevalence of actual use, 15 drugs cannot be recommended to be included on the revised OPF since the actual use was both <0.2%, and an alternative in the same clinical class and route category is recommended for inclusion.

Of all 17 oral skeletal muscle relaxants preparations reported to be used by athletes, 1 drug was recommended for inclusion based on the cut-off criteria and rules for inclusion (see Table 74).

Table 74 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for oral skeletal muscle relaxants

Skeletal muscle relaxants: Oral				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Tizanidine	17	0.28%	23%
Excluded	Chlorzoxazone	8	0.13%	33%
Excluded	Cyclobenzaprine	8	0.13%	44%
Excluded	Thiocolchicoside	6	0.10%	52%
Excluded	Methocarbamol + Paracetamol	5	0.08%	59%
Excluded	Muscle relaxant (non-descript)	5	0.08%	65%
Excluded	Tolperisone	5	0.08%	72%
Excluded	Methocarbamol	4	0.06%	77%
Excluded	Orphenadrine	4	0.06%	83%
Excluded	Metaxalone	3	0.05%	87%
Excluded	Pridinol	2	0.03%	89%
Excluded	Sirdalud	2	0.03%	92%
Excluded	Chlorzoxazone + Paracetamol	1	0.02%	93%
Excluded	Chlorzoxazone + Paracetamol + Aceclofenac	1	0.02%	95%
Excluded	Chlorzoxazone + Paracetamol + Diclofenac	1	0.02%	96%
Excluded	Chlorzoxazone + Paracetamol + Ibuprofen	1	0.02%	97%
Excluded	Eperisone	1	0.02%	99%
Excluded	Hexafluronium	1	0.02%	100%
Excluded	Baclofen	0	0.00%	

Skeletal muscle relaxants: Topical

There were no topical skeletal muscle relaxants used by athletes, and as such they are not recommended for inclusion. These drugs are not currently listed on the OPF.

Massage and physical therapy preparations: Topical

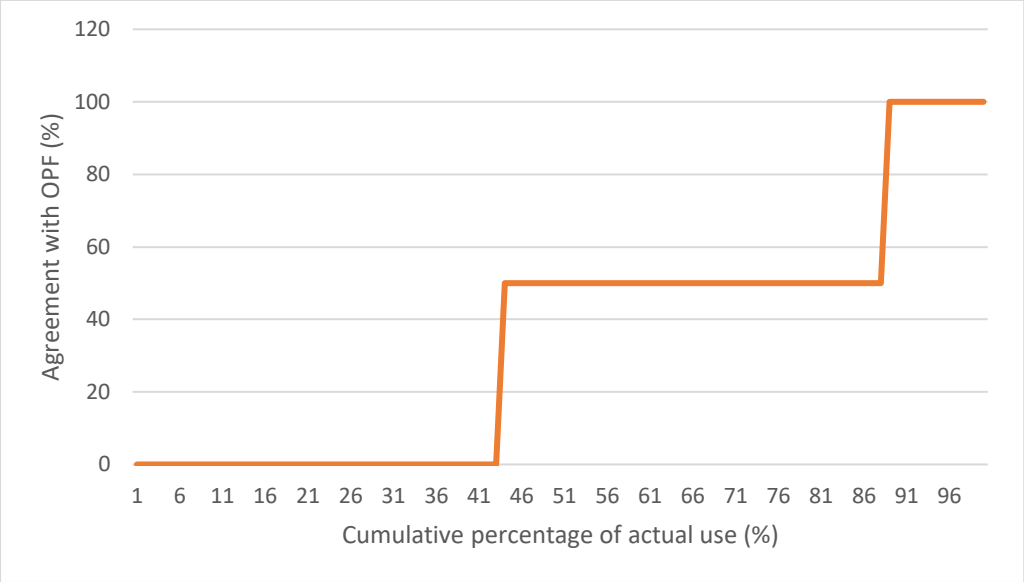


Figure 45 The relationship between cumulative percentage of actual use of drugs, with percentage of agreement with the drugs on the OPF (%) for topical massage and physiotherapy preparations

By examining Figure 45 above, we see that by considering the top 89% of actual-use drugs maximises the percentage of agreement with the OPF up to 100%. The top 89% of actual-use drugs included 2 preparations already currently listed on the OPF, and 3 drugs that are not currently listed in formulary (Table 75).

Table 75 Report from the Formulary Medication Match Website for 89% top actual use for topical massage and physiotherapy preparations

Currently listed in OPF and used by athletes	Not currently listed in OPF but used by athletes	Currently listed in OPF but not used by athletes
Menthol Methylsalicylate + Menthol	Capsaicin Dimetidine Methylsalicylate	

These preparations fall into two main categories: topical cooling agents, and topical warming agents. Menthol is recommended as the representative example of a cooling agent and given that the other topical warming agents had equal prevalence of <0.2%, the team importation data was used to select the example. The most common imported warming preparation was

topical capsaicin, which was imported by 25 of 117 countries (21.4%), and as such was recommended as the representative example of a topical warming agent.

It should be noted that for a sample population of this size, the use of these topical preparations was likely to be vastly under-reported and might be explained by the fact that these were less likely to be declared on doping control forms as they were not considered by athletes to be a medication or supplement.

Of all 6 preparations reported to be used by athletes, 4 drugs were excluded based on the cut-off criteria and rules for inclusion (see Table 76).

Table 76 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for topical massage and physical therapy preparations

Massage and physical therapy preparations: Topical				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Menthol	4	0.06%	44%
Included	Capsaicin	1	0.02%	56%
Excluded	Dimetidine	1	0.02%	67%
Excluded	Methylsalicylate	1	0.02%	78%
Excluded	Methylsalicylate + Menthol	1	0.02%	89%
Excluded	Trolamine salicylate	1	0.02%	100%

General anaesthetics with analgesia: Inhalation

There were no general anaesthetics with analgesia for inhalation reported to be used by athletes. There are two examples of these drugs currently listed on the OPF (Table 77).

Table 77 Report from the Formulary Medication Match Website for 1% top actual use for general anaesthetics with analgesia

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
		Methoxyflurane Nitrous oxide + Oxygen

There is no documented usage for general anaesthetic drugs for inhalation in the actual-use datasets used for this study, as they do not provide a comprehensive account of drugs used in emergency settings. However, this class of drugs is required for immediate treatment of certain clinical conditions that may present in the emergency setting at the games. As such, clinical guidelines for use of drugs for emergency care must prevail in terms of selection of emergency drugs for the formulary.

Inclusions and exclusions

Both nitrous oxide + oxygen, and methoxyflurane inhalation are recommended for continued inclusion on the OPF based on their use for emergency treatment.

Table 78 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for general anaesthetics with analgesia by inhalation

General anaesthetics with analgesia: Inhalation				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Methoxyflurane	0	0.00%	
Included	Nitrous oxide + Oxygen	0	0.00%	

General anaesthetics with analgesia: Injection

There were no general injectable anaesthetics with analgesia reported to be used by athletes. There is 1 example of these drugs (ketamine) currently listed on the OPF (Table 79).

Table 79 Report from the Formulary Medication Match Website for 1% top actual use for general anaesthetics with analgesia for injection

Currently listed in OPF and used by athletes	**Not currently listed in OPF but used by athletes**	**Currently listed in OPF but not used by athletes**
		Ketamine

Similar to inhaled anaesthetic drugs, there is no documented usage in the actual-use datasets used for this study, as they do not provide a comprehensive account of drugs used in emergency settings. However, this class of drugs is required for immediate treatment of certain clinical conditions that may present in the emergency setting at the games. As such, clinical guidelines for use of drugs for emergency care must again prevail in terms of selection of emergency drugs for the formulary.

Ketamine injection is recommended for continued inclusion on the OPF based on its use for emergency treatment (Table 80).

Table 80 Summary of inclusion or exclusion recommendations for the revised OPF, prevalence of use, and cumulative % of actual-use drugs for general anaesthetics with analgesia

General anaesthetics with analgesia: Injection				
Status	**Drug**	**Frequency (n)**	**Prevalence (%) (6155 athletes)**	**Cumulative (%)**
Included	Ketamine	0	0.00%	

4.4 THE RECOMMENDED REVISED OPTIMISED OPF

The resulting recommended list of PI medications for inclusion on the OPF is shown in Table 81 and contains a total of 48 preparations. The 9 newly added preparations are indicated below in bold.

Table 81 Revised recommended PI medications for inclusion on the OPF

OPF Class	Route	Drug
01.1.1 NSAID	Injection	Diclofenac Ketorolac
	Oral	Aspirin Diclofenac Ibuprofen **Ketoprofen*** Ketorolac Loxoprofen Meloxicam Naproxen
	Rectal	Diclofenac
	Topical	Diclofenac Ibuprofen
	Transdermal	**Diclofenac***
01.1.2 COX-2 inhibitor	Oral	Celecoxib **Etoricoxib***
01.1.3 Non-opioid analgesic	Oral	Paracetamol
01.2 Opioid analgesics	Injection	Fentanyl Morphine Tramadol
	Oral	Codeine Codeine + Paracetamol Tramadol
01.3 Medicines for neuropathic pain	Oral	Duloxetine Gabapentin **Amitriptyline***
01.4 Corticosteroids for intra-articular use	Injection	**Betamethasone*** Dexamethasone Triamcinolone
01.5 Local anaesthetics	Injection	Lidocaine
	Topical	Lidocaine
	Transdermal	Lidocaine
01.5.1 Local anaesthetics + vasoconstrictor	Injection	Lidocaine + Epinephrine
02.1 Corticosteroids for oral use	Oral	Prednisolone
03.1 Benzodiazepines	Injection	Diazepam

	Injection	Midazolam
	Oral	**Alprazolam***
		Brotizolam*
		Diazepam
		Lorazepam
	Rectal	Diazepam
03.2 Skeletal muscle relaxants	Oral	**Chlorzoxazone***
		Tizanidine
10.9 Massage and physical therapy preps	Topical	**Capsaicin***
		Menthol
23.1.2 General anaesthetics with analgesia	Inhalation	Methoxyflurane
		Nitrous oxide + Oxygen
	Injection	Ketamine

*Newly added preparations

DELETED MEDICATIONS

The following table shows the 13 preparations which are recommended for deletion.

Table 82 PI medications recommended for deletion from the OPF

OPF Class	**Route**	**Drug**
01.1.3 Non-opioid analgesic	Rectal	Paracetamol
01.2 Opioid analgesics	Oral	Dihydrocodeine
		Hydromorphone
01.3 Medicines for neuropathic pain	Oral	Nortriptyline
		Pregabalin
01.4 Corticosteroids for intra-articular use	Injection	Hydrocortisone
01.5.1 Local anaesthetics + vasoconstrictor	Injection	Bupivacaine + Epinephrine
02.1 Corticosteroids for oral use	Oral	Beclometasone
		Dexamethasone
03.1 Benzodiazepines	Injection	Lorazepam
	Oral	Midazolam
03.2 Skeletal muscle relaxants	Oral	Baclofen
10.9 Massage and physical therapy preps	Topical	Methylsalicylate + Menthol

Impact of implementation of the revised list in the same population

If the revised list of PI medications was implemented for the same athlete study population (n=6155) across the Tokyo 2020 and Beijing 2022 Olympic Games, it would lead to a 7% improvement in the numbers of athletes taking PI medications who could have their exact

PI medication requirements met by the OPF (n=244). For the original OPF PI list, 2704 of 3423 (79%) of athletes taking PI medications could have their PI medications met by the OPF, compared to the revised OPF PI list where 2948 of 3423 (86%) athletes could have their exact medications met.

4.5 VALIDATING THE REVISED OPF

4.5.1 Results of the team drug importation review

This section describes the results of the review of the lists of medications teams imported into Japan and China for use during the Tokyo 2020 and Beijing 2022 Olympic Games. These results were used to further validate the recommended revised OPF as presented in the previous section.

Over both games, a total of 156 of 205 (76.1%) NOC teams (including the Refugee Olympic Team) imported medications to be used as team stock while in the respective host countries. Teams that did not import any medications were likely to rely solely on the medications available from the athlete village pharmacy while in the host country.

In total, 13,706 athletes, or 96.2% of the total athlete population of both games, were expected to be covered by these imported team medications under the care of their NOC medical teams. In other words, these imported stock medications were what the medical teams of each NOC expected to be potentially needed to treat athletes of their teams while in the host country. These findings demonstrate the widespread applicability of the importation data to the vast majority of athletes across both Games.

Of all unique importation declarations made, there were a total of 1747 declarations made by NOC teams for stock PI medications across both games (Tokyo: n=1248; Beijing n=499). It was these PI medication importation declarations which were used to assess and validate the recommended revised OPF list.

Table 83 Number of athletes in teams importing stock, and total unique PI import declarations

Games	Number of unique PI importation declarations	Number of countries importing medications	Number of athletes in teams importing medications	Total participating NOCs	% NOCs importing medications	Total participating athletes	% athletes covered by imported team medications
Tokyo	1,248	152	10,987	205	74.1%	11,420	96.2%
Beijing	499	57	2,719	82	69.5%	2,834	96.0%
Tokyo + Beijing	1,747	156	13,706	205	76.1%	14,254	96.2%

Comparison between games of imported declarations of PI medications

Table 84 below shows a summary of the importation declarations of PI medications in each OPF class, as a proportion of the total number of unique team importation declarations for PI medications. This table was analysed using pairwise comparisons, but any category with a column proportion of zero or one was not used in the comparisons. The tests were adjusted for all pairwise comparisons using the Bonferroni correction to reduce the likelihood of false-positive results.

There was a significant association between the importation of PI medications in Beijing and Tokyo ($p < 0.05$). But the comparison shows significant differences in the importation of benzodiazepines and massage and physical therapy preparations between the two games. Beijing had a higher proportion of benzodiazepine importation (3.8%) than Tokyo (1.9%). And Tokyo had a higher proportion of massage and physical therapy product importation (8.1%) compared with Beijing (3.8%). There was no difference in the importation of other PI categories between each Games.

These two differences can potentially be explained by the local customs and importation rules in place for each Games. In Japan, benzodiazepines were considered a ''controlled substance'' and so the importation of these drugs was complex, which may have deterred teams from importing them, rather, relying on the athlete village pharmacy to access them if needed.[11] The process for importation of benzodiazepines was much easier in China where just a simple declaration was required.[195] Furthermore, for Japan it was required to declare all ''quasi drugs'', which included any topical preparation (with or without an active drug).[11] As a result,

the declarations for massage and physical therapy products containing non-drug ingredients was likely to have resulted in greater declarations in Tokyo compared with Beijing.

Table 84 Unique team import declarations of PI medications by OPF class in Beijing and Tokyo

OPF class	Beijing	Tokyo
01.1.1 NSAID	216 (43.3%)	581 (46.6%)
01.1.2 COX-2 inhibitor	15 (3.0%)	55 (4.4%)
01.1.3 Non-opioid analgesic	49 (9.8%)	106 (8.5%)
01.2 Opioid analgesics	28 (5.6%)	50 (4.0%)
01.3 Medicines for neuropathic pain	2 (.4%)	3 (.2%)
01.4 Corticosteroids for intra-articular use	48 (9.6%)	90 (7.2%)
01.5 Local anaesthetics	57 (11.4%)	111 (8.9%)
01.5.1 Local anaesthetics + vasoconstrictor	1 (.2%)	0 (0.0%)[a]
02.1 Corticosteroids for oral use	15 (3.0%)	35 (2.8%)
03.1 Benzodiazepines	19 (3.8%)	24 (1.9%)
03.2 Skeletal muscle relaxants	26 (5.2%)	85 (6.8%)
10.9 Massage and physical therapy preparations	19 (3.8%)	101 (8.1%)
23.1.2 General anaesthetics with analgesia	4 (.8%)	7 (.6%)
Total	499 (100.0%)	1248 (100.0%)

P<0.05; [a] Not used in the comparisons

The NOC team drug importation declarations across the Tokyo 2020 and Beijing 2022 Olympic Games were tabulated by OPF class and route of administration, against frequency, prevalence, and cumulative percentage of use within each OPF class and route category. This information was used as a deciding factor in the recommendations for inclusion on the revised OPF in instances where the prevalence of actual use by athletes was equal. These data are presented in the table below showing the NOC team importation declarations by frequency, % of drugs within each OPF class and route category, and prevalence of team importation.

Table 85 NOC team importation declarations by frequency, % of drugs within each OPF class and route category, and prevalence of team importation.

OPF Class	Route	Drug	Countries importing (n=156)	n%	Prevalence
01.1.1 NSAID	**Injection**	Diclofenac	45	41.7%	29%
		Ketorolac	18	16.7%	12%
		Ketoprofen	17	15.7%	11%
		Piroxicam	9	8.3%	6%
		Dexketoprofen	8	7.4%	5%
		Meloxicam	7	6.5%	4%
		Aspirin	3	2.8%	2%
		Lornoxicam	1	.9%	1%
		Loxoprofen	0	0.0%	0%
		Total	108	100.0%	
	Oral	Diclofenac	82	16.7%	53%
		Ibuprofen	77	15.7%	49%
		Aspirin	72	14.6%	46%
		Naproxen	41	8.3%	26%
		Meloxicam	29	5.9%	19%
		Ketoprofen	25	5.1%	16%
		Nimesulide	23	4.7%	15%
		Ketorolac	17	3.5%	11%
		Mefenamic acid	15	3.0%	10%
		Dexketoprofen	14	2.8%	9%
		Aceclofenac	12	2.4%	8%
		Piroxicam	12	2.4%	8%
		Indomethacin	10	2.0%	6%
		Flurbiprofen	8	1.6%	5%
		Lornoxicam	8	1.6%	5%
		Aspirin + Paracetamol	7	1.4%	4%
		Naproxen + Esomeprazole	5	1.0%	3%
		Dexibuprofen	4	.8%	3%
		Diclofenac + Misoprostol	4	.8%	3%
		Tenoxicam	4	.8%	3%
		Acemetacin	3	.6%	2%
		Ibuprofen + Paracetamol	3	.6%	2%
		Loxoprofen	3	.6%	2%
		Propyphenazone + Paracetamol	3	.6%	2%
		Tiaprofenic acid	2	.4%	1%
		Aceclofenac + Paracetamol	1	.2%	1%
		Diclofenac + Carisoprodol	1	.2%	1%
		Diclofenac + Omeprazole	1	.2%	1%
		Diclofenac + Paracetamol	1	.2%	1%
		Diclofenac + Paracetamol + Carisoprodol	1	.2%	1%
		Etodolac	1	.2%	1%

		Ketoprofen + Paracetamol	1	.2%	1%
		Ketoprofen + Paracetamol + Carisoprodol	1	.2%	1%
		Niflumic acid	1	.2%	1%
		Aminophenazone	0	0.0%	0%
		Analgesic (non-descript)	0	0.0%	0%
		Antiinflammatory (non-descript)	0	0.0%	0%
		Nabumatone	0	0.0%	0%
		NSAID (non-descript)	0	0.0%	0%
		Total	492	100.0%	
	Rectal	Diclofenac	14	66.7%	9%
		Indomethacin	3	14.3%	2%
		Piroxicam	2	9.5%	1%
		Ketoprofen	1	4.8%	1%
		Nimesulide	1	4.8%	1%
		Total	21	100.0%	
	Topical	Diclofenac	75	53.2%	48%
		Ketoprofen	22	15.6%	14%
		Ibuprofen	11	7.8%	7%
		Etofenamate	5	3.5%	3%
		Flurbiprofen	5	3.5%	3%
		Diethylamine salicylate	4	2.8%	3%
		Indomethacin	4	2.8%	3%
		Piroxicam	4	2.8%	3%
		Dexketoprofen	2	1.4%	1%
		Nimesulide	2	1.4%	1%
		Phenylbutazone	2	1.4%	1%
		Aceclofenac	1	.7%	1%
		Etodolac	1	.7%	1%
		Hydroxyethyl salicylate	1	.7%	1%
		Ibuprofen + Menthol	1	.7%	1%
		Ketorolac	1	.7%	1%
		Loxoprofen	0	0.0%	0%
		Naproxen	0	0.0%	0%
		Total	141	100.0%	
	Transdermal	Diclofenac	24	68.6%	15%
		Ketoprofen	5	14.3%	3%
		Flurbiprofen	4	11.4%	3%
		Loxoprofen	1	2.9%	1%
		Piroxicam	1	2.9%	1%
		Total	35	100.0%	
01.1.2 COX-2 inhibitor	**Injection**	Parecoxib	4	100.0%	3%
		Total	4	100.0%	3%
	Oral	Etoricoxib	38	57.6%	24%
		Celecoxib	27	40.9%	17%
		Rofecoxib	1	1.5%	1%
		Parecoxib	0	0.0%	0%
		Total	66	100.0%	

01.1.3 Non-opioid analgesic	**Injection**	Metamizole	25	86.2%	16%
		Paracetamol	3	10.3%	2%
		Nefopam	1	3.4%	1%
		Total	29	100.0%	
	Oral	Paracetamol	94	77.7%	60%
		Metamizole	27	22.3%	17%
		Total	121	100.0%	
	Rectal	Paracetamol	5	100.0%	3%
		Total	5	100.0%	
01.2 Opioid analgesics	**Injection**	Tramadol	10	66.7%	6%
		Morphine	4	26.7%	3%
		Naloxone	1	6.7%	1%
		Fentanyl	0	0.0%	0%
		Total	15	100.0%	
	Intranasal	Fentanyl	1	100.0%	1%
		Total	1	100.0%	
	Oral	Tramadol	28	45.2%	18%
		Tramadol + Paracetamol	11	17.7%	7%
		Codeine	9	14.5%	6%
		Codeine + Paracetamol	7	11.3%	4%
		Dihydrocodeine	3	4.8%	2%
		Codeine + Diclofenac	1	1.6%	1%
		Morphine	1	1.6%	1%
		Tilidine	1	1.6%	1%
		Tilidine + Naloxone	1	1.6%	1%
		Codeine + Paracetamol + Aspirin	0	0.0%	0%
		Codeine + Paracetamol + Ibuprofen	0	0.0%	0%
		Dihydrocodeine + Paracetamol	0	0.0%	0%
		Tramadol + Dexketoprofen	0	0.0%	0%
		Total	62	100.0%	
	Transdermal	Fentanyl	0	0.0%	0%
		Total	0	0.0%	
01.3 Medicines for neuropathic pain	**Oral**	Gabapentin	3	60.0%	2%
		Amitriptyline	2	40.0%	1%
		Duloxetine	0	0.0%	0%
		Nortriptyline	0	0.0%	0%
		Pregabalin	0	0.0%	0%
		Total	5	100.0%	
01.4 Corticosteroids for intra-articular use	**Injection**	Dexamethasone	30	21.7%	19%
		Triamcinolone	30	21.7%	19%
		Betamethasone	28	20.3%	18%
		Methylprednisolone	26	18.8%	17%
		Hydrocortisone	12	8.7%	8%
		Prednisolone	10	7.2%	6%
		Methylprednisolone + Benzocaine	1	.7%	1%
		Methylprednisolone + Lidocaine	1	.7%	1%

		Cortisone	0	0.0%	0%
		Total	138	100.0%	
01.5 Local anaesthetics	**Injection**	Lidocaine	61	58.1%	39%
		Bupivacaine	23	21.9%	15%
		Procaine	8	7.6%	5%
		Ropivacaine	8	7.6%	5%
		Mepivacaine	4	3.8%	3%
		Levobupivacaine	1	1.0%	1%
		Anaesthetic (non-descript)	0	0.0%	0%
		Mesocaine	0	0.0%	0%
		Prilocaine	0	0.0%	0%
		Trimecaine	0	0.0%	0%
		Total	105	100.0%	
	Topical	Lidocaine	28	62.2%	18%
		Lidocaine + Prilocaine	11	24.4%	7%
		Benzocaine	4	8.9%	3%
		Dibucaine	1	2.2%	1%
		Procaine	1	2.2%	1%
		Articaine	0	0.0%	0%
		Lidocaine + Chlorhexidine	0	0.0%	0%
		Total	45	100.0%	
	Transdermal	Lidocaine	14	77.8%	9%
		Lidocaine + Menthol	2	11.1%	1%
		Lidocaine + Prilocaine	2	11.1%	1%
		Total	18	100.0%	
01.5.1 Local anaesthetics + vasoconstrictor	**Injection**	Lidocaine + Adrenaline	1	100.0%	1%
		Lidocaine + Epinephrine	0	0.0%	0%
		Total	1	100.0%	
02.1 Corticosteroids for oral use	**Oral**	Prednisolone	28	56.0%	18%
		Methylprednisolone	10	20.0%	6%
		Dexamethasone	7	14.0%	4%
		Prednisone	3	6.0%	2%
		Betamethasone	1	2.0%	1%
		Triamcinolone	1	2.0%	1%
		Fludrocortisone	0	0.0%	0%
		Total	50	100.0%	
03.1 Benzodiazepines	**Injection**	Diazepam	6	66.7%	4%
		Midazolam	3	33.3%	2%
		Total	9	100.0%	
	Oral	Diazepam	14	41.2%	9%
		Bromazepam	6	17.6%	4%
		Lorazepam	3	8.8%	2%
		Alprazolam	2	5.9%	1%
		Midazolam	2	5.9%	1%
		Oxazepam	2	5.9%	1%
		Brotizolam	1	2.9%	1%
		Clonazepam	1	2.9%	1%

		Etizolam	1	2.9%	1%
		Lormetazepam	1	2.9%	1%
		Triazolam	1	2.9%	1%
		Cinolazepam	0	0.0%	0%
		Estazolam	0	0.0%	0%
		Phenazepam	0	0.0%	0%
		Total	34	100.0%	
03.2 Skeletal muscle relaxants	**Injection**	Thiocolchicoside	8	72.7%	5%
		Tolperisone	2	18.2%	1%
		Orphenadrine	1	9.1%	1%
		Baclofen	0	0.0%	0%
		Total	11	100.0%	
	Oral	Tolperisone	16	16.3%	10%
		Tizanidine	14	14.3%	9%
		Thiocolchicoside	13	13.3%	8%
		Cyclobenzaprine	11	11.2%	7%
		Methocarbamol	6	6.1%	4%
		Orphenadrine	6	6.1%	4%
		Orphenadrine + Paracetamol	6	6.1%	4%
		Methocarbamol + Paracetamol	4	4.1%	3%
		Chlorzoxazone	3	3.1%	2%
		Eperisone	3	3.1%	2%
		Baclofen	2	2.0%	1%
		Chlorzoxazone + Paracetamol	2	2.0%	1%
		Mephenoxalone	2	2.0%	1%
		Metaxalone	2	2.0%	1%
		Methocarbamol + Aspirin	2	2.0%	1%
		Thiocolchicoside + Paracetamol	2	2.0%	1%
		Chlorzoxazone + Paracetamol + Diclofenac	1	1.0%	1%
		Cyclobenzaprine + Lysine cloxinate	1	1.0%	1%
		Mefenoxalon	1	1.0%	1%
		Methocarbamol + Ibuprofen	1	1.0%	1%
		Chlorzoxazone + Paracetamol + Aceclofenac	0	0.0%	0%
		Chlorzoxazone + Paracetamol + Ibuprofen	0	0.0%	0%
		Hexafluronium	0	0.0%	0%
		Muscle relaxant (non-descript)	0	0.0%	0%
		Pridinol	0	0.0%	0%
		Sirdalud	0	0.0%	0%
		Total	98	100.0%	
	Topical	Thiocolchicoside	2	100.0%	1%
		Total	2	100.0%	
10.9 Massage and physical therapy preparations	**Topical**	Menthol	27	23.1%	17%
		Capsaicin	25	21.4%	16%
		Butane + Propane	17	14.5%	11%
		Methylsalicylate	17	14.5%	11%

		Ethyl chloride	8	6.8%	5%
		Camphor + Menthol	7	6.0%	4%
		Methylsalicylate + Menthol	5	4.3%	3%
		Cold spray	4	3.4%	3%
		Trolamine salicylate	3	2.6%	2%
		Capsaicin + Menthol	2	1.7%	1%
		Camphor	1	.9%	1%
		Cold gel	1	.9%	1%
		Dimetidine	0	0.0%	0%
		Total	117	100.0%	
	Transdermal	Capsaicin	1	33.3%	1%
		Menthol	1	33.3%	1%
		Methylsalicylate	1	33.3%	1%
		Total	3	100.0%	
23.1.2 General anaesthetics with analgesia	**Inhalation**	Methoxyflurane	10	100.0%	6%
		Total	10	100.0%	
	Injection	Ketamine	1	100.0%	1%
		Total	1	100.0%	

Comparison of imported PI medications with the recommended revised OPF

The importation dataset was used to compare and validate the proposed recommendations for the revised OPF. The graphs below illustrate the prevalence of team importation for the range of medications in each OPF category. The bars of the graphs have been colour coded to visualise the drugs which were recommended for inclusion on the revised OPF through the analysis of the actual-use drug datasets. Green indicates the drugs that were recommended for the next OPF.

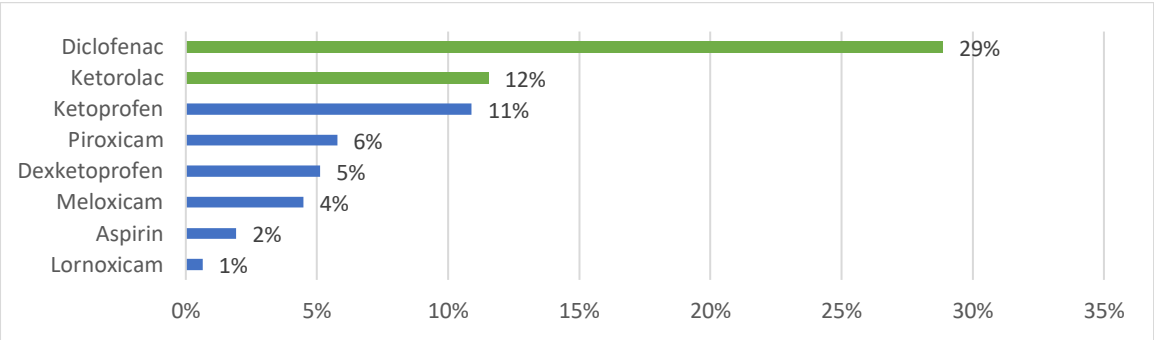


Figure 46 Prevalence (%) of countries importing various injectable NSAID drugs (n=156) [green: listed in revised OPF]

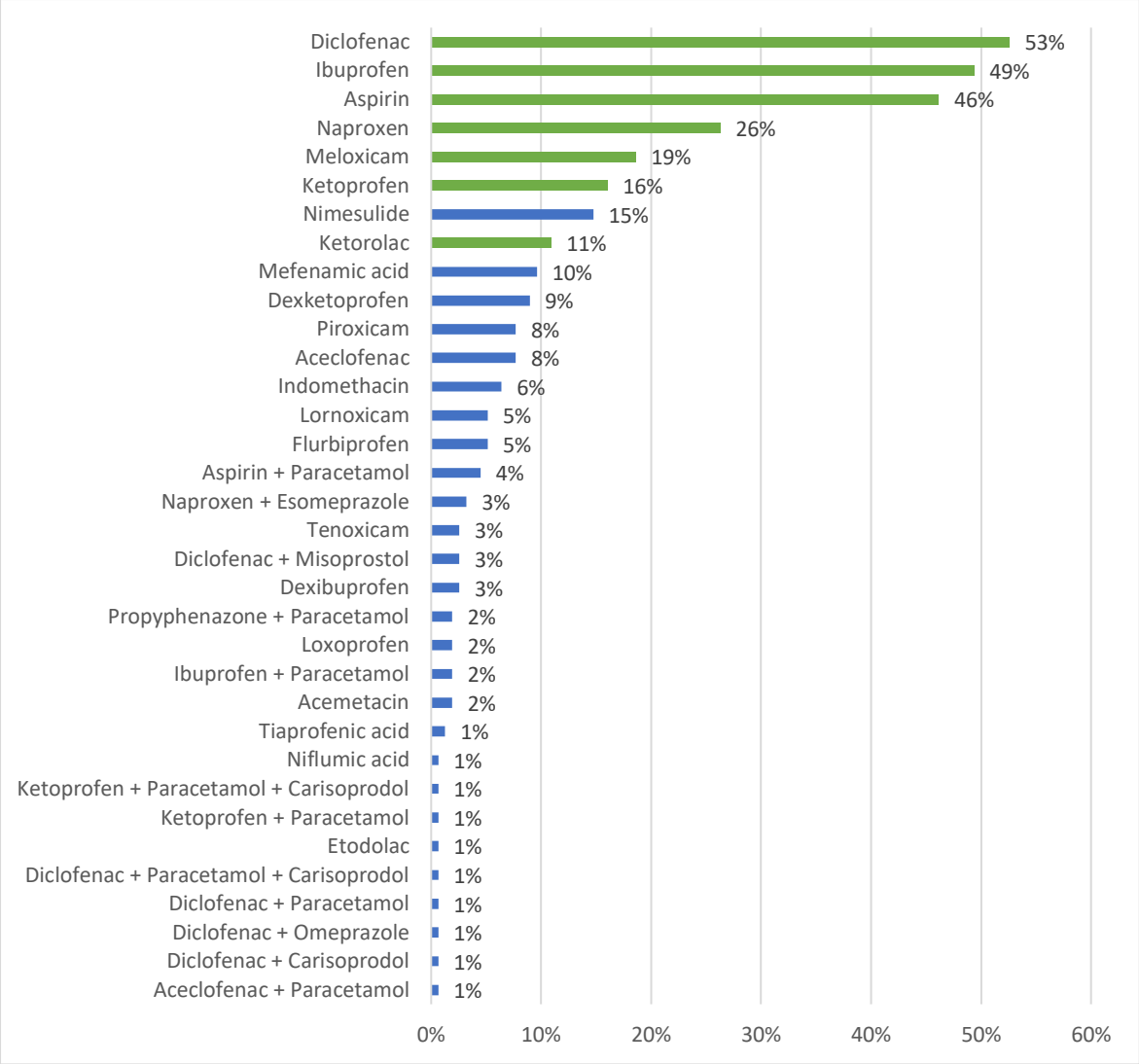


Figure 47 Prevalence (%) of countries importing various oral NSAID drugs (n=156) [green: listed in revised OPF]

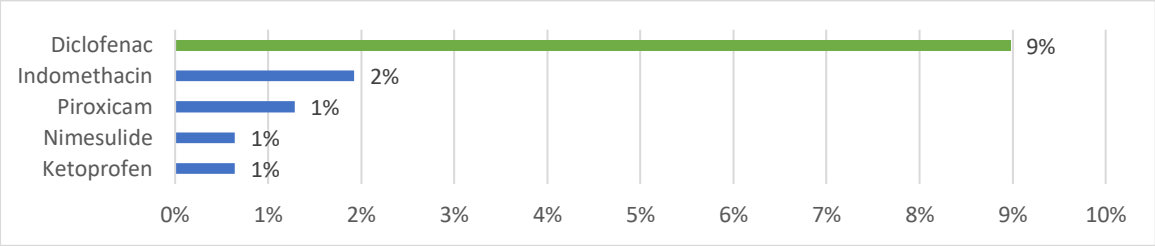


Figure 48 Prevalence (%) of countries importing various rectal NSAID drugs (n=156) [green: listed in revised OPF]

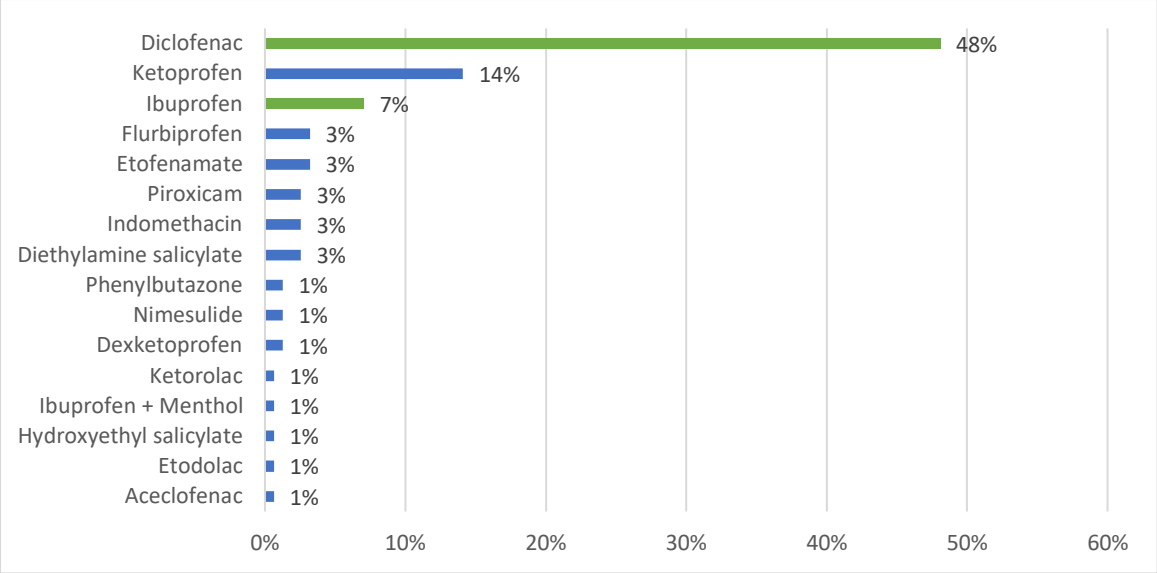


Figure 49 Prevalence (%) of countries importing various topical NSAID drugs (n=156) [green: listed in revised OPF]

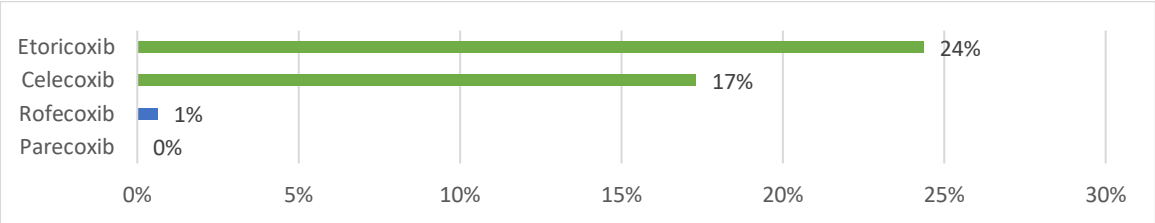


Figure 50 Prevalence (%) of countries importing various oral COX-2 inhibitor drugs (n=156) [green: listed in revised OPF]

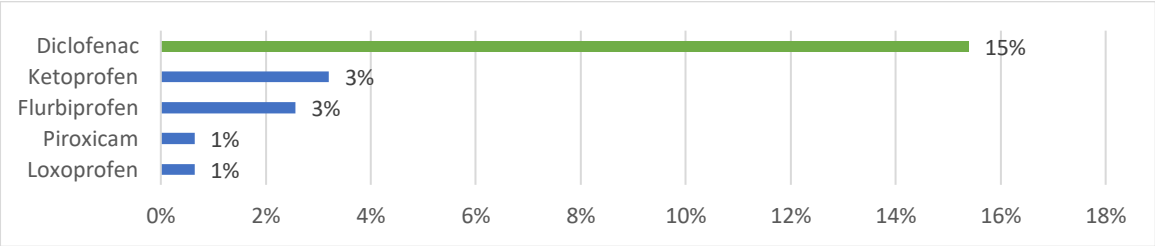


Figure 51 Prevalence (%) of countries importing various transdermal NSAIDs (n=156) [green: listed in revised OPF]

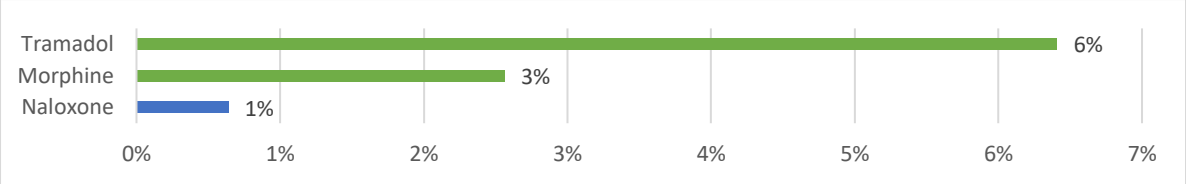


Figure 52 Prevalence (%) of countries importing various injectable opioid drugs (n=156) [green: listed in revised OPF]

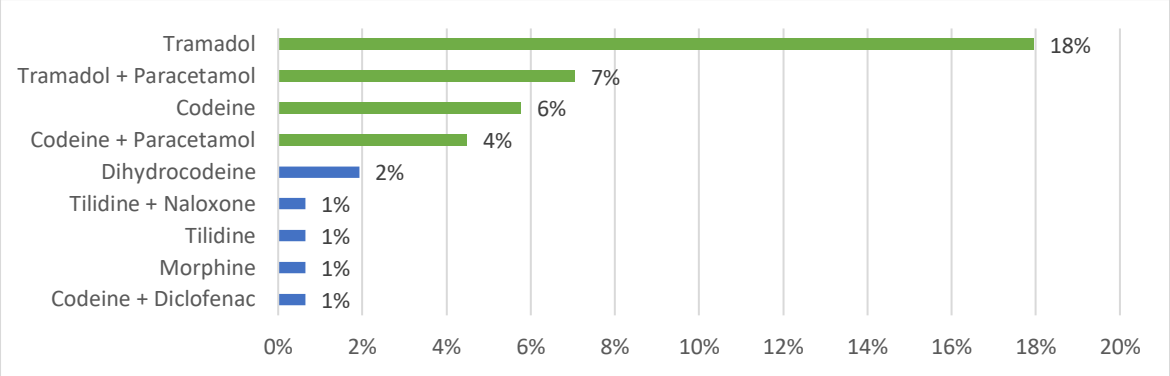


Figure 53 Prevalence (%) of countries importing various oral opioid drugs (n=156) [green: listed in revised OPF]

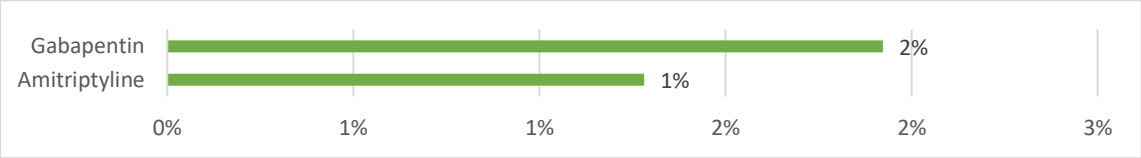


Figure 54 Prevalence (%) of countries importing various medicines for neuropathic pain (n=156) [green: listed in revised OPF]

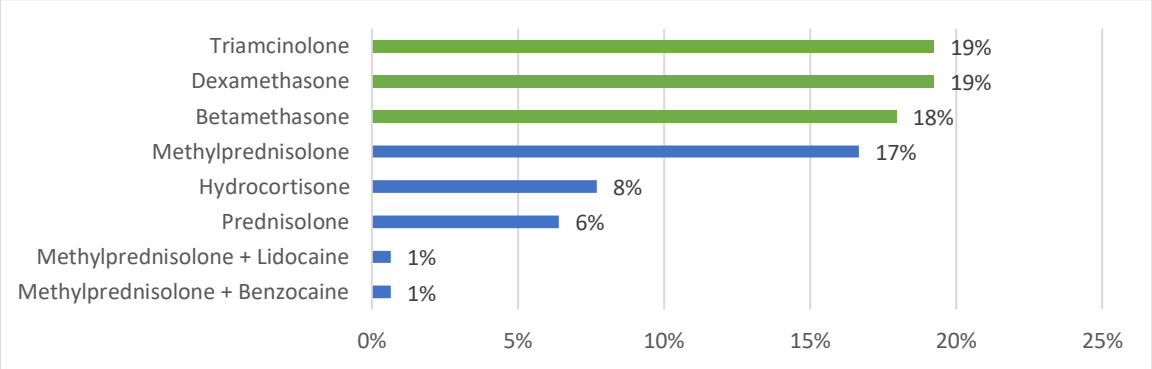


Figure 55 Prevalence (%) of countries importing various injectable corticosteroids (n=156) [green: listed in revised OPF]

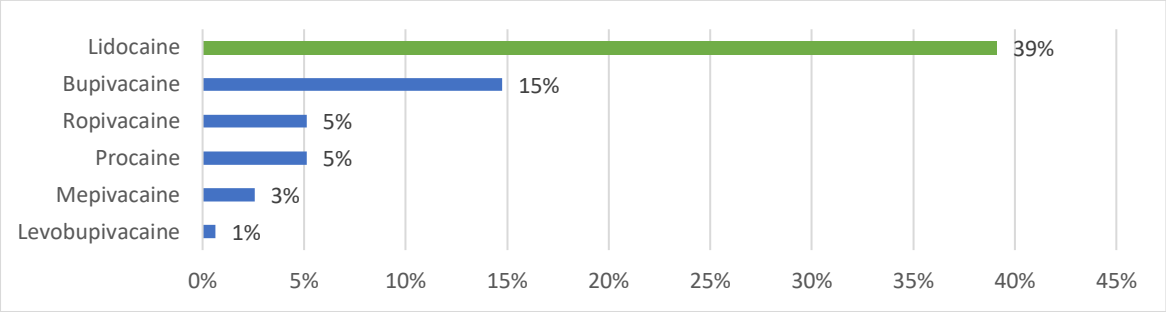


Figure 56 Prevalence (%) of countries importing various injectable local anaesthetics (n=156) [green: listed in revised OPF]

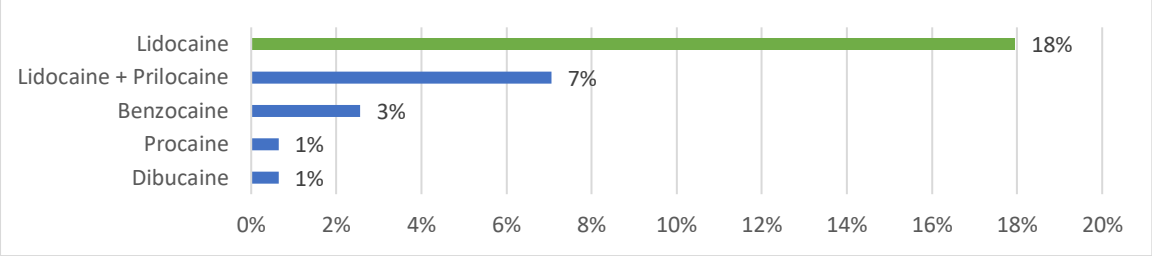


Figure 57 Prevalence (%) of countries importing various topical local anaesthetics (n=156) [green: listed in revised OPF]

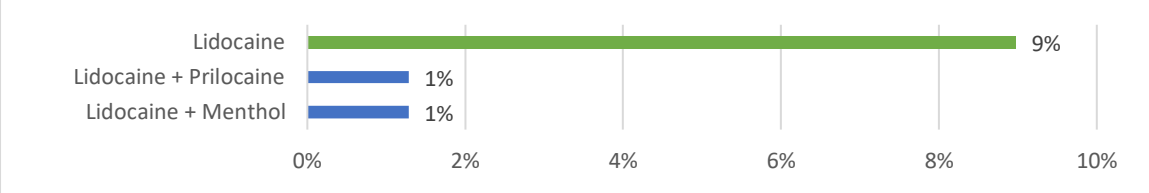


Figure 58 Prevalence (%) of countries importing various transdermal local anaesthetics (n=156) [green: listed in revised OPF]

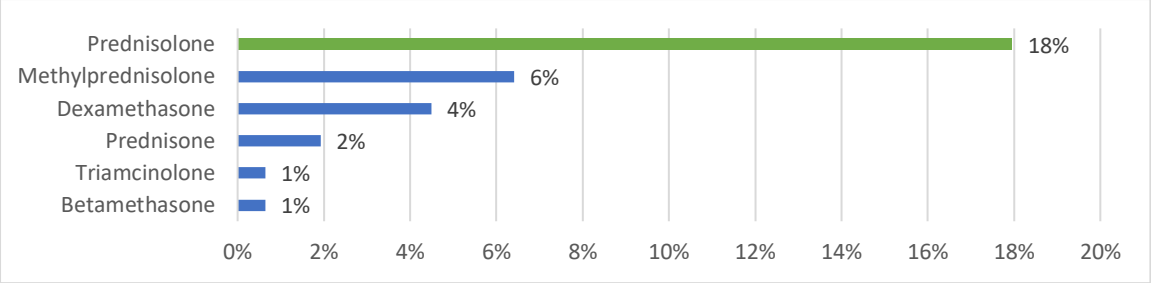


Figure 59 Prevalence (%) of countries importing various oral corticosteroids (n=156) [green: listed in revised OPF]

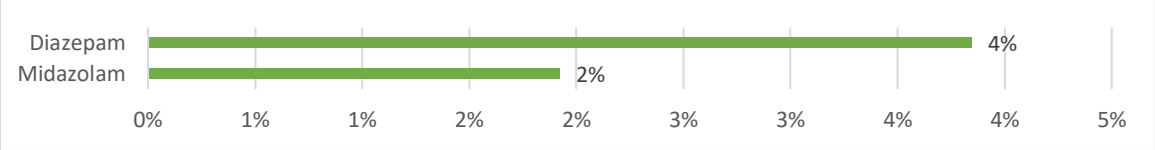


Figure 60 Prevalence (%) of countries importing various injectable benzodiazepines (n=156) [green: listed in revised OPF]

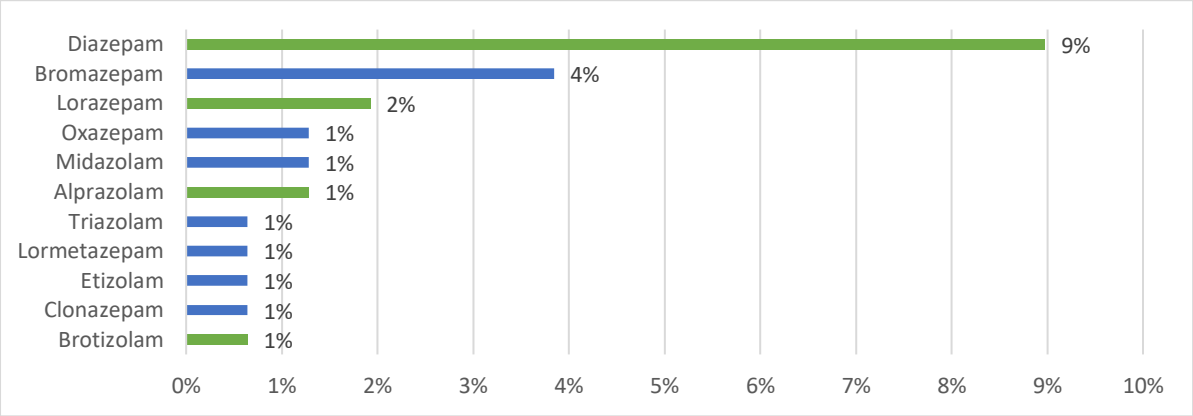


Figure 61 Prevalence (%) of countries importing various oral benzodiazepines (n=156) [green: listed in revised OPF]

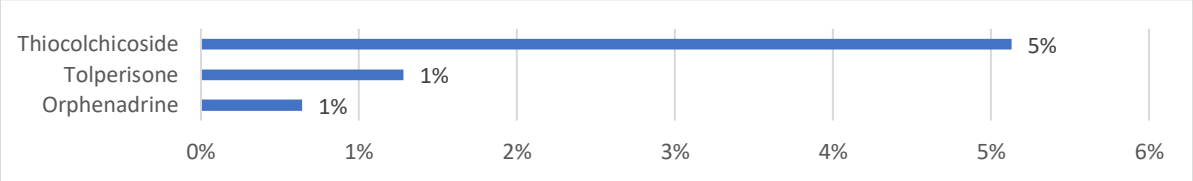


Figure 62 Prevalence (%) of countries importing various injectable skeletal muscle relaxants (n=156)

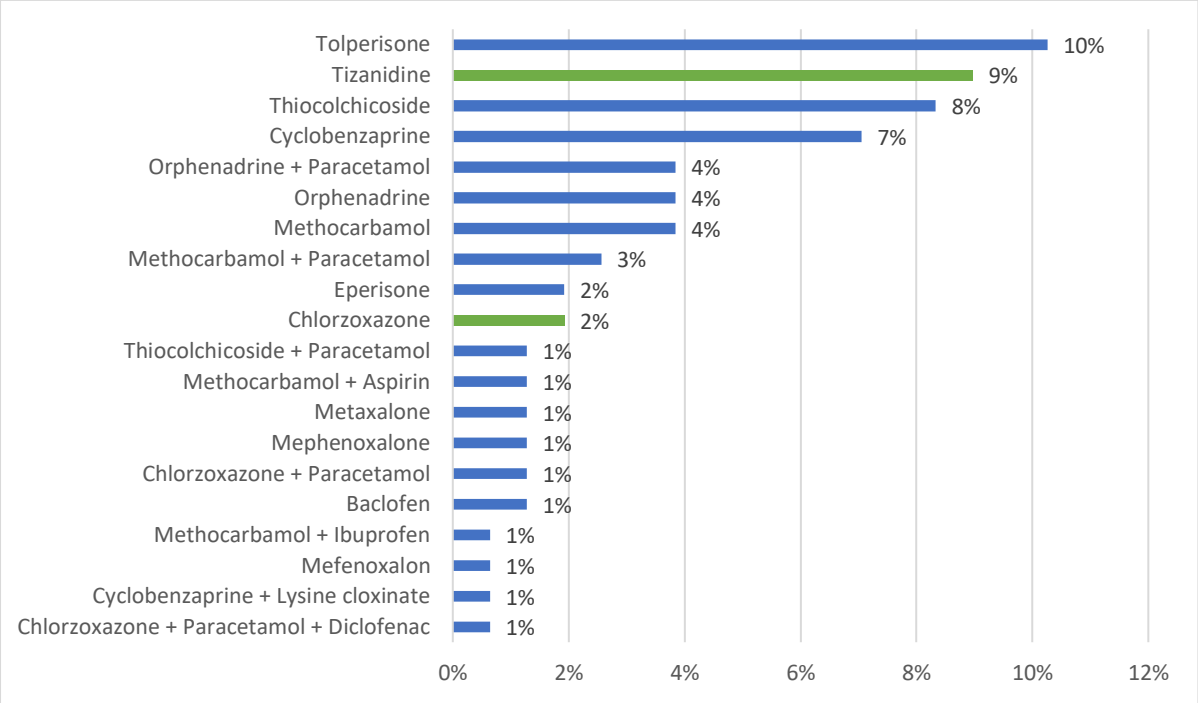


Figure 63 Prevalence (%) of countries importing various oral skeletal muscle relaxants (n=156) [green: listed in revised OPF]

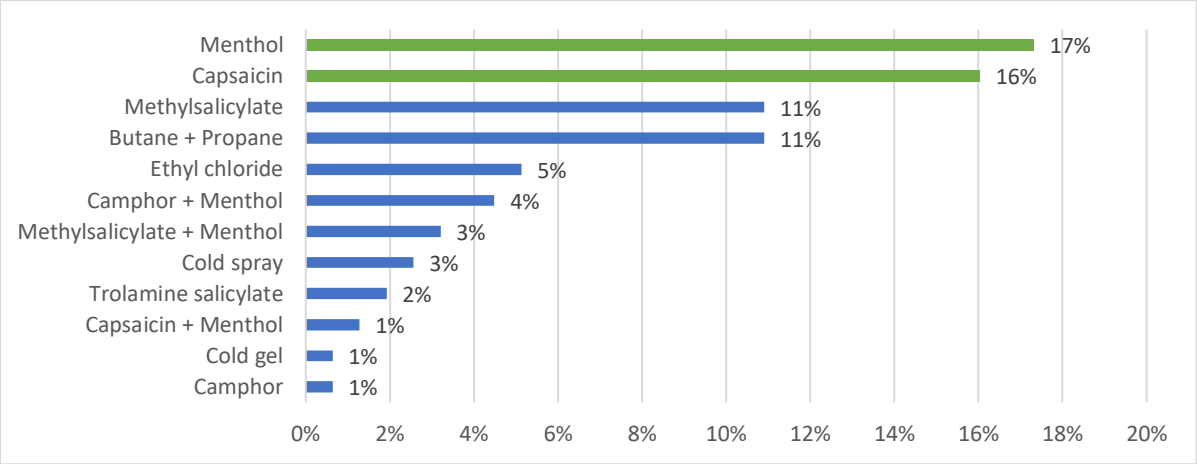


Figure 64 Prevalence (%) of countries importing various massage and physical therapy preparations (n=156) [green: listed in revised OPF]

For classes where only one type of drug was imported (not presented by a graph).

- For injectable COX-2 inhibitors, 3% (n=4) of countries imported parecoxib only.
- For intranasal opioid analgesics, 1% (n=1) of countries imported fentanyl only.
- No countries imported transdermal opioid analgesics.
- For topical skeletal muscle relaxants, 1% (n=2) of countries imported thiocolchicoside.
- For general anaesthetics by inhalation, 6% (n=10) of countries imported methoxyflurane.
- For general anaesthetics by injection, 1% (n=1) of countries imported ketamine.

4.5.2 Results of the team physician survey

This section presents the survey results of team physicians who participated in either the Tokyo or Beijing Olympic and Paralympic Games. These findings provide an understanding of the perspectives of team physicians in relation to medication use and preferences at these major international sporting events. In addition to the team importation data, these results were used to further validate the recommended revised OPF (as presented in Section 4.4).

Size of sample population

The sample population consisted of 382 team physicians, from an expected 415 physicians who were informed of and might be expected to complete the survey, giving a response rate of 92%. There were 279 team physician respondents from the Tokyo 2020 Olympic and Paralympic Summer Games (Olympics: n=200; Paralympics: n=79), and 103 team physician respondents from the Beijing 2022 Olympic and Paralympic Winter Games (Winter Olympics: n=87; Winter Paralympics: n=16).

Table 86 Number of team physician survey respondents from the Tokyo 2020 and Beijing 2022 Olympic and Paralympic Games.

Tokyo 2020			**Beijing 2022**			
Olympics	Paralympics	Total	Winter Olympics	Winter Paralympics	Total	Grand total
200	79	279	87	16	103	382

The survey results include responses from a diverse range of team physicians from 120 different countries who attended either the Tokyo 2020 or Beijing 2022 Games. The distribution of team physician respondents across countries and games is presented in Table 87 below.

Table 87 Distribution of team physician respondents by country and games.

	Beijing 2022			Tokyo 2020			Grand total (n=382)
Country	Olympics	Paralympics	Total	Olympics	Paralympics	Total	
Algeria	0	0	0	1	1	2	2
Angola	0	0	0	0	1	1	1
Argentina	0	0	0	5	0	5	5
Armenia	0	0	0	1	0	1	1
Australia	1	2	3	1	2	3	6
Austria	6	0	6	1	1	2	8
Azerbaijan	0	0	0	1	0	1	1
Bahamas	0	0	0	1	0	1	1
Bahrain	0	0	0	0	1	1	1
Bangladesh	0	0	0	1	0	1	1
Barbados	0	0	0	1	0	1	1
Belarus	1	0	1	7	1	8	9
Belgium	0	1	1	1	1	2	3
Bosnia and Herzegovina	0	0	0	0	1	1	1
Botswana	0	0	0	1	0	1	1
Brazil	1	0	1	4	2	6	7
Bulgaria	1	0	1	1	0	1	2
Canada	9	1	10	8	1	9	19
Central African Republic	0	0	0	1	2	3	3
Chad	0	0	0	1	0	1	1
Chile	0	0	0	3	1	4	4
Chinese Taipei	0	0	0	2	1	3	3
Colombia	0	0	0	4	1	5	5
Costa Rica	0	0	0	0	1	1	1
Côte d'Ivoire	0	0	0	0	1	1	1
Croatia	0	1	1	1	1	2	3
Cuba	0	0	0	1	1	2	2
Cyprus	0	0	0	1	0	1	1
Czech Republic	2	0	2	1	1	2	4
Denmark	1	0	1	1	1	2	3
Dominican Republic	0	0	0	2	1	3	3
Ecuador	0	0	0	1	1	2	2
Egypt	0	0	0	1	3	4	4
Eritrea	0	0	0	3	0	3	3
Estonia	0	0	0	1	1	2	2

Ethiopia	0	0	0	1	1	2	2
Fiji	0	0	0	1	0	1	1
Finland	1	1	2	1	0	1	3
France	1	1	2	10	4	14	16
Gambia	0	0	0	1	0	1	1
Georgia	0	0	0	1	1	2	2
Germany	6	1	7	6	0	6	13
Ghana	0	0	0	1	0	1	1
Great Britain	2	0	2	7	4	11	13
Greece	0	0	0	1	0	1	1
Guatemala	0	0	0	1	0	1	1
Honduras	0	0	0	1	0	1	1
Hong Kong, China	0	0	0	1	0	1	1
Hungary	1	0	1	0	1	1	2
Iceland	1	0	1	0	0	0	1
India	0	0	0	1	1	2	2
Indonesia	0	0	0	0	1	1	1
Ireland	0	0	0	4	1	5	5
Islamic Republic of Iran	0	0	0	1	0	1	1
Israel	0	0	0	1	1	2	2
Italy	4	0	4	1	4	5	9
Jamaica	1	0	1	1	0	1	2
Japan	3	2	5	8	0	8	13
Jordan	0	0	0	1	0	1	1
Kazakhstan	1	0	1	0	0	0	1
Kenya	0	0	0	1	0	1	1
Latvia	1	0	1	2	1	3	4
Libya	0	0	0	0	1	1	1
Lithuania	1	0	1	2	1	3	4
Luxembourg	0	0	0	1	0	1	1
Madagascar	0	0	0	0	1	1	1
Malawi	0	0	0	0	1	1	1
Mali	0	0	0	0	1	1	1
Malta	0	0	0	1	0	1	1
Mexico	0	0	0	1	0	1	1
Montenegro	0	0	0	1	0	1	1
Morocco	0	0	0	0	1	1	1
Mozambique	0	0	0	1	0	1	1
Nepal	0	0	0	1	0	1	1
Netherlands	1	1	2	5	0	5	7
New Zealand	1	0	1	3	1	4	5
Niger	0	0	0	1	0	1	1
Nigeria	0	0	0	2	1	3	3
Norway	2	1	3	1	0	1	4
Palau	0	0	0	1	0	1	1
Panama	0	0	0	1	0	1	1
Papua New Guinea	0	0	0	1	0	1	1

Paraguay	0	0	0	1	0	1	1
People's Republic of China	4	2	6	3	0	3	9
Peru	0	0	0	1	1	2	2
Philippines	0	0	0	1	1	2	2
Poland	0	0	0	1	1	2	2
Portugal	0	0	0	2	1	3	3
Puerto Rico	0	0	0	2	1	3	3
Refugee Olympic Team	0	0	0	1	0	1	1
Republic of Korea	1	0	1	2	0	2	3
Republic of Moldova	0	0	0	1	0	1	1
Romania	1	0	1	1	0	1	2
Russian Federation	6	0	6	2	0	2	8
Rwanda	0	0	0	1	0	1	1
Saudi Arabia	0	0	0	1	1	2	2
Senegal	0	0	0	1	0	1	1
Serbia	1	0	1	2	1	3	4
Seychelles	0	0	0	1	0	1	1
Singapore	0	0	0	1	1	2	2
Slovakia	2	1	3	1	1	2	5
Slovenia	3	0	3	2	1	3	6
South Africa	0	0	0	4	2	6	6
Spain	1	0	1	5	0	5	6
Sri Lanka	0	0	0	1	0	1	1
Sweden	1	1	2	1	1	2	4
Switzerland	3	0	3	1	0	1	4
Thailand	0	0	0	1	1	2	2
Trinidad and Tobago	0	0	0	2	0	2	2
Turkey	0	0	0	1	0	1	1
Uganda	0	0	0	1	1	2	2
Ukraine	1	0	1	1	0	1	2
United Arab Emirates	0	0	0	0	1	1	1
United States of America	14	0	14	8	4	12	26
Uruguay	0	0	0	1	0	1	1
Uzbekistan	0	0	0	7	0	7	7
Venezuela	0	0	0	0	1	1	1
Vietnam	0	0	0	1	0	1	1
Zambia	0	0	0	0	1	1	1
Zimbabwe	0	0	0	1	0	1	1

Number of athletes under the care of each team physicians

Team physicians were asked how many athletes were under their care while at the games. The majority of physicians (67.3%, n=255) reported taking care of 50 or fewer athletes. A smaller proportion (12.4%, n=47) were responsible for 50 to 100 athletes, while 11.9% (n=45)

cared for 101 to 200 athletes. Only 8.4% of physicians (n=32) reported that they care for over 200 athletes over the course of the games.

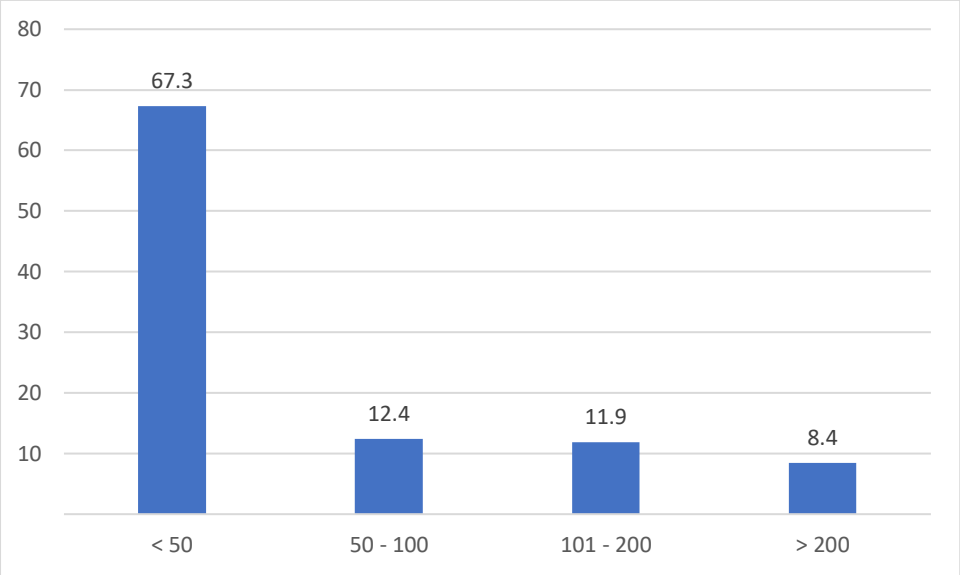


Figure 65 Number of athletes under the care of team physicians (%) at the games

Clinical specialty of team physicians

Team physicians were asked what their primary clinical specialty was. The majority of physicians specialised in sports medicine (47.6%, n=182), followed by orthopaedics (18.6%, n=71), general practice primary care (8.6%, n=33), sports medicine surgery (7.9%, n=30), and emergency medicine (3.9%, n=15). There were a mix of 15 other specialties represented by a smaller number of physicians.

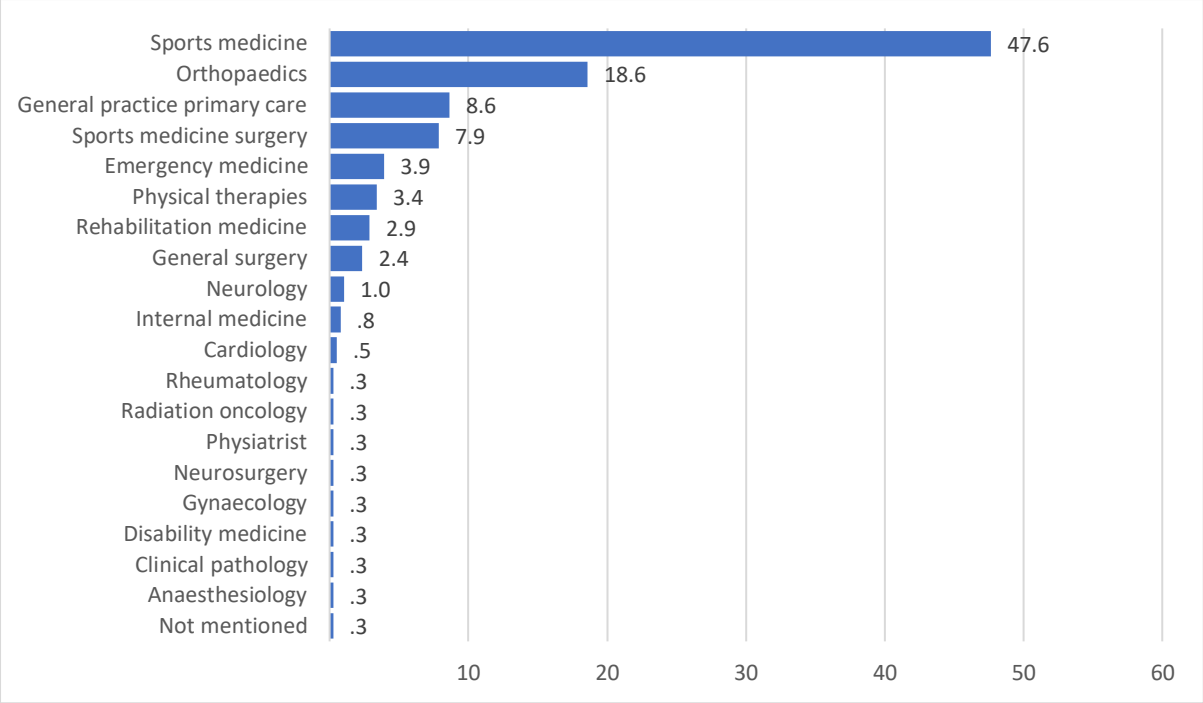


Figure 66 Clinical specialty of team physicians (%) working at the games

Coverage of overall prescribing needs of the OPF

Team physicians were asked approximately what proportion of their overall prescriptions could be covered by the medicines on the games formulary for the athletes under their care. Of the 381 responding physicians, 76.1% (n=290) stated that most (>75%) or all of their prescribing needs were covered by the formulary. Only 10.2% (n=39) of respondents indicated that less than 25% or none of their prescriptions were covered by the games formulary.

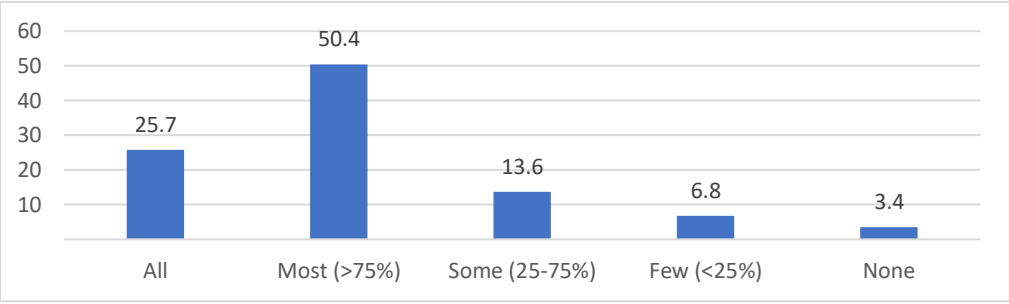


Figure 67 Coverage of overall prescribing needs of formulary versus number of physicians (%)

Coverage of overall prescribing needs from imported team stock

Team physicians were asked what proportion of prescriptions for the athletes under their care could be covered by their team's own stock of medicines. Of the 379 responding physicians, 84.7% (n=321) reported that most (>75%) or all prescriptions could be covered by their own stock. Only 4.7% (n=18) reported that less than 25% of their prescriptions could be covered by their own stock.

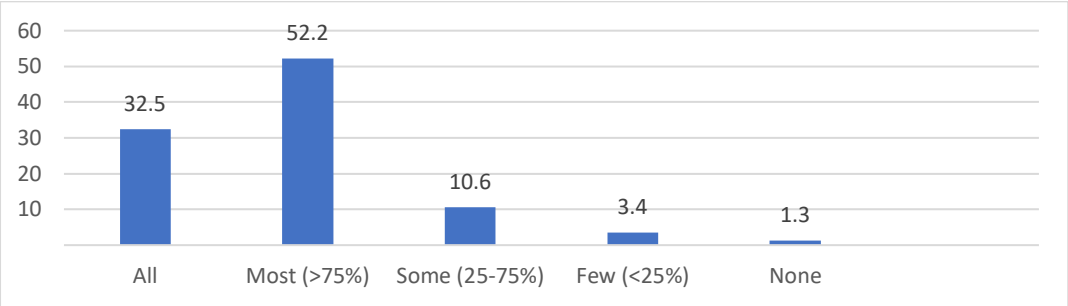


Figure 68 Coverage of overall prescribing needs of NOC team stock versus number of physicians (%)

Expected use of the games pharmacy service

Team physicians were asked what proportion of the medicines they prescribe for athletes do they expect to be obtained from the polyclinic pharmacy in the athlete village. Of 379 team physician respondents, 19.3% (n=73) reported that most (>75%) or all prescriptions would be obtained from the polyclinic pharmacy. A total of 70.9% (n=269) stated that either few (<25%) or no prescriptions would be expected to be obtained via the polyclinic pharmacy.

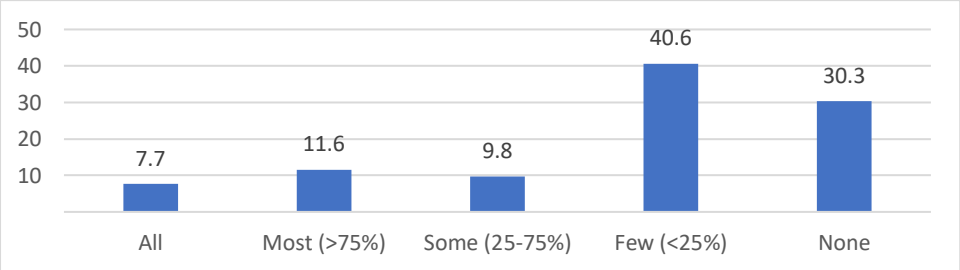


Figure 69 Proportion of medicines expected to be obtained from polyclinic pharmacy versus number of physicians (%)

Expected prescribing of analgesic or anti-inflammatory drugs for athletes

Team physicians were asked approximately what percentage of athletes under their care do they expect to require analgesic or anti-inflammatory medications for sports-related conditions during the course of the games.

The results show that of the 379 respondents, the majority of physicians (66%, n=250) expected 0-30% of athletes to require analgesic or anti-inflammatory medication during the games. A smaller proportion (21.6%, n=82) expected 31-60% of athletes to require the medication, while even less (12.4%, n=47) expected 61-100% of athletes to require these types of medications.

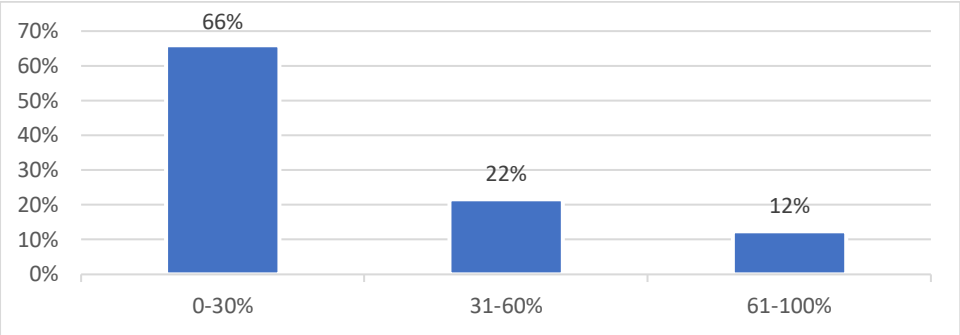


Figure 70 Percentage groupings of athletes in NOC versus athletes (%) expected to require PI medications for sports-related injury during the games

Coverage of medications for pain and inflammation on the Olympic & Paralympic medicines formulary

Team physicians were asked what proportion of their expected PI medications for sports-related conditions could be covered by the medicines in the games formulary. Of 379 physician respondents, 73% (n=277) reported either most (>75%) or all of their PI prescriptions could be covered by the existing formulary. Only 16.7% (n=63) indicated that less than 25% of their prescriptions could be covered.

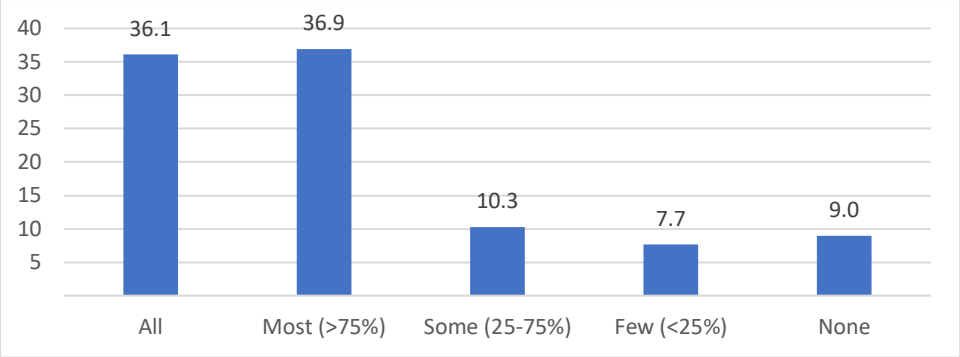


Figure 71 Proportion of prescribing needs of PI medications covered by the formulary per physician (%)

The next section covers the questions in the survey related to specific medication preferences or frequency of use by team physicians. The drugs recommended for inclusion in the revised OPF are presented as green bars on the graphs below in order to help compare the revised recommended OPF list of medications with the preferences and use of medications by team physicians. This comparison is used to further validate the proposed revised OPF recommendations, as presented in the discussion section that follows.

Oral medicines

Use of oral non-opioid or NSAIDs

Team physicians were asked which oral non-opioid or NSAIDs they had prescribed in the last 12 months for sports-related conditions in athletes. All physicians reported they had prescribed paracetamol (100%, n=381), with diclofenac (78.2%, n=298) and ibuprofen (77.4%, n=295) also being used by the majority of respondents. Naproxen (42.3%, n=161), celecoxib (36.7%, n=140), meloxicam (25.7%, n=98) was also commonly used. Other drugs were used by less than 25% of physicians in the previous 12 months.

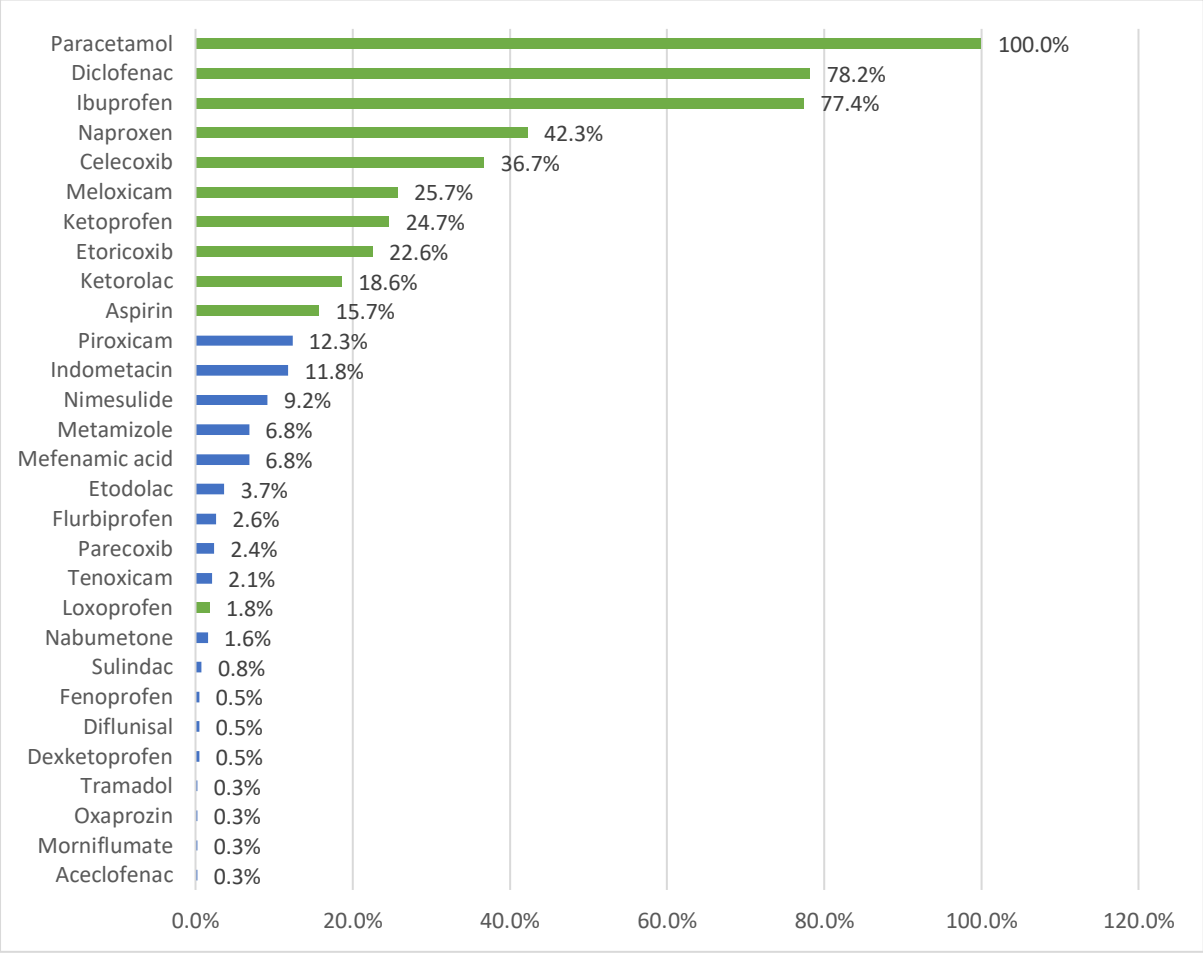


Figure 72 Proportion (%) of team physicians prescribing ORAL non-opioid or NSAIDs in the last 12 months (n=381) [green: listed in revised OPF]

Use of oral opioid analgesic drugs

Team physicians were asked which oral opioid analgesic drugs they had prescribed in the previous 12 months to for sports-related conditions in athletes. The most commonly prescribed drugs were oral tramadol (40.8%, n=122) and oral codeine (26.4%, n=79). Other drugs in this class were prescribed by less than 6% of physicians.

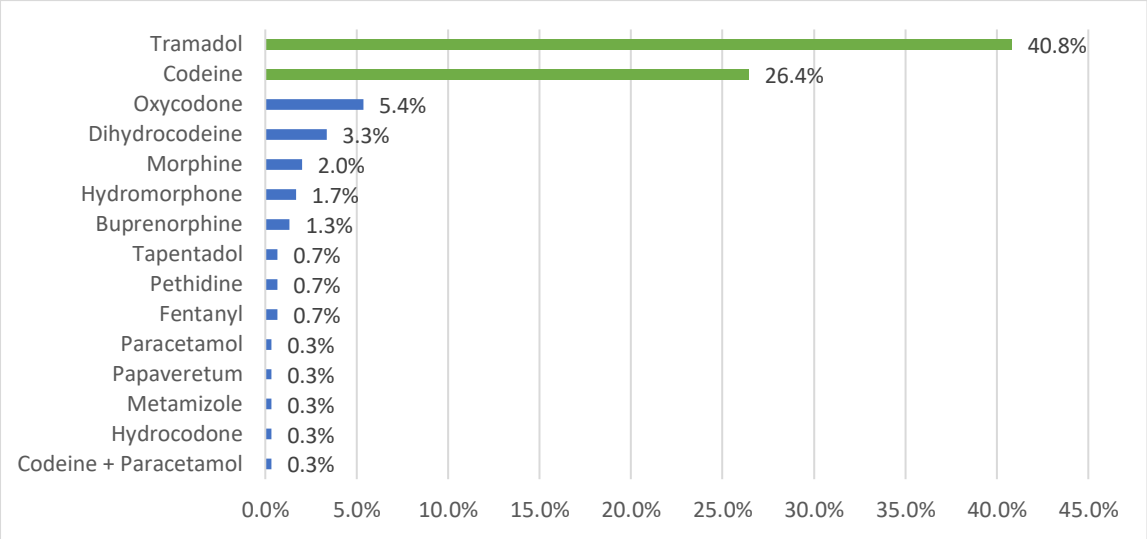


Figure 73 Proportion (%) of team physicians prescribing ORAL opioid analgesic drugs in the last 12 months (n=381) [green: listed in revised OPF]

Oral medicines for mild to moderate pain without inflammation

Team physicians were asked which oral medicine they most frequently prescribe for mild to moderate pain (without inflammation) for sports-related conditions in athletes. The most commonly prescribed drugs included paracetamol (85.3%, n=324), ibuprofen (43.2%, n=164), diclofenac (31.3%, n=119) and naproxen (16.1%, n=61). Other drugs for this clinical indication were used by less than 10% of physicians.

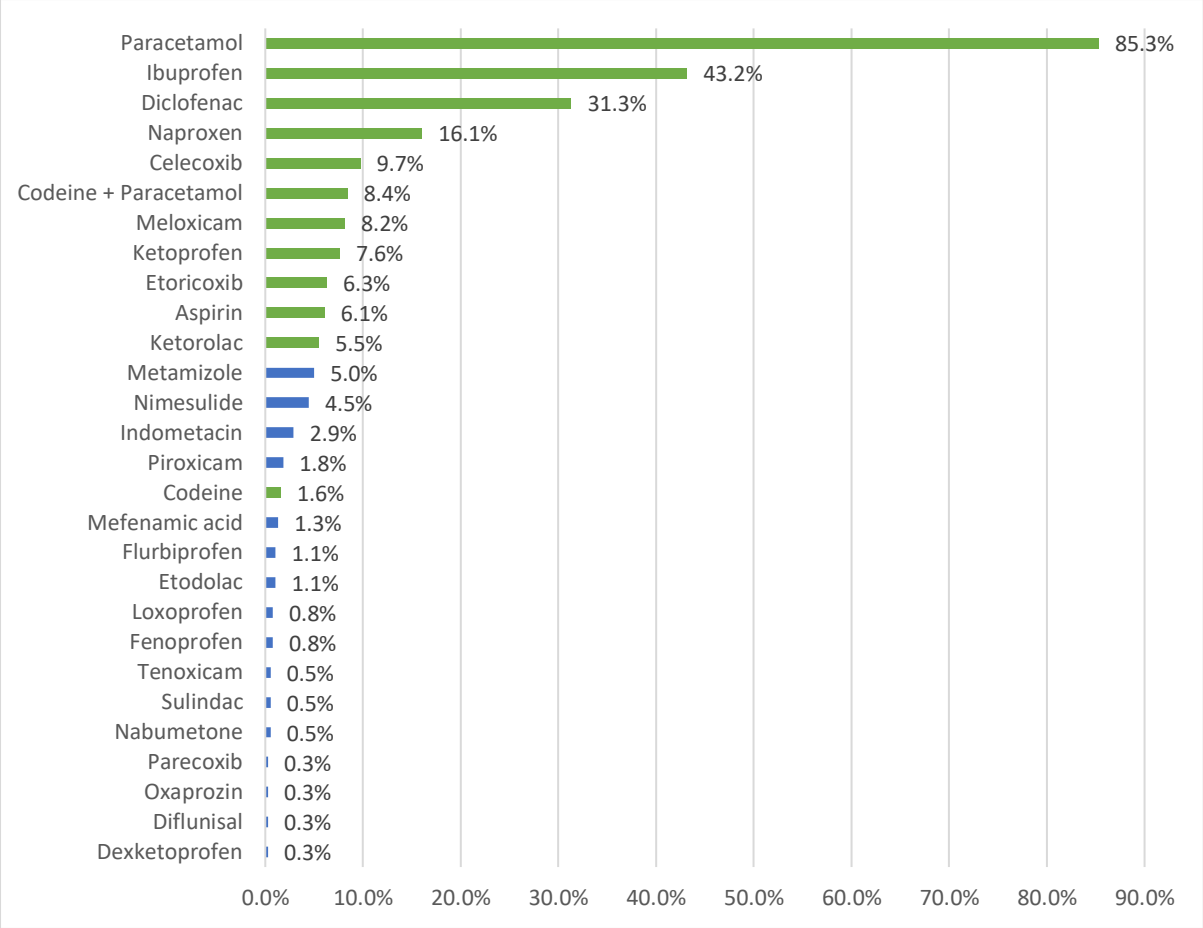


Figure 74 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for mild to moderate pain (without inflammation) for sports-related conditions in athletes (n=380) [green: listed in revised OPF]

Oral medicine for moderate to severe pain without inflammation

Team physicians were asked which oral medicine they most frequently prescribed for moderate to severe pain (without inflammation) for sports-related conditions in athletes. The most common prescribed drugs were paracetamol (44.7%, n=170), diclofenac (36.1%, n=137), tramadol (32.6%, n=124), codeine + paracetamol as a combination formulation (30.8%, n=117) and ibuprofen (30.5%, n=116). Other drugs were prescribed by less than 15% of physicians for this clinical indication.

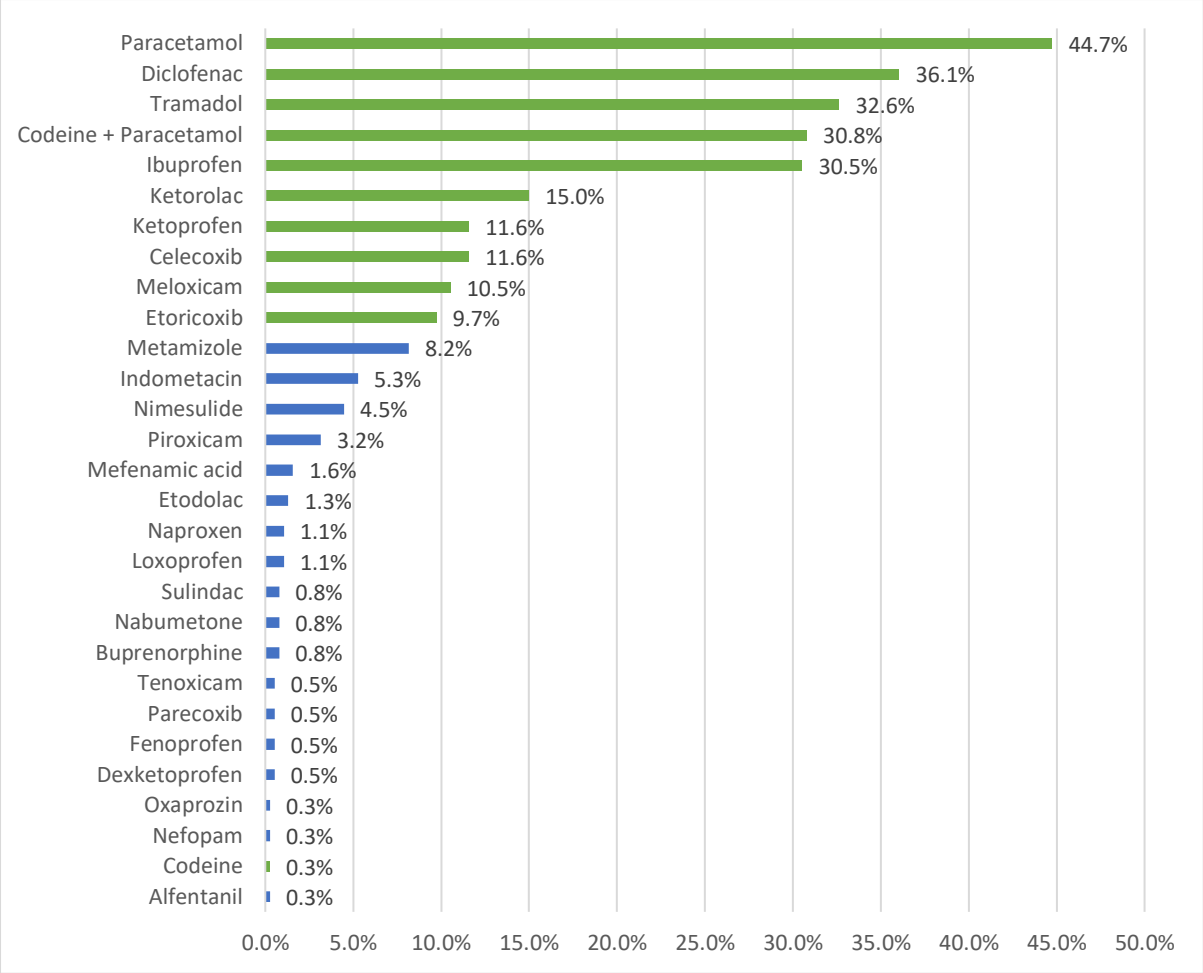


Figure 75 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for moderate to severe pain (without inflammation) for sports-related conditions in athletes (n=380) [green: listed in revised OPF]

Oral medicine for mild to moderate pain with inflammation

Team physicians were asked which oral medicine they most frequently prescribe for mild to moderate pain with inflammation for sports-related conditions in athletes. The most commonly prescribed drugs included ibuprofen (55.6%, n=212), diclofenac (55.4%, n=211), paracetamol (40.2%, n=153), naproxen (24.4%, n=93), celecoxib (19.2%, n=73), and ketoprofen (15.2%, n=58). Other drugs were prescribed by less than 15% of physicians.

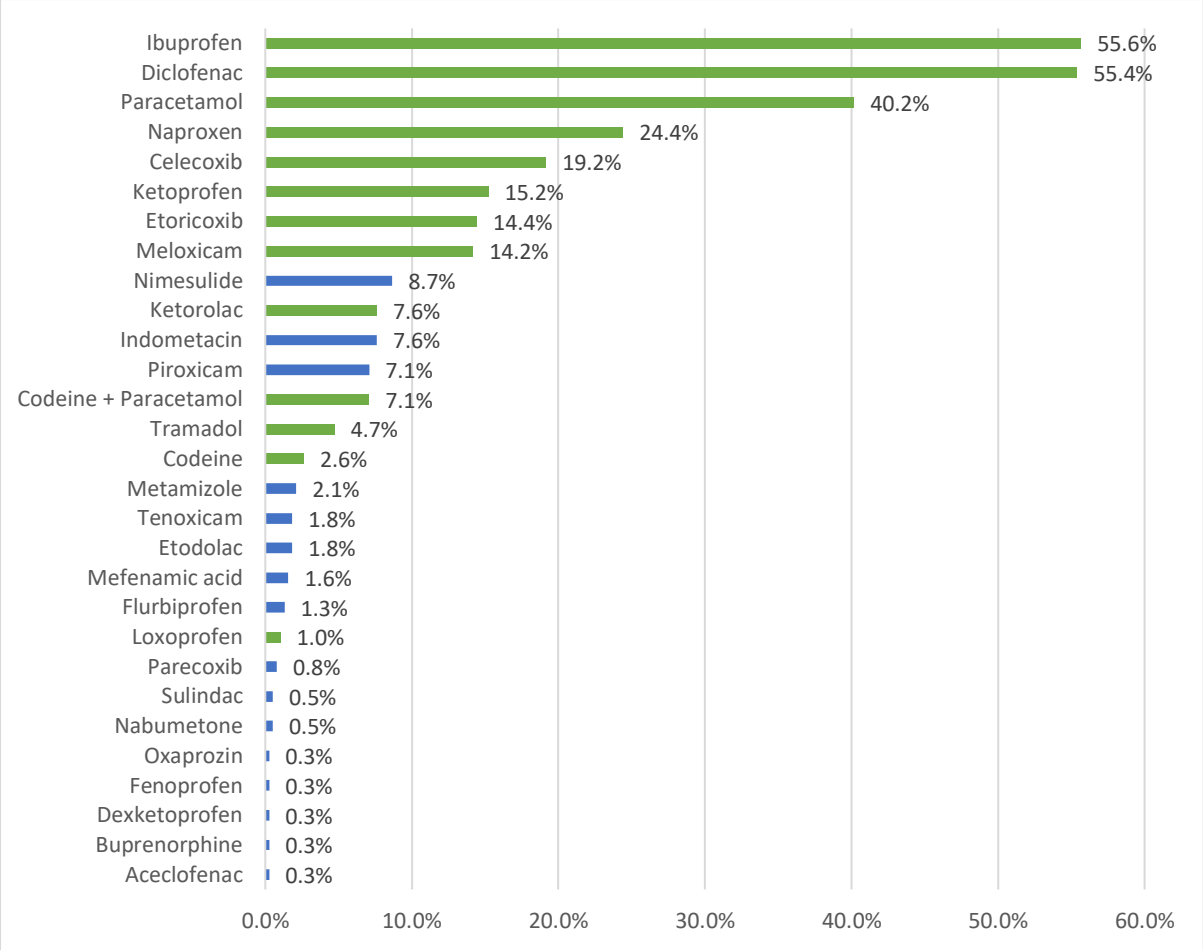


Figure 76 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for mild to moderate pain with inflammation for sports-related conditions in athletes (n=381) [green: listed in revised OPF]

Oral medicine for moderate to severe pain with inflammation

Team physicians were asked which oral medicine they most frequently prescribe for moderate to severe pain with inflammation for sports-related conditions in athletes. The most commonly prescribed medicines included diclofenac (54.9%, n=208), ibuprofen (38.0%, n=144), paracetamol (31.4%, n=119), tramadol (25.1%, n=95), ketoprofen (22.4%, n=85), celecoxib (22.4%, n=85), naproxen (21.6%, n=82), codeine + paracetamol (21.4%, n=81) and etoricoxib (18.5%, n=70). Other drugs were prescribed by less than 15% of physicians.

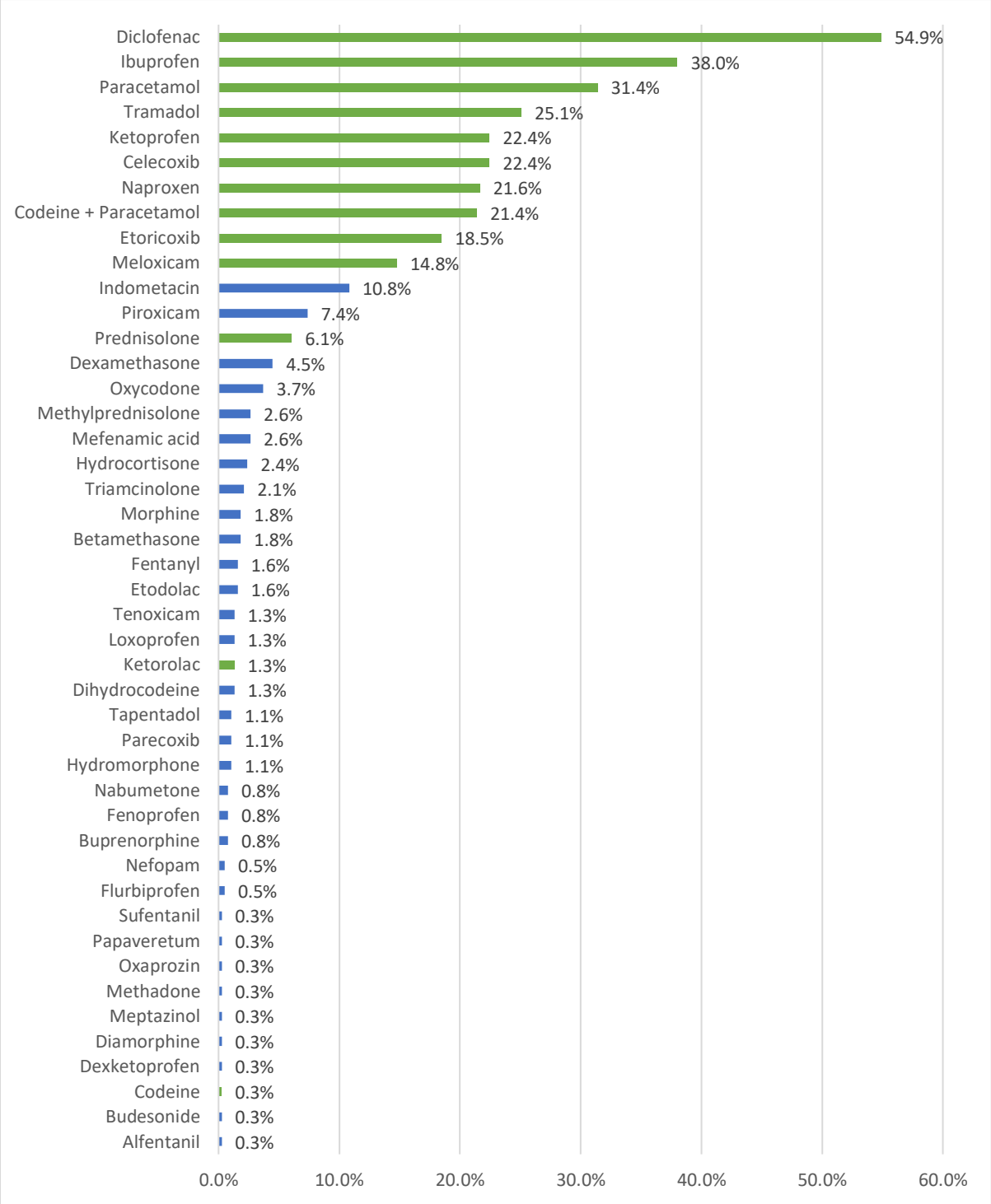


Figure 77 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for moderate to severe pain with inflammation for sports-related conditions in athletes (n=379) [green: listed in revised OPF]

Oral medicines for neuropathic pain

Team physicians were asked which oral medicine they would most frequently prescribe for neuropathic pain in athletes. The most commonly prescribed drugs included gabapentin (46.6%, n=172), pregabalin (45.0%, n=166), diclofenac (25.2%, n=93), tramadol (21.4%, n=79), and amitriptyline (21.1%, n=78). Other drugs were prescribed by less than 14% of physicians for the treatment of neuropathic pain.

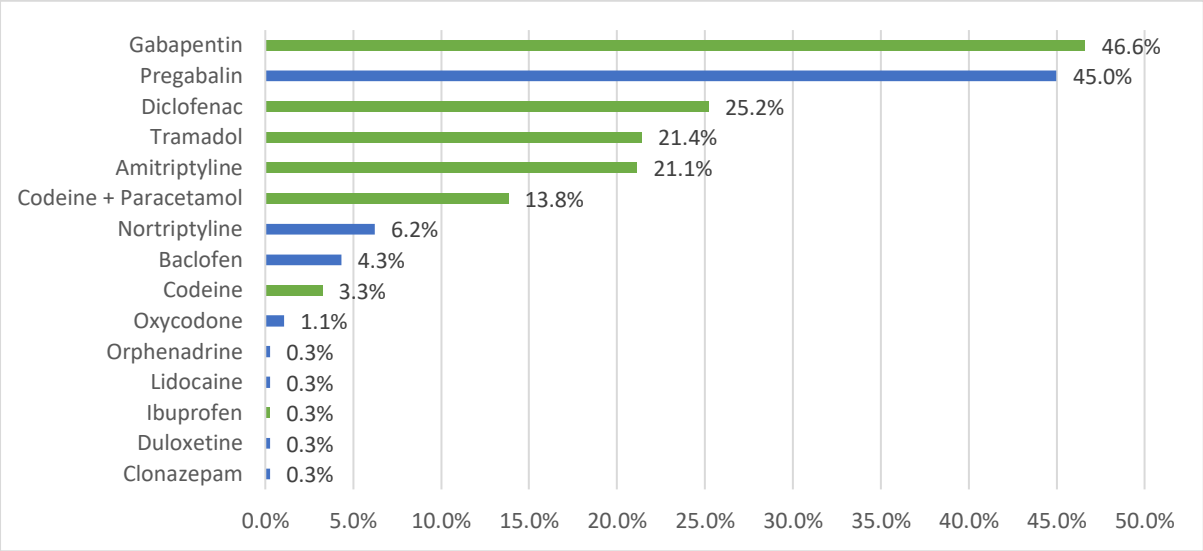


Figure 78 Proportion (%) of team physicians reporting their most frequently prescribed ORAL medicine for neuropathic pain in athletes (n=369) [green: listed in revised OPF]

Oral skeletal muscle relaxants

Team physicians were asked which skeletal muscle relaxants they had prescribed in the last 12 months for sports-related conditions in athletes. The most commonly prescribed medications were diazepam (25.0%, n=70), cyclobenzaprine (21.8%, n=61), baclofen (9.6%, n=55), and tizanidine (18.2%, n=51). Other drugs in this category were prescribed by less than 14% of responding physicians.

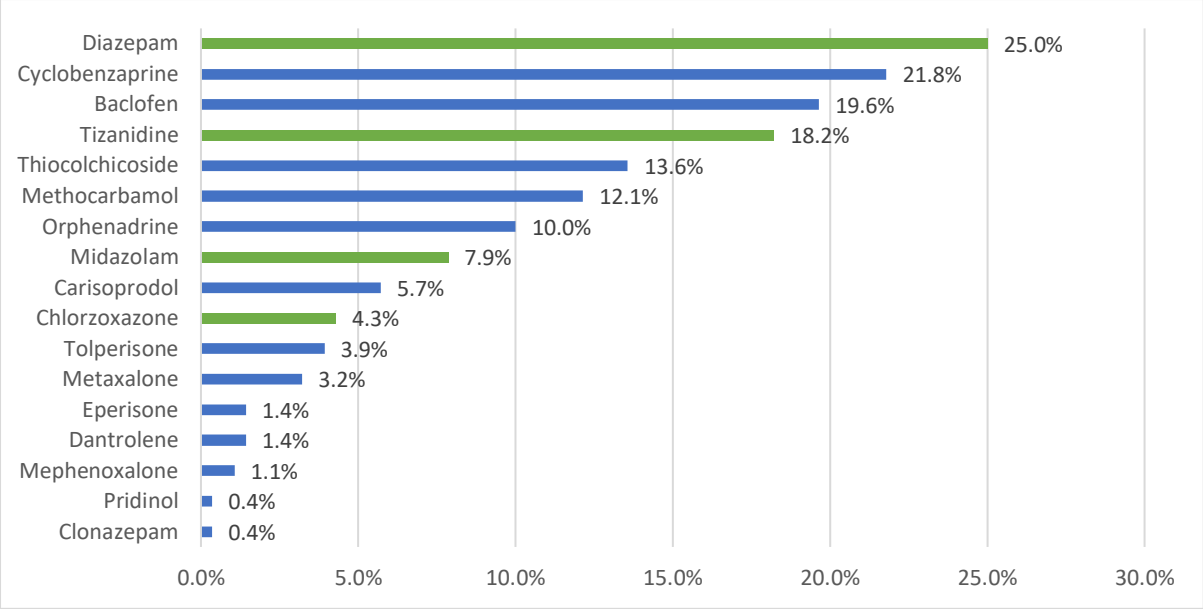


Figure 79 Proportion (%) of team physicians reporting which skeletal muscle relaxants they had prescribed in the last 12 months for sports-related conditions in athletes (n=280) [green: listed in revised OPF]

Injectable medicines

Injectable non-opioid and non-steroidal anti-inflammatory drugs (NSAIDs)

Team physicians were asked which injectable non-opioid and non-steroidal anti-inflammatory drugs (NSAIDs) they had prescribed in the last 12 months for sports-related conditions in athletes. The most commonly prescribed medications were diclofenac (48.7%, n=148), ketorolac (23.0%, n=70) and ketoprofen (15.5%, n=47). Other injectable drugs in these categories were prescribed by less than 15% of physicians.

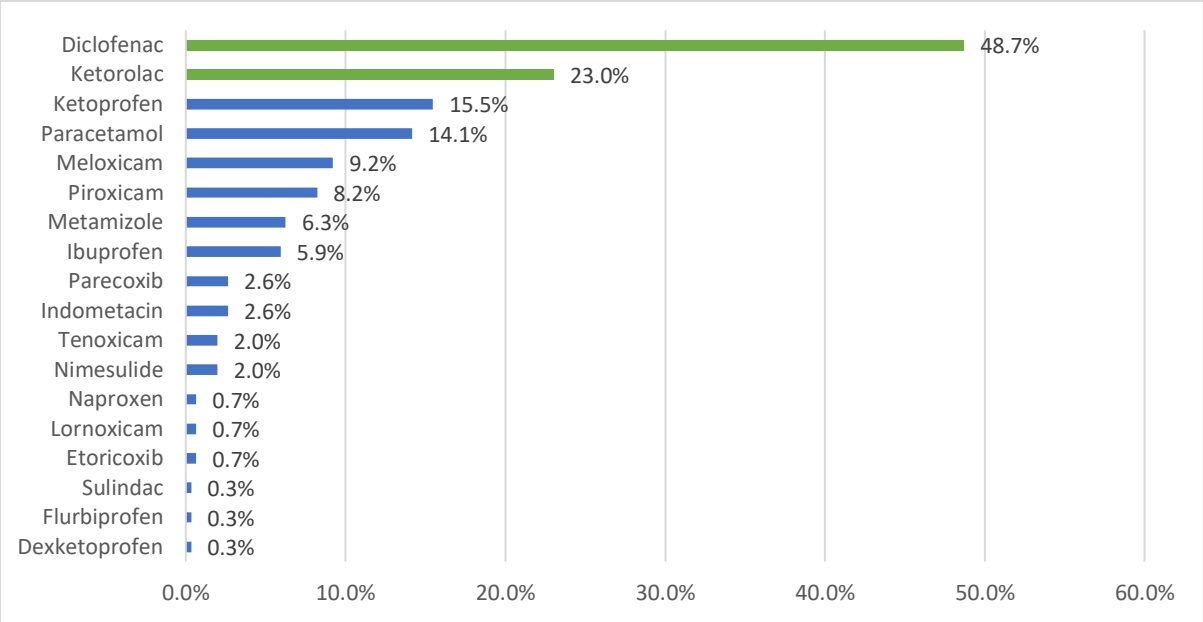


Figure 80 Proportion (%) of team physicians reporting which INJECTABLE non-opioid and non-steroidal anti-inflammatory drugs (NSAIDs) they had prescribed in the last 12 months for sports-related conditions in athletes (n=304) [green: listed in revised OPF]

Injectable opioid analgesic drugs

Team physicians were asked which injectable opioid analgesic drugs they had prescribed in the last 12 months for sports-related conditions in athletes. Tramadol was the most prescribed injectable opioid analgesic drug (18.3%, n=46), followed by much lower prescribing of morphine (3.6%, n=9) and fentanyl (3.6%, n=9), and even lower prescribing of other drugs in this class.

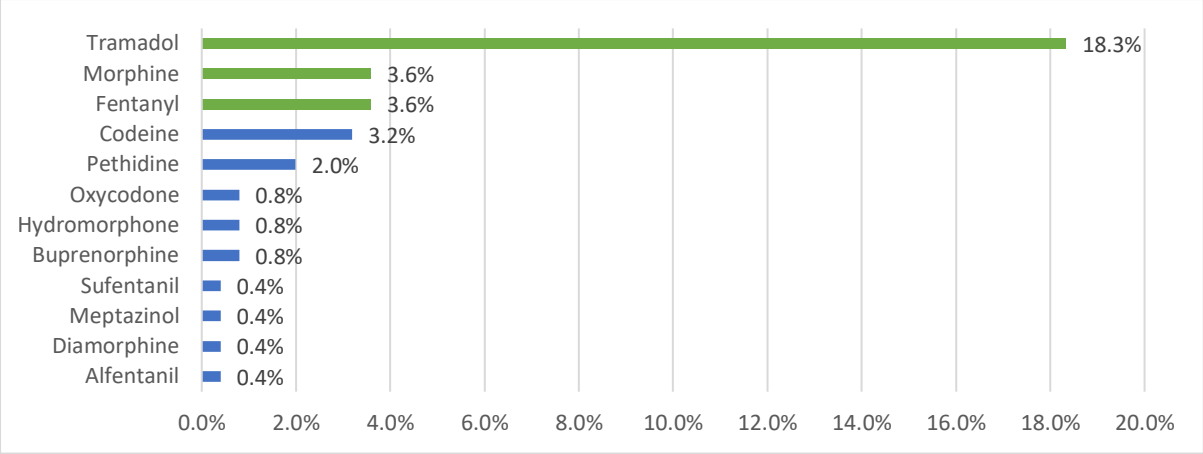


Figure 81 Proportion (%) of team physicians reporting which INJECTABLE opioid analgesic drugs they had prescribed in the last 12 months for sports-related conditions in athletes (n=251) [green: listed in revised OPF]

Injectable medicine for moderate to severe pain without inflammation

Team physicians were asked which injectable medicine they most frequently prescribe to athletes for moderate to severe pain without inflammation due to sports-related conditions. The most commonly prescribed drugs included diclofenac (28.1%, n=99), paracetamol (19.0%, n=67), ketorolac (17.0%, n=60) and tramadol (16.5%, n=58). Other injectable drugs for this clinical indication were prescribed by less than 15% of responding physicians.

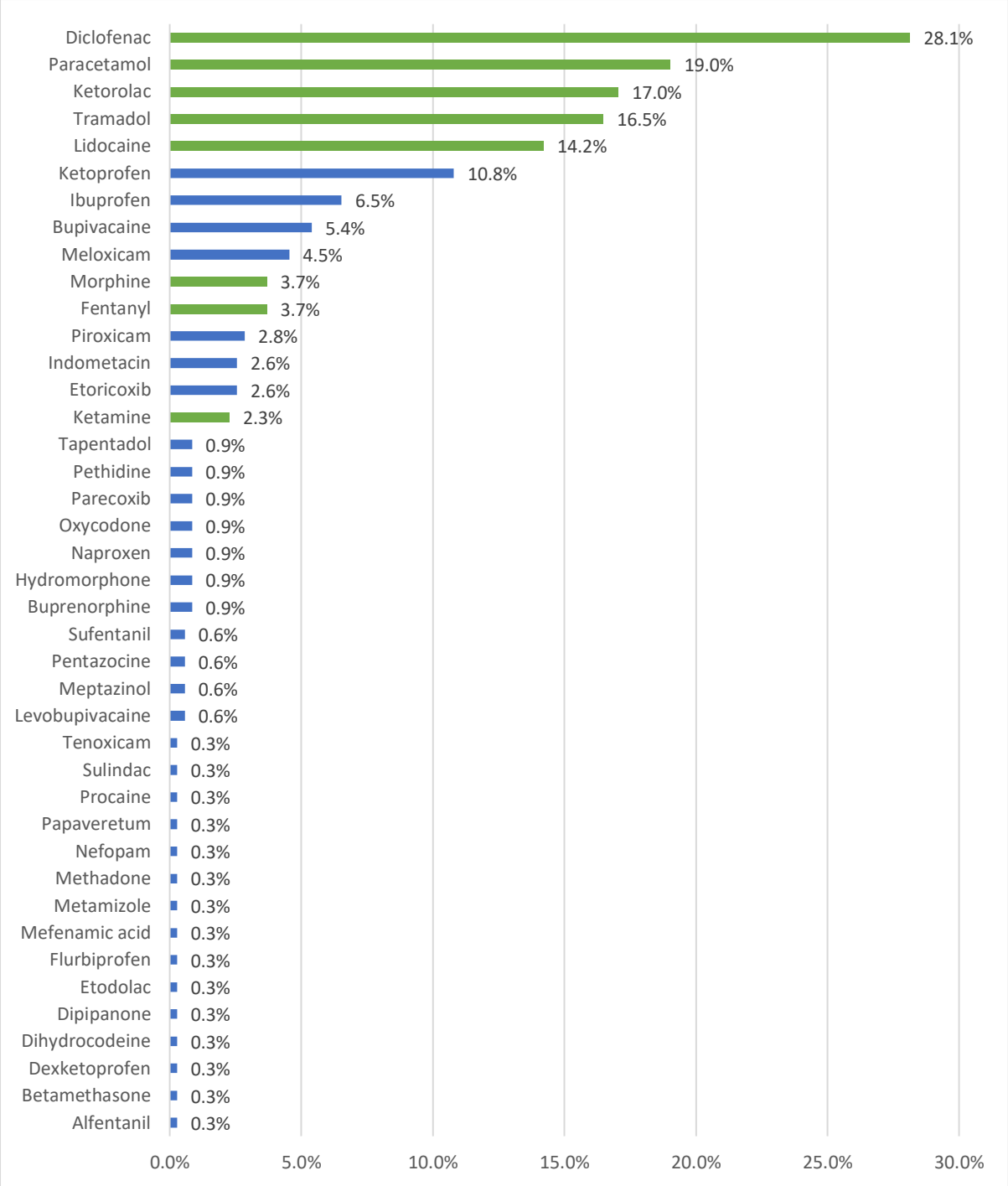


Figure 82 Proportion (%) of team physicians reporting which INJECTABLE medicine they most frequently prescribe to athletes for moderate to severe pain without inflammation due to sports-related conditions (n=352) [green: listed in revised OPF]

Injectable medicine for moderate to severe pain with inflammation

Team physicians were asked which injectable medicine they most frequently prescribe to athletes for moderate to severe pain with inflammation due to sports-related conditions. The

two most commonly prescribed drugs by far were diclofenac (41.4%, n=149) and ketorolac (20.3%, n=73). Other injectable drugs for this clinical indication were prescribed by less than 14% of physicians.

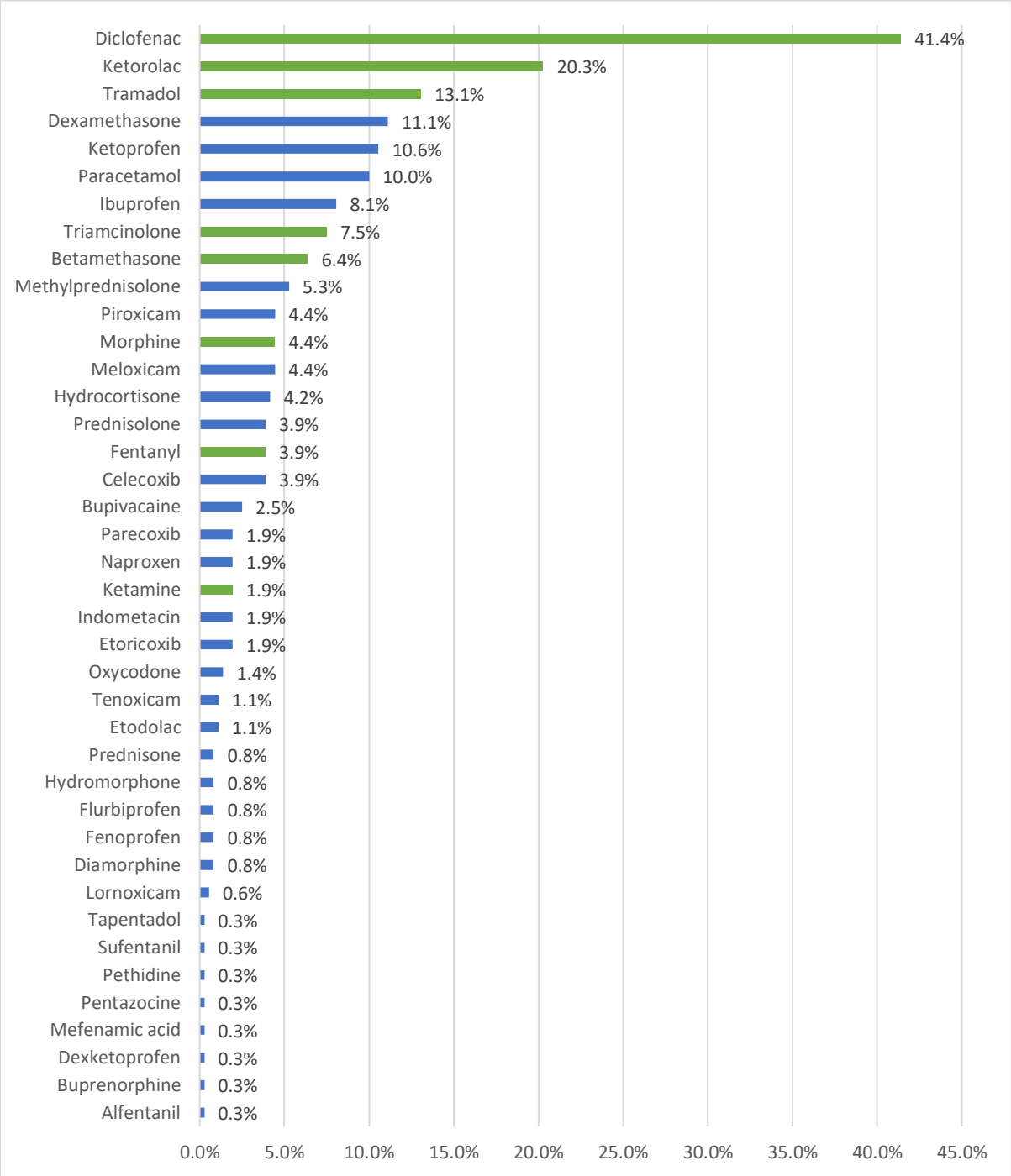


Figure 83 Proportion (%) of team physicians reporting which INJECTABLE medicine they most frequently prescribe to athletes for moderate to severe pain with inflammation due to sports-related conditions (n=360) [green: listed in revised OPF]

Glucocorticoid medicines for local injection

Team physicians were asked which glucocorticoid medications they most frequently administer to athletes by local injection (e.g. intra-articular) for inflammation due to sports injury. The four most prescribed drugs include triamcinolone (36.8%, n=131), betamethasone (22.2%, n=79), dexamethasone (21.1%, n=75) and methylprednisolone (20.8%, n=74). Other injectable glucocorticoids for local administration were prescribed by less than 10% of physicians.

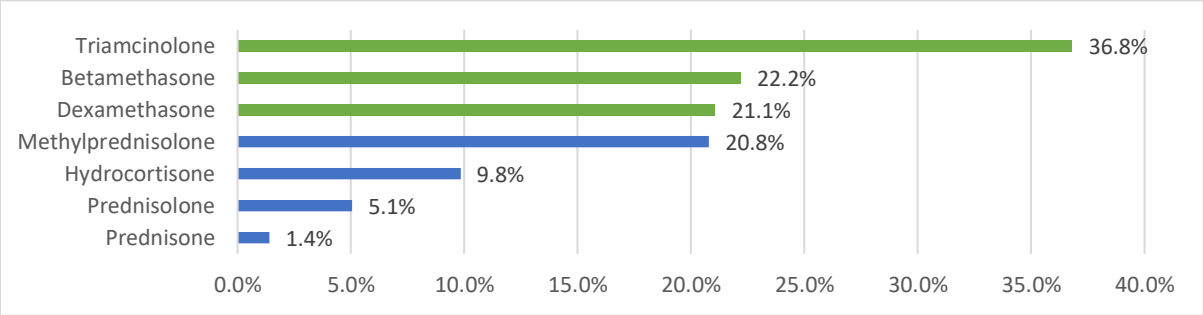


Figure 84 Proportion (%) of team physicians reporting which glucocorticoid medications they most frequently administer to athletes by local injection (e.g., intra-articular) for inflammation due to sports injury (n=356) [green: listed in revised OPF]

Local anaesthetic for local injection into a joint

Team physicians were asked which local anaesthetic drug they most frequently administer to athletes by local injection into a joint (e.g. intra-articular) for pain due to sports injury. The most commonly prescribed drug by far was lidocaine (70.1%, n=255), followed by bupivacaine (23.1%, n=84). Other local anaesthetic drugs for local injection were prescribed by less than 10% of team physicians.

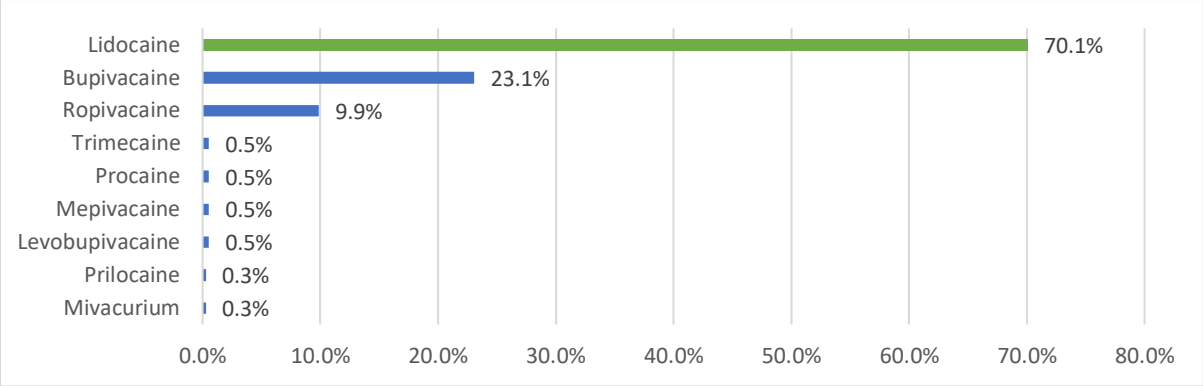


Figure 85 Proportion (%) of team physicians reporting which local anaesthetic drug they most frequently administer to athletes by local injection into a joint (e.g., intra-articular) for pain due to sports injury (n=364) [green: listed in revised OPF]

Local anaesthetic for local injection into soft tissue

Team physicians were asked which local anaesthetic drug they most frequently administer to athletes by local injection into soft tissue for sports-related conditions. The most commonly prescribed drug by far was lidocaine (74.0%, n=268), followed by bupivacaine (23.2%, n=84). Other drugs were prescribed by less than 7% of physician respondents for this indication.

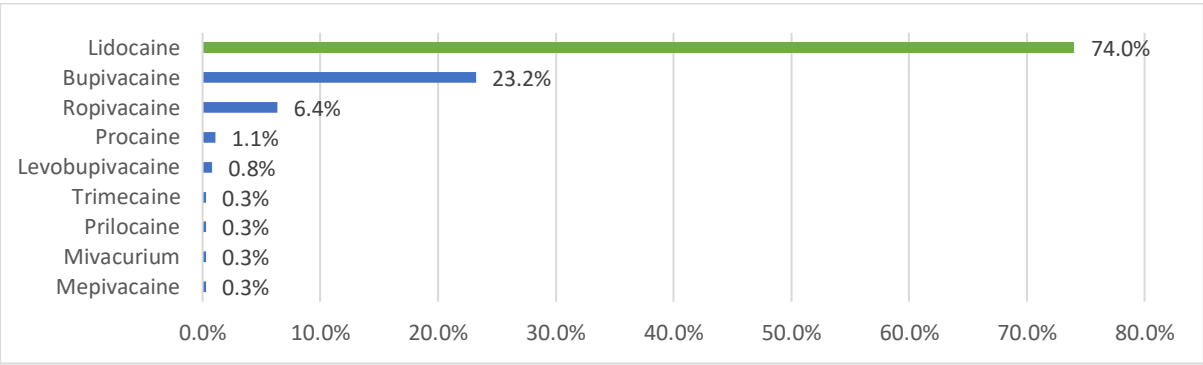


Figure 86 Proportion (%) of team physicians reporting which local anaesthetic drug they most frequently administer to athletes by local injection into soft tissue for sports-related conditions (n=362) [green: listed in revised OPF]

Urgent or emergency treatment

Emergency analgesia for severe pain on the field of play

Team physicians were asked which medicine they prefer to use for emergency analgesia for severe pain on the field of play due to serious injury in athletes. The most commonly preferred drugs were tramadol injection (36.6%, n=132), morphine injection (20.2%, n=73), fentanyl injection (15.8%, n=57), ketamine injection (11.4%, n=41) and methoxyflurane for inhalation (11.1%, n=40). Other drugs for this use were preferred by less than 8% of physicians.

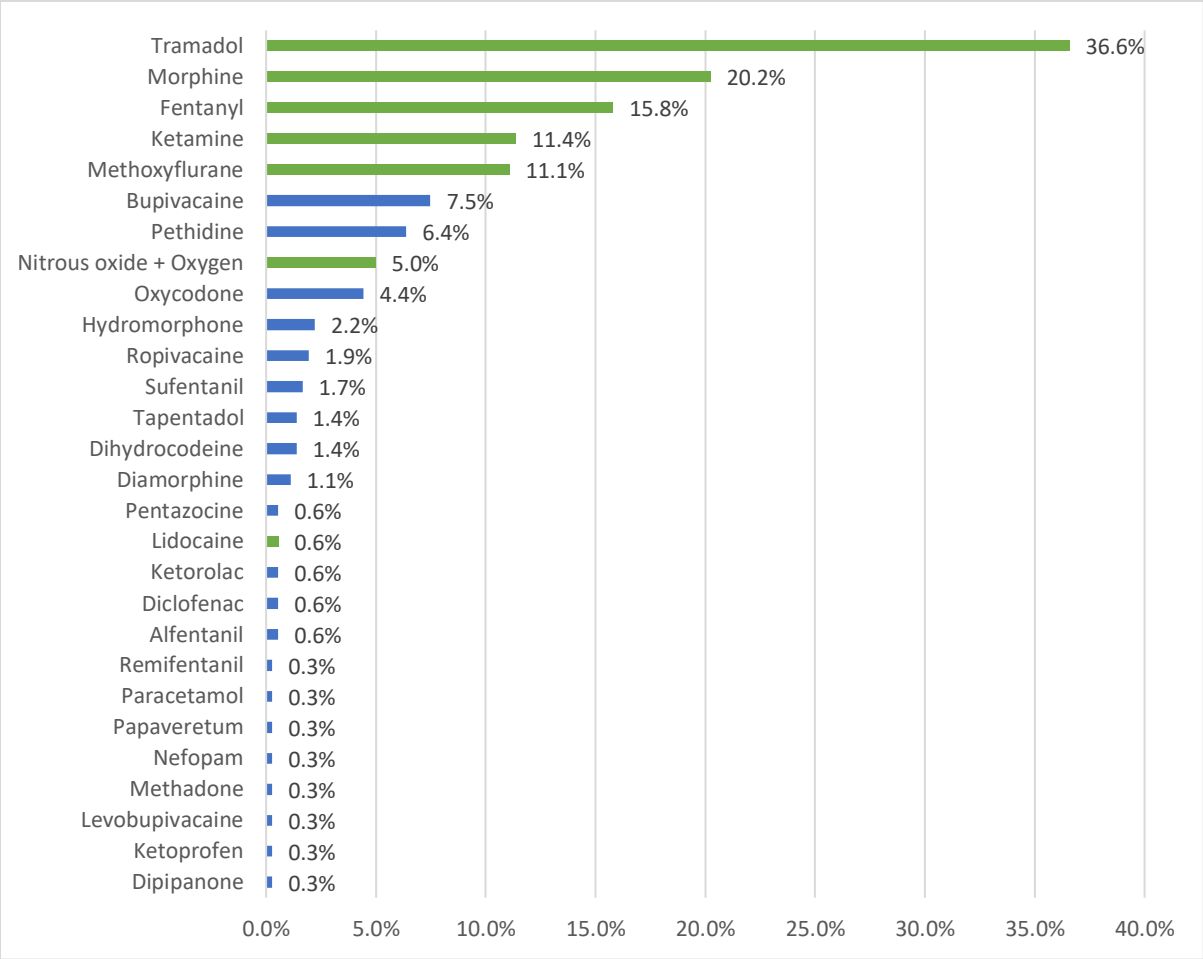


Figure 87 Proportion (%) of team physicians reporting which medicine they prefer to use for emergency analgesia for severe pain on the field of play due to serious injury in athletes (n=361) [green: listed in revised OPF]

Analgesia with sedation requiring rapid onset on the field of play

Team physicians were asked which medication they prefer to use for analgesia with sedation requiring rapid onset on the field of play. The most commonly preferred drugs were fentanyl (22.8%, n=81), tramadol (19.4%, n=69), morphine (16.9%, n=60) and ketamine (15.4%, n=55). Other drugs for this use were preferred by less than 10% of physicians.

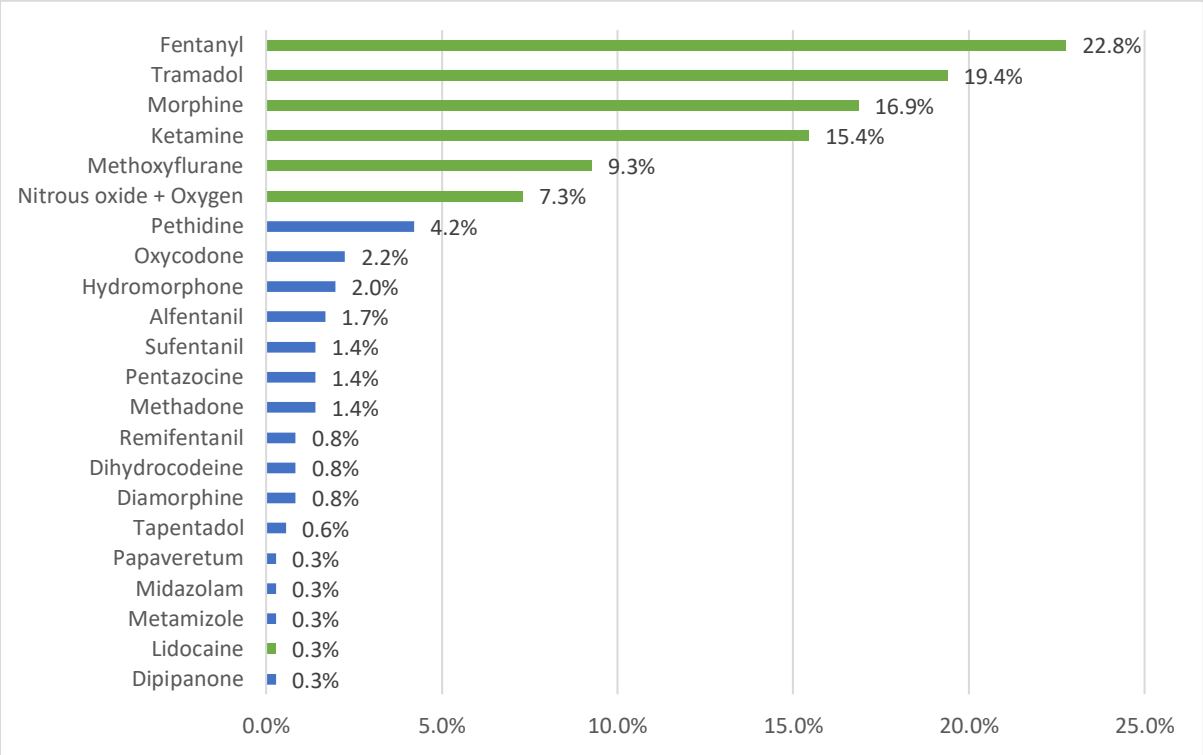


Figure 88 Proportion (%) of team physicians reporting which medication they prefer to use for analgesia with sedation requiring rapid onset on the field of play (n=356) [green: listed in revised OPF]

Topical medicines

Topical medicines for pain and inflammation

Team physicians were asked which topical medicine they most frequently prescribe for pain and inflammation due to sports-related conditions. The three most commonly prescribed drugs were NSAIDs including diclofenac (78.2%, n=297), ibuprofen (33.4%, n=127) and ketoprofen (27.1%, n=103). Other drugs included lidocaine (23.2%, n=88), menthol (21.1%, n=80) and capsaicin (15.8%, n=60). Other topical medicines for pain and inflammation were prescribed by less than 12% of responding physicians.

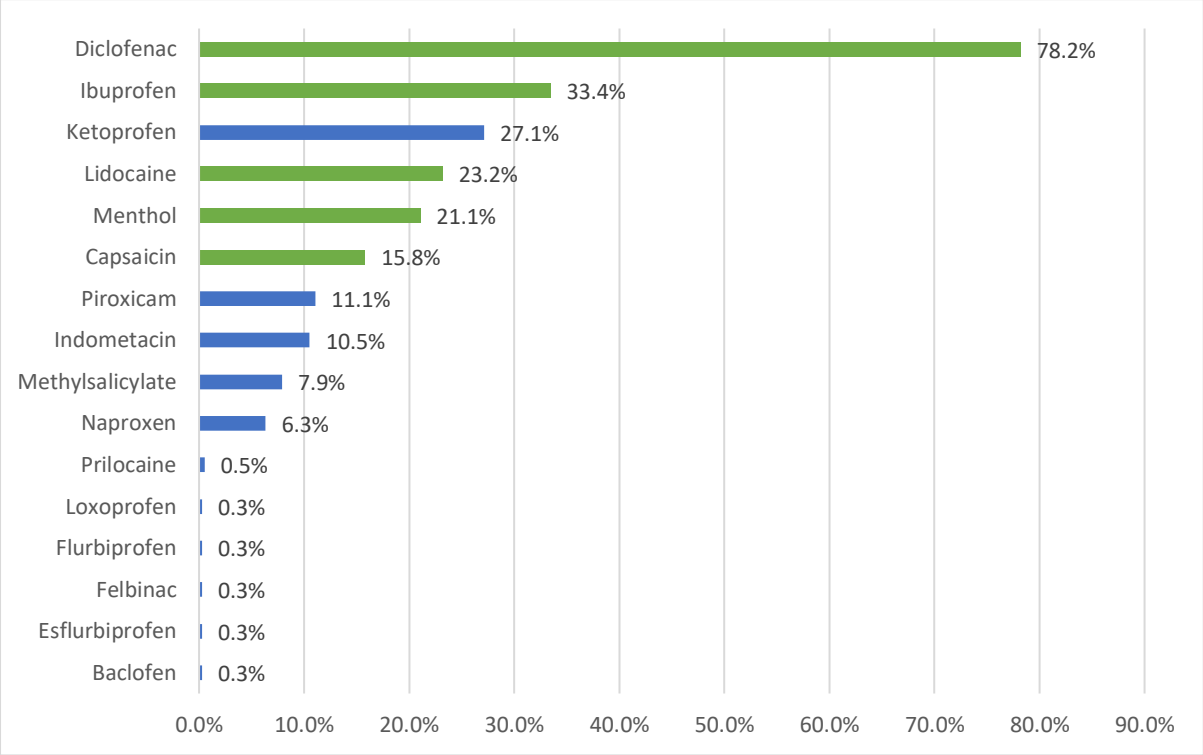


Figure 89 Proportion (%) of team physicians reporting which topical medicine they most frequently prescribe for pain and inflammation due to sports-related conditions (n=380) [green: listed in revised OPF]

Potential for follow-up studies with the sample population

Of all respondents, 77.2% (n=295) agreed that they would be happy to be contacted in the future to participate in follow-up studies for this project or similar research.

4.6 DISCUSSION

Prior to Tokyo 2020, for every edition of the Olympic Games, a completely new set of drugs was put together, through a different selection process each time, undertaken by medical experts in each host country.

As such, medicines available to the athletes at each edition of the Olympic Games has varied, and it is no wonder that over the many editions of the Olympic Games, teams have opted to bring their own medicines in their entirety rather than try to count on the local provision. The culture of teams importing most of their stock drugs, rather than obtaining them locally, can only be changed through provision of a more relevant selection of drugs that are used internationally and that are matched to the clinical need of the athletes attending the games. This was the primary reason why the OPF was developed in the first instance.

Phase Two of this research involved evaluating the prevalence of actual medicine use by athletes across both the Tokyo and Beijing Olympics and comparing it to the existing OPF to identify potential improvements to the OPF in terms of better representing the medicines athletes are taking. Through the addition of new drugs and the removal of others, a revised OPF was recommended to be implemented at future games which better meets the needs of the athletes. Subsequently, the resulting formulary was compared to the prescribing preferences and anticipated drug use of team physicians through a review of imported team medicines and the survey of team physicians to further validate the applicability of the revised recommended formulary.

In addition, through this study a comprehensive picture of the prevalence of the use of drugs for pain and inflammation across different demographics and home regions of the athletes at the Olympic Games was presented.

4.6.1 General findings

Prevalence of PI drug use by athletes

The findings of the study provide valuable insights into the prevalence of PI medication use among athletes participating in the Olympic Games. The results demonstrate a significant difference in PI medication use between athletes competing in the Tokyo 2020 Summer Games and the Beijing 2022 Olympic Winter Games. At the Summer Olympics, the prevalence of PI medication use was significantly higher (39.4%), compared the Winter Olympics (29.3%; $p<0.001$). The overall prevalence of athletes across both Games in the combined study population of 6155 athletes was 36.7%.

It is interesting to note that the IOC Injury and Illness Surveillance Study reported that of the 11,315 athletes followed up during the Tokyo 2020 Summer Olympics, 9% incurred an injury during the games,[40] and of 2,848 athletes followed up during the Beijing 2022 Winter Olympics, 10% incurred an injury during the course of the Games.[41] This difference in prevalence of PI medication use compared with known rates of games-time injury suggests that the conditions being treated are likely to pre-existing from before the start of the games.

The results show that the use of PI medications among athletes varies significantly across different OPF classes and routes of administration. Oral NSAIDs were identified as the most prevalent class and route of PI medication, with 25.6% of athletes reporting their use, followed by other oral non-opioid analgesics with a prevalence of 9.8%. These findings are consistent with previous studies looking at use of medications by athletes at major games which also indicated that NSAIDs are the most commonly used medication for pain management and inflammation control compared to other classes of drugs.[25]

This relatively high prevalence of PI medication use by athletes compared to other types of medications highlights the importance of the need to provide a comprehensive and evidence-based selection of PI medicines to be available for prescribing through the polyclinic pharmacy during the games. It is essential that any formulary must present the safest and most effective treatment options for the athlete and provide team physicians with a range of

drugs that meets their prescribing choices. The formulary must be representative of the most common drugs that are required and used by athletes, and which are being actively prescribed by the physicians that care for them from practically every country of the world. Given that PI medications are some of the most commonly used types of treatments for athletes in the games setting compared to other drugs that are listed on the OPF, a more comprehensive range of these drugs is justified, and the selection process used to determine which drugs are on the list should consider the types of drugs that are actually being used by athletes and prescribed by their physicians.

The formulary must also provide options for continuation of treatment for athletes while they are away from home in the host country of the games. As shown by the doping control form declarations, which require a declaration of medications used in the prior 7 days, many athletes are already on some sort of drug treatment regimen prior to arriving at the games. Many of these athletes will require ongoing treatment with the same drugs, or closely matched clinical alternatives while at the games. The selection of drugs for the formulary must provide for this, and is another reason why the formulary must best represent the spectrum of treatments that athletes are already taking before they arrive at the games.

For this reason, a formulary at the Olympic Games will have a wider selection of drugs within a clinical class to account for this. This can be seen on the resulting recommended OPF within the NSAID category, which are taken by 27% of all athletes at the Games ($p<0.001$). To be able to provide a continuation of treatment for most athletes, there are multiple drugs with broadly similar clinical indication provided for some routes. For example, there are 7 types of oral NSAIDSs provided, which in effect will cover 93% of all types oral NSAIDs declared by athletes.

Unique approach to an Olympic medicines formulary

The approach to selection of drugs for an Olympic formulary is somewhat different to that applied to other clinical setting such as local hospitals or local primary care clinics. For these local community settings, often just a single example of a drug within a pharmacological class and route of administration is provided for prescribing, based on clinical and cost

effectiveness, and local availability. By limiting the range of drugs on local formularies, the prescribing of treatments can be influenced to ensure that local populations receive what is considered the best choice of drug, within the wider healthcare budget.

The influence of the OPF on medicines use

However, for a temporary, short-term medical service as is provided for the Olympic Games, limiting the selection of drugs for the formulary may have a number of effects. Firstly, it will influence the drugs that teams carry with them to the games, as if a drug that is preferred for prescribing in one of the participating countries, but not provided on the formulary, they will likely import it themselves. Teams are informed of the games formulary around 6 months prior to the Games, and so have plenty of time to review the list and plan and prepare their own stock to import for their team. As can be seen by the team physician survey, 84.7% (n=321) of team physicians reported that most (>75%) or all of their prescriptions could be covered by their own stock and 70.9% (n=269) stated that either few (<25%) or no prescriptions would be expected to be obtained via the polyclinic pharmacy. Therefore, by limiting the choice of drugs on the games formulary, the influence on prescribing will likely be limited, but will result in more teams bringing more of the drugs they choose to prescribe if they are not accessible through the host country medical services.

Shifting the balance of medicines sourcing

By comparing the limited list of drugs on the pharmacy dispensing records, with the extensive number of examples provided through the doping control form declarations, it is clear that most of the drugs for PI were obtained through sources outside of the games pharmacy service.[196 197] As shown by this study, across both the Tokyo and Beijing Olympic Games, 91% (n=3155) of unique records of actual PI use for athletes came through doping control form declarations and needle use declarations, compared with only 9% (n=308) of unique PI actual-use records for athletes recorded through the games pharmacy service.[196 197] This clearly illustrates that currently there is a greater reliance on sources of medicines outside of those provided through the host country medical services.

A truly successful games formulary would result in all team physicians from every country using the medicines provided by the host country for the treatment of their athletes. But given the variance in medical and prescribing practice around the world, a one-stop formulary solution will be difficult to ever achieve through a single, rational list of drugs at this event. However, by providing a selection of drugs that meets the majority of clinical needs and prescribing choice, the shift in reliance on the medicines of the host country compared to imported medicines can be slowly instigated.

To shift the sourcing of medicines to local sources, and to decrease the need for teams to import vast quantities of medicines, the trust in the pharmacy services at major games needs to be gradually improved. The standardisation of the formulary is a major step towards achieving this trust by reassuring team physicians that their needs can be met locally.[12 13]

In addition, improved awareness strategies and early communication to inform teams about what medicines will be locally available while at the games is necessary so that they can prepare just the minimum set of drugs to import, reducing the medications they carry to specialist medicines needed for patients with long-term or pre-existing conditions which are not available at the games.[12] Reducing the need to import medicines to a Games will inevitably lead to reduced cost, reduce wastage and a significant reduction of the carbon footprint that results in the transport of multiple large stocks of medicines to the host country.

Considerations for prohibited drugs in sport

The status of medications according to the *WADA List of Prohibited Substances and Methods*[145] may also be an influencing factor on the types of PI medications prescribed to athletes. For example, some opioid analgesic drugs are prohibited to be taken by athletes during the in-competition period, including for example, oxycodone, oxymorphone, and hydromorphone. And glucocorticoid drugs are prohibited to be taken by systemic routes of administration including oral, rectal and injectable routes. The prevalence of both strong opioid medications and systemic glucocorticoid use is thus very low compared to other drugs

that are not prohibited in athletes, although they can still be used for essential medical treatment if a Therapeutic Use Exemption (TUE) is applied for their use.[198]

The use of tramadol at the time of the Tokyo 2020 and Beijing 2022 Olympic Games was permitted for competing athletes and represented 35% of all opioid analgesics used by athletes. However, from 1 January 2024, the use of Tramadol is prohibited during the in-competition period in sport, and a TUE will be required to be applied for athletes taking this drug.[146] It is likely that the prevalence of tramadol use in athletes will significantly decrease during 2024, and we will observe a shift in analgesic prescribing across all sports to other permitted alternatives.

Differences in PI use between males and female athletes

The results indicate a higher prevalence of PI medication use among female athletes (44.1%) compared to male athletes (30.0%). The observed difference was statistically significant ($p<0.001$), indicating that female athletes are more likely to use PI medications than males in the Olympic Games setting. The results also revealed differences in males and females between use of medications within specific medication classes, with the most significant disparities observed in the use of NSAIDs and non-opioid analgesics. Female athletes demonstrated a higher prevalence of NSAID use (33.4%) compared to male athletes (26.0%; $p<0.001$). Similarly, the use of non-opioid analgesics was more prevalent among female athletes (13.3%) than male athletes (7.8%; $p<0.001$).

These findings are not unique to the sport setting. The US Centers for Disease Control and Prevention (CDC) reported that in any 30-day period, prescription pain medication use of any type was higher among women (12.6%) compared with men (8.7%), with multiple non-opioid use also higher among women (6.2%) than among men (3.8%) as established through a national survey in the US from 2015-2018.[199] In a similar survey in Sweden, 34.8% of women and 21.4% of men had used pain medications during a 2 week period (n=5404).[200]

This finding is particularly interesting given that the IOC Injury and Illness Study reported no significant difference in overall injury incidence between women (8.6 injuries per 100

athletes) and men (9.6 injuries per 100 athletes) at the Tokyo 2020 Olympic Games,[40] and similarly no significant difference in overall injury incidence between women (10.0 injuries per 100 athletes) and men (8.7 injuries per 100 athletes) at the Beijing 2022 Olympic Winter Games.[41] While the injury rates between male and female athletes have been shown to be similar, the reliance on PI medications, specifically NSAIDs and non-opioid analgesics, is significantly higher among female athletes. This disparity warrants further investigation to understand whether the underlying reasons are related to physiological differences in pain perception and management between males and females, or social or cultural differences in the selection and prescribing of treatments for male versus female athletes, to ensure optimal and equitable medical support for all athletes, irrespective of their sex.

Differences in PI use between age groups

This study examined the prevalence of PI medication use among athletes across different age groups. The results revealed a significant difference in PI medication use between age groups ($p<0.001$), suggesting that age may play a significant role in the prevalence of PI medication use among athletes. The findings indicate that older athletes had a higher prevalence of PI medication use compared to younger athletes. The highest prevalence of PI medication use was observed among athletes aged 30-34 (42.0%), followed closely by those aged 35-39 (41.8%) and 40 and over (39.8%). In contrast, the lowest prevalence rates were found among athletes aged 19 and under (27.4%) and those aged 20-24 (31.7%).

These findings highlight that age affects the use of PI medication use among athletes. These results could indicate an increased susceptibility to pain or injury in older athletes due to the physiological wear and tear associated with long-term sports involvement. This result might also suggest that older athletes, having more experience in their sports, may be more knowledgeable and willing to use PI medications for managing injuries and maintaining performance.

Conversely, the relatively lower prevalence of PI medication use among younger athletes might be attributable to their generally better physical health and potentially reduced

exposure over time to strenuous training and competition schedules. It could also reflect a lesser awareness or willingness among these age groups to use PI medications.

While this study provides interesting insights, it also raises important questions for future research and the need to further explore the reasons for these age-related disparities in PI medication use to understand whether physiological, psychological, or educational factors are involved. The study also brings to light the potential need for strategies to minimise the reliance on PI medications, particularly among older athletes. These could include increased emphasis on injury prevention, proper rest and recovery techniques, and education around appropriate use of medicines and also non-pharmacological pain management strategies.

Differences in PI use between global regions

The study examined the prevalence of pain intervention (PI) medication use among athletes across various global regions, with the findings indicating a significant variation in PI medication use between regions ($p<0.0001$). The Pacific region had the highest prevalence, with 52.2% of athletes reporting PI medication use, followed by South America at 43.4%. In contrast, the Asia region showed the lowest prevalence rate of 28.0%.

These findings suggest that region-specific factors might play some role in the observed pattern of PI medication use. Such factors might include differences in the sports played and their risks, varying attitudes toward medication use, differences in medical practice, cultural attitudes towards pain management, prescribing preferences of team physicians, or healthcare access and medicines availability.

Given that the OPF needs to cater to athletes from every region of the world, the regional variation in drug use was not factored into the selection process for drugs on the revised OPF, but rather a unified global approach was taken. However, should the OPF be adapted for use at regional or national events by any organisation, then analysis of PI medication use at country-level could be considered to ensure the formulary is best tailored to the needs of athletes in that region.

Differences in PI use between Summer and Winter Olympics

The results of this research indicate that there is no significant difference between the actual use of PI medications by athletes between the Summer and Winter Olympics for all OPF classes, except for corticosteroids for intra-articular use, which showed a significantly higher prevalence of use in Tokyo (3.5%) compared to Beijing (1.4%) ($p<0.05$). This finding suggests that the type and prevalence of PI medications is broadly consistent across both games, indicating that the approach to a unified list of medicines on the OPF is appropriate and can continue to be recommended for both the Summer and Winter Olympic Games going forward.

The reduction of use injectable corticosteroids during the Beijing 2022 compared to Tokyo 2020 can be explained by the introduction of a new regulation by WADA prior to the Beijing 2022 Olympics. From 1 January 2022, according to the 2022 *WADA List of Prohibited Substances and Methods*, all injectable glucocorticoids were designated as prohibited during the in-competition period in all sports, unless a Therapeutic Use Exemption was applied for their use.[201] The introduction of this rule has likely influenced the choice of treatments, where since 1 January 2022, physicians were opting for permitted alternatives rather than have to submit a TUE requiring justification of the use of any injectable corticosteroid.

4.6.2 Selecting the PI medications for inclusion on the revised OPF

The study showed that the majority of the drugs currently represented on the OPF were actually used to varied extents by athletes at the games. However, the results indicated that there were some drugs frequently used by athletes that were not included on the current OPF, and there were some drugs listed on the current OPF that were rarely used by athletes during these two major events. By systematically applying the cut-off threshold for inclusion to each separate OPF class and route subset, we were able to recommend a revised list of drugs for inclusion on the OPF. This approach ensured that the recommended drugs were more relevant to the athlete population and the unique demands of athletes in the Olympic Games setting.

Recommending drugs for inclusion on the revised OPF

Using the Formulary Medication Match Website report (see Appendix 4) for each cut-off threshold for each class and route category, the set of drugs for the recommended revised edition of the OPF were made. Drugs used by athletes within the cut-off were included (green and orange coded). Drugs not used by athletes (red coded) were recommended to be deleted from the OPF.

The color-coded report allowed for easy identification of drugs that were used by athletes and already on the OPF (green), drugs that were used by athletes but not currently on the OPF (orange), and drugs currently listed on the OPF but not used at the selected cut-off threshold (red). This dynamic tool was not only been key in the evaluation of the current OPF compared to actual drug usage by athletes, but it can also be used by future games organisers to make informed decisions about the appropriate drugs to include in future editions of the OPF.

Application of the exception rules

In order to ensure patient safety and minimise duplication of drugs with the same indication and route of administration, specific exceptions were adopted to guide the inclusion of drugs on the revised OPF. These exceptions considered the frequency of drug use, potential clinical alternatives, potential risks and harms to athlete health, and the necessity of essential drugs for emergency or life-threatening conditions.

These exception rules enabled a reasonable rationalisation of numerous examples of medications with a category into a more efficient list to be stocked at the games. It enabled preparations with low prevalence of athlete use to be omitted in favour of other interchangeable clinical alternatives. But the rules enabled drugs for emergency use, such as morphine, to be retained on the formulary despite few or no records of athlete use, as they were deemed essential for emergency treatment. The rules enabled a number of combination products (such as tramadol + paracetamol) to be omitted due to low prevalence of use, but with the individual drugs remaining as treatment options in their single-agent formulations.

The exception rules also resulted in nimesulide, piroxicam and metamizole being excluded due to safety concerns.

For multiple drugs within the same class and route, the cut-off value of 0.2% prevalence worked well to provide a manageable list of drugs that could be realistically stocked at the Olympic Games, while addressing the vast majority of athlete needs. However, when applying the OPF to the next Olympic Games, the prevalence data should be used in conjunction with the list of drugs to inform the procurement and stock levels kept in the polyclinic pharmacy. For example, for oral NSAIDS, ibuprofen was used by 9.52% of athletes compared to meloxicam used by 0.8% of athletes. As such, the anticipated volume of stock purchased for the games should reflect this, with a roughly 10-fold higher volume of ibuprofen stocked than meloxicam. This approach to procurement of medication stock should prove effective in ensuring minimum wastage and lowest costs.

4.6.3 Validation of the revised OPF using drug importation records

Comparison of imported team medications with the revised OPF

Comparing the lists of drugs on the revised OPF with the prevalence of drugs imported as team stock, we observed a high level of agreement between the two datasets. The revised OPF was found to include most frequently stocked medications in 94% (17 of 18) clinical categories represented on the OPF.

For example, for the NSAID category which was the most common class of drugs used in the Olympic Games setting,[196 197] the 2 most frequently stocked NSAID injections were included on the revised OPF including diclofenac (29%, n=45) and ketorolac (12%, n=18). The 6 most frequently stocked oral NSAIDs were included on the revised OPF including diclofenac (53%, n=82), ibuprofen (49%, n=77), aspirin (46%, n=72), naproxen (26%, n=41), meloxicam (19%, n=29), ketoprofen (16%, n=25) and ketorolac (11%, n=17). In addition, the most frequently stocked rectal, topical, and transdermal NSAIDs were included, which were diclofenac (rectal: 9%, n=14; topical: 48%, n=75; transdermal: 15%, n=24).

However, some medications and routes were not included on the revised OPF due to safety concerns (including rofecoxib, metamizole, nimesulide and piroxicam)[188 190 194 186 187 188] or because of lack of evidence of actual use in athletes (including injectable COX-2 inhibitors, intranasal opioids, rectal paracetamol, topical skeletal muscle relaxants, and transdermal preparations for massage or physical therapy).

These results indicate that the revised OPF, which was derived from the actual drug use patterns of athletes, is broadly consistent with the medications that NOC medical teams expect to be potentially needed during the Olympic Games. This suggests that the revised OPF is also well-suited to meet the anticipated prescribing needs of the team physicians during the Olympic Games.

The strong agreement between the revised OPF and the importation data further validates our approach in revising the formulary based on actual drug use data collected during the Tokyo 2020 and Beijing 2022 Olympic Games, and the methodology used to determine the cut-off threshold for inclusion. This validation provides additional evidence that our approach to revising the OPF was reliable and can be used to inform decisions about the appropriate drugs to include on the formulary for future Olympic Games.

The current extent of importation of stock drugs by teams, and the responses provided through the team physician survey indicate a general preference among team physicians to rely on their own stock, with the likely intention to ensure their prescribing preferences can always be met. However, in providing a list of drugs which can be accessed via the pharmacy in the athlete village, matched to what team physicians are prescribing for athletes, the burden on NOC medical teams to import their own stock of additional medications can be greatly reduced.

4.6.4 Validation of the revised OPF through the team physician survey

This part of the study aimed to evaluate the revised list of drugs on the OPF against the results of the team physician survey, which was a cross-sectional study undertaken during the Tokyo

2020 and Beijing 2022 Olympic and Paralympic Games. The survey explored the most preferred and frequently prescribed medications and routes of administration for various pain and inflammation indications for sports-related conditions in athletes.

The sample size consisted of 382 team physicians, of a total of 415 physicians who were invited to participate in the study, giving a response rate of 92%. The total number of team physicians attending either of the games was not able to be accurately determined, as team physicians were not uniquely identified from other team members through the games accreditation systems. However, it was known that many team physicians worked at both the Olympic and Paralympic Games, and some for both the Tokyo and Beijing editions of the games. The responding team physicians represented 120 (58%) of the 205 different countries participating. Although the study sought completion of the survey from a team physician from every team who had one accompanying them, it was recognised that some teams did not have a team physician accompanying them to the games. However, the range of countries of respondents of the survey presented a good cross-section of countries, with every populated continent of the world represented.

One of the key findings of the survey was that the majority of team physicians (76.1%, n=290 of 382) reported that most or all of their general prescribing needs were covered by the existing set of drugs provided by the existing OPF. Furthermore, 73% (n=277) reported that most or all of their prescriptions for pain and inflammation could be covered by the existing OPF. This result indicates that in its original format, the existing OPF was already reasonably effective in addressing the majority of PI medication needs of athletes during the games from the team physician perspective. However, to evaluate whether the revised OPF better meets their prescribing needs, the same survey should be repeated at future editions of the games after the implementation of the revised optimised OPF.

The survey results also highlighted that the majority of team physicians (66%, n=250) expected that 30% or less of athletes would require PI medications, while 21.6% (n=82) of 382 physicians expected that 31-60% of athletes would need such medications. However, through the analysis of the actual-use data, the prevalence of PI medication usage among the 6,155

athletes in the study population was found to be 36.7% ($p<0.001$), meaning that the physicians surveyed generally underestimated the proportion of athletes who would require PI medications during the games.

Given that much of the drug use was self-reported by athletes, this potentially indicates that in some cases, athletes might be taking PI medications that have been either self-prescribed or obtained via multiple prescribers, which may account for the higher usage indicated by the evidence of actual use, compared with the survey. This is entirely conceivable as a number of the most commonly reported PI medications, including for example, paracetamol which was used by 9.3% (n=571) of athletes, and ibuprofen used by 9.5% (n=586) of athletes, are readily available to purchase over-the-counter in pharmacies and supermarkets around the world.

Comparison of physician prescribing preferences with the revised OPF

Overall, the findings of the team physician survey demonstrate that the revised OPF was well aligned with the prescribing preferences of team physicians. For every clinical indication presented in the survey, every one, or more, of the topmost frequently prescribed medications were included on the revised OPF. In addition, the revised OPF provided the most frequently prescribed drugs for oral, injectable, and topical medicines. This suggests that the revised OPF could effectively address both the clinical need and the vast majority of prescribing preferences of team physicians when treating athletes for pain and inflammation due to sports-related conditions.

However, there were a few instances where some of the top-prescribed medications were not included on the revised OPF. For example, the second and third most frequently prescribed oral skeletal muscle relaxants were not included in the revised OPF due to evidence of lower actual use by athletes. In such cases, alternative medications were included on the revised OPF based on evidence of higher prevalence of use among athletes.

4.7 CONCLUSION

This phase of research aimed to recommend a list of PI medications that would provide an optimal formulary of essential medicines to be implemented at future Olympic Games. Through this study, the existing OPF was revised by comparing it with a dataset representing the prevalence of actual drug usage in 6155 athletes attending the Tokyo 2020 and Beijing 2022 Olympic Games, which was collated through analysis of declarations of medicines use on the doping control forms, polyclinic pharmacy dispensing reports, and declaration of injections administered by the team physicians during both events.

The study dynamically applied a systematic cut-off threshold for inclusion to recommend a revised list of drugs for each OPF class and route, ensuring that selected drugs were more relevant to the athlete population in the Olympic Games setting (see Table 81). The resulting set of PI medications takes into account exceptions for inclusion to ensure patient safety and minimise duplication of drugs on the OPF with the same indication and route of administration, while also providing a selection of medicines that meets the medication needs of the majority of athletes.

The resulting revised OPF was subsequently assessed using two approaches: a comparative analysis of the medications imported by teams (n=156) as stock for use at the Tokyo and Beijing Olympic Games, and a survey involving team physicians (n=382) examining their prescribing practices relating to pain and inflammation management in athletes. The study found that the revised OPF covers the vast majority of the PI medications that Olympic medical teams carry as stock, and is closely aligned with the prescribing preferences of the majority of team physicians for treating athletes for pain and inflammation due to sports-related conditions. These comparisons provide robust validation for the study's approach in recommending a suitable formulary that meets the needs of athletes in the Olympic Games setting.

The study also involved the development of an online visualisation tool (Appendix 4. The Formulary Medication Match Website), to compare any medicines formulary against

prevalence of drug use in any population. This dynamic tool can be continued to be used by future Olympic Games organisers to make informed decisions about the appropriate drugs to include in any future editions of the OPF to constantly revise the selection of drugs to ensure athletes' current needs are always met.

Finally, a number of drugs with known harmful risks for athletes, but which are still being prescribed and taken by athletes, were identified through this research. This warrants specific actions and further education within the sports healthcare community to actively caution against their use.

Overall, this study provided a quantitative measure to determine the selection of drugs for the revised formulary with a clear cut-off for inclusion or exclusion. The results and methodology are reproducible, and a new model has been developed, which includes an interactive online tool, that can be applied to future Olympic Games to constantly revise the selection of drugs to ensure the athletes' current needs are always met. Ultimately, the revised OPF will provide athletes with access to the medications they require during the Olympic Games, reduce the risks to health from harmful drugs, while reducing the burden on NOC medical teams to import their own stock of additional medications.

CHAPTER 5. GENERAL DISCUSSION: THE ESSENTIAL & OPTIMAL FORMULARY

All of the objectives set out at the outset of this research were met over the course of a 4-year period. The first phase of research, which acted as a proof-of-concept pilot study, was undertaken during the Minsk 2019 European Games, and focussed on athletes and their physicians from 50 European countries, competing in summer sports. The second phase of the research was undertaken at the Tokyo 2020 Olympic Games and the Beijing 2022 Olympic Winter Games and focussed on athletes, and their physicians, from 205 countries covering every winter and summer Olympic sport.

The data collection process was complex, but comprehensively covered all available and reliable sources of drug usage data at the games, with the exception of personal physician-patient medical consultation and emergency paramedic treatment records. The data collection was successfully undertaken to plan, despite a delay in the research due to the postponement of the Tokyo Olympics by a year and consisted of the following components to comprehensively assess the research question: i) medications declared by athletes on doping control forms, ii) pharmacy dispensing reports from athlete village pharmacy, iii) injection declaration forms from the Tokyo 2020 and Beijing 2022 Olympic Games, and iv) Review of declarations of imported team medication stock. In addition, a cross-sectional survey of team physicians across European, Olympic and Paralympic games was successfully delivered to plan.

5.1 Review of the research aims

The first aim of the research was to determine whether the OPF met the clinical needs of the athlete patients, and the prescribing expectations of team physicians relating to the use of PI medications for the treatment of musculoskeletal sports injury.

It was through the body of research conducted in Phase One at the European Games, where we were able to first ascertain the extent of use of medications for treatment of pain and/or

inflammation by athletes through the component involving the review of declared medications on the doping control form. The results showed that 23.1% (n=231) of athletes had used one or more PI medications in the previous 7 days, with NSAIDs accounting for 70.8% and non-opioid analgesics accounting for 19.4% of them, providing evidence of a high prevalence of use of these medications compared to the general population, which been reported to be around 10% for analgesic medication use.[199] These results highlight the importance of having a comprehensive formulary in terms of PI medications to meet the high demands of athletes in this environment.

More importantly, the aim of the study was to understand whether formulary met the clinical needs of the athletes, with the results of the doping control form review at the European Games providing a clear account of this. For all PI medications declared by athletes, 80.0% (n=252) were specifically listed on the OPF, showing that the OPF could meet their needs in the majority of cases, but that there was room for improvement in terms of providing an even better match of more medications. However, the review of the other 20% of medications not listed on the OPF showed that a large proportion (18.7%, n=59) could substituted with an acceptable alternative from the OPF, in the same pharmacological class and clinical indication. Only 1.3% (n=4) of all medication declarations did not have any suitable therapeutic alternative on the OPF.

This key finding showed that the OPF was already reasonably effective in meeting the clinical needs of the athletes, but improvements could be made to provide an even more targeted set of PI medicines that reflect the specific examples of drugs that athletes were known to take. The subsequent research conducted in Phase Two was the basis for determining what these improvements should be, based on direct evidence of athlete use.

The pharmacy dispensing data reviewed at the European Games, were less enlightening in terms of assessing whether the OPF matched what athletes were taking at the games. The reason for this was that the vast majority of drugs dispensed by the pharmacy were already on the OPF, and so physicians could only prescribe these options. This component of study could therefore not assess whether the preferred treatment or an exact match was available,

or whether a substituted drug was prescribed. It did, however, provide further evidence to validate the extent of use of various PI medications, including NSAIDs, which represented 68% of all PI medications dispensed from the pharmacy, which closely corresponded with the proportion of NSAIDs declared through the doping control forms (70%). It also enabled a side understanding of the demands of athletes from various sports, and the use of pharmacy services by non-athletes at the games.

The datasets collected in Phase One at the European Games relating to imported team stock, and the results of the team physician survey enabled us to address the second part of the aims to understand whether the OPF met the prescribing expectations of team physicians. The review of imported team medication stock showed that 36% of all PI medications were listed on the OPF, but 44% could be covered by a suitable alternative in the same therapeutic class for the same indication. And of all physicians completing the team physician survey, 68.3% (n=41) indicated that 75-100% of PI medications they preferred to prescribe were covered by the OPF. These components showed that the preferences of the physicians were already largely met, but again, could be improved.

The aims relating to Phase Two of the research conducted during Tokyo 2020 and Beijing 2022 were to test to what extent the OPF matched the needs of athletes in the Olympic environment and to propose revisions to the OPF to present a revised and optimised set of essential PI medications based on actual athlete drug usage, to better meet the clinical needs of the athletes.

To assess this question in the main body of research in Phase Two at the Olympic Games, a completely different methodology was applied. In this phase, the existing OPF was compared to a much wider dataset representing direct evidence of PI medication use to establish prevalence, collected through multiple sources, and combined into a single dataset including: doping control forms, pharmacy dispensing records, and injection administration, which was a new set of data unique to this phase. The study involved a category-by-category comparison of each class of medications on the OPF list with the dataset representing prevalence of athlete use. Similar to the results of the European Games study, this analysis showed that the

majority of the PI drugs on the OPF were being used by athletes to varied extents, and the results (Section 4.3.2) also identified those which were not used at all.

The difference between the assessment of this aim in Phase Two, compared to Phase One was that in Phase Two, the prevalence in a population of 6155 Olympic athletes was determined for every medication listed on the OPF, plus any other PI medication athletes were taking but not listed. The focus of this phase was not to quantify the number of clinical substitutions could be made from the existing OPF to meet their needs (as was done in Phase One), but rather to move forward with constructing a new and optimised set of PI medications for the OPF based on first principles, best matched to the prevalence data that was available.

By systematically applying the prevalence-based threshold for inclusion of PI medications on the OPF, a revised list of 48 PI medications was recommended, with 9 new drug formulations added to the OPF, and 13 deleted (Table 81). This revised list of PI medications fully met the clinical needs of all athletes at the Olympic Games through either an exact match or a suitable clinical alternative in every case, with the exception of a small number of drugs with significant known risks or harms. An overall reduction of the numbers of medication preparations on the OPF was also achieved, but with a more targeted selection of drugs, which will inevitably lead to efficiencies and cost savings for future Olympic organisers.

Subsequent to the development of the revised set of PI medications, which was based on prevalence of use, the review of the imported team medications and the results of the team physician survey were used to evaluate to what extent this revised set of PI medications also met the prescribing expectations of the team physicians. This new revised list was found to include most frequently stocked medications by teams in 94% of therapeutic clinical categories represented. And for every clinical indication presented in the survey, 100% of the topmost frequently prescribed medications were included on the revised OPF. This suggested that the revised OPF could effectively address both the clinical need and the vast majority of prescribing preferences of team physicians when treating athletes for pain and inflammation due to sports-related conditions.

The final aim of this PhD research was also to establish a quantitative, reproducible approach to the selection of medicines for the OPF which could be implemented for future games to enable continual update the OPF over time to reflect the changing medication needs of athletes. This aim has been met through this research.

A systematic approach has been developed that will inevitably revolutionise the way medicines are selected for the Olympics, with immediate effect, starting from the Paris 2024 Olympic Games. One of the most innovative developments from this study was the introduction of the Formulary Medication Match Website, an online visualisation tool that can compare any medicines formulary against the prevalence of drug use in any population to inform the selection of medicines. This tool will be made available to the IOC to empower future Olympic Games organisers to continually update and improve the formulary, ensuring athletes' needs are always met (see Appendix 4).

Following the completion of this research, the revised resulting set of PI medicines for the OPF was recommended to the IOC for inclusion on the OPF, which when implemented will lead to a more optimised formulary that better serves the PI medication needs of elite athletes from around the world while they are at the games.

5.2 Review of the research methodology

The methodology used to address the research question evolved significantly over the course of the four years of research, with some major lessons being learnt from Phase One and subsequently applied to the main body of research conducted in Phase Two. The following section provides a review of the strengths and limitations of the methodology used for each component of the research, followed by an overall review of how each component was analysed in each phase.

5.2.1 Discussion of methodology for each component of research

i) Review of medications declared on doping control forms

The doping control form data provided the most extensive source of direct evidence of medication use by athletes, but several limitations must be acknowledged. Firstly, the accuracy of the data relied on the honesty of individual athletes declaring their personal substance use over the past 7 days, with substance use extending beyond a 7-days not captured as declaration of longer-term use was not required. Athletes generally attend major games from the opening to the close of the athlete village, which is usually about 14 days, and so the entire time period of the European Games may not necessarily be represented by these data.

It should be noted that at the Tokyo 2020 and Beijing 2022 Olympics, athletes were requested to stay for a reduced period of time to minimise the population of the village as a preventative measure during the Covid-19 pandemic; they were asked to arrive 2 days prior to the competition and leave within 2 days after, and so the declared data for the Olympics was probably fully representative of what they took while at the games. Should this study be repeated in the future, these factors should be recognised.

The doping control form data was only collected from athletes who had been selected for doping control testing. As a result there was not an equal balance of athletes from all participating countries, the reason being that the testing strategy at the games is based on known doping risks and can skew the balance of athletes tested, for example, athletes competing in sports with a higher risk of doping will be more likely selected for testing, and those from countries where doping has historically occurred may also be tested more.[202] Despite these limitations, the sample size was sufficiently large enough to at least include some athletes from every sport, and most (97%) countries participating in the games.

It should be acknowledged that since athletes knew that their declarations were being used for anti-doping purposes, there could be potential under-reporting or intentionally providing misinformation; if athletes were taking a substance, whether it be permitted or prohibited,

with the intention to cheat, it would be highly unlikely they would declare it on the form. This was not a significant concern for the study as most medications used for pain and/or inflammation are not prohibited in sport, with the exception of some opioid analgesics (such as morphine and fentanyl), which were unlikely to be reported on doping control forms anyway as they are used medically in the emergency setting.

A significant challenge encountered was the legibility and language of the handwritten declarations, with misspelled names and references to unregulated or unlicensed medicines. In instances where the identity of the substance required confirmation or was in a non-English language, resources such as *Google Translate*, *Martindale*,[171] manufacturer's official product information, and various Internet searches were employed to verify the identity of the declared products. The reliability of these resources varied, and so a hierarchy of resources used was in place as a quality control mechanism. *Martindale* was used as the primary reference where possible, which provided trusted information about medicines licenced in 43 countries,[171] followed by official manufacturer's product information. General internet searches were only used if these trusted sources could not provide confirmation of identity of the substance. The issue of handwriting legibility and potential error due to manual transcription was greatly reduced for Phase Two at the Olympic Games as the data were collected via an electronic form.

ii) Review of pharmacy dispensing reports from athlete village pharmacy

The pharmacy prescription data were provided electronically as an output of the pharmacy dispensing system, and so the identification of substances did not require the same level of translation and interpretation as the doping control form declarations. It was a highly reliable source of all medicines dispensed through the athlete village pharmacy, which was already in a format ready for analysis.

A potential for bias may be that the pharmacy was not accessed in the same way by different teams. The data show that some teams used the pharmacy extensively, but others rarely used the pharmacy at all. As a standalone dataset, the pharmacy data is therefore not representative of athletes from every sport or country. For example, at the European Games,

prescriptions for Belarusian patients accounted for 24.4% of prescriptions, because this was the primary source of medicines for the team. Other teams relied on imported stock medicines as their supply, which can be seen by the use of pharmacy by some of the larger teams present – at the European Games, the Great Britain team had 100 members,[183] but did not access the athlete village pharmacy at all.

Another potential for bias may have been that the athlete collected the medication from the pharmacy but never took it, although given that medications were for the treatment of pain or inflammation, which usually warrant immediate treatment, this type of bias was unlikely.

iii) Review of injection declarations

The inclusion of this set of data was specific for the Olympic Games. During the pilot phase at the European Games, this additional potential source of evidence of medication used was identified, and permission sought from the IOC to use this Phase Two. The data were provided as an export from the secure IOC electronic submission platform used by team physicians to submit the declarations to the IOC Medical and Scientific Commission. As such, were in a format that required minimal translation or data processing prior to analysis.

Given this was self-declared data, there was the potential for under-reporting. The low compliance of team physicians to the *IOC Needle Policy* has been reported through previous studies; fewer than 20% of NOCs submitted an injection declaration during the Sochi 2014 and PyeongChang 2018 Olympic Games.[203] At the Tokyo 2020 Olympics, only 12% of NOCs submitted a declaration.[204] The reasons for lack of submissions from some NOCs can be explained by the following reasons: a) some small NOCs do not have their own physician; b) athletes from NOCs who did not submit, were treated in the athlete village polyclinic where declarations were not required; c) that injections were not administered to athletes at all in some NOCs. Despite serious disciplinary consequences by the IOC, including sanctions for physicians if they are found to not comply with the policy,[28 29] the rate of compliance with the *IOC Needle Policy* is not fully understood, and so these data may not fully represent every injection actually administered to athletes during the games.

iv) Review of imported team stock medications

The declaration of imported medications was required by law in both Belarus, Japan, and China. At each games, this process is strictly enforced by the respective national Customs authorities, with all drug stock imported requiring an official permit, and inspections of stock made at the border at the point of entry.[11 195] For each games, the respective organising committees coordinated the declaration process in collaboration with the national authorities. As such, the reliability and validity of the data obtained was assured through a legal mandate. A structured template was used at each games to record the generic drug name, formulation, and quantity, which enabled the data to be easily processed.

The most significant limitation with this set of data was that the declarations did not necessarily represent actual use of the medication by athletes – it was not determined to what extent the stock medicines were ever used. The only way to determine what was used would be either: a) through the athlete medical records kept by the team physicians, or; b) through a review comparing the exported stock with the original import lists. Athlete medical records were not available for this study, and exported stock was not required to be declared, and so this level of understanding was unachievable through this research. For these reasons, this set of data was omitted in Phase Two as a source to determine prevalence of medication use, but rather used as a method of validation in terms of whether team stock expectations could be met by the revised set of PI medications.

v) Cross-sectional survey of team physicians

The online survey format was chosen for this component of the study given the scalability of the format in order to reach physicians who were located across various sites at each games. Most team physicians were based in the athlete village, but depending on the sports of the athletes under their care, a large number were also based at competition venues across the host city, or at satellite villages in other parts of the country. An online survey allowed all physicians at the games an opportunity to access the survey to participate in the study, which could be completed at their own pace. The fact that a similar survey had been successfully conducted during the Rio 2016 Olympic Games was also evidence that the format was effective in this setting.[25] Other formats were also originally considered, including focus

groups, and face-to-face interviews, but were considered too logistically challenging to be able to achieve in the games environment.

The recruitment strategies for the survey proved effective, with a very high response rate of 92% when conducted at the Olympic and Paralympic Games. The reason for such a high rate may have been somewhat attributed to the endorsement that the IOC and IPC senior medical and scientific directors gave to the survey at the team physicians meetings at each games, which probably served as a motivating factor for many of the respondents. However historically, participation in other research activities conducted by the IOC, including the IOC Injury and Illness Surveillance Study,[40 41] have always achieved a strong compliance by most NOCs, and thus a good response was expected for this survey. The sample size was, however, limited by: a) the numbers of team physicians attending the meetings in the athlete village, and; b) the list of personal email contact that the IOC and IPC medical departments had for the team physicians, and so the sample did not include every physician attending the games.

After the pilot phase at the European Games, the team physician survey underwent improvements to the format and questions. The results of the survey delivered at the European Games highlighted that there were a number of additional drugs being prescribed by team physicians than were not listed as options to select on the survey form, as they were identified through a free-type response. As a result, the form was improved and expanded to be more comprehensive of potential drugs for the various clinical indications asked by the survey questions.

In addition, it was realised that the multiple-choice answers enabling only a single response were too restrictive, as team physicians indicated that they often have a menu of drug options for the same clinical indication, in order to best tailor the treatment to the individual patient's needs. As such, the survey was modified to enable respondents to select more than one drug when answering questions, which resulted in findings that were more inclusive of the physicians wider choices.

In Phase One at the European Games, the survey was only delivered in English, which was the official language of these games. But for Phase Two, the translation of the survey into multiple languages including French, Spanish, Russian and Japanese for the version conducted at the Olympic Games ensured accessibility to a wider number of physicians, which also potentially contributed to the high response rate.

A limitation of this survey was the reliance on self-reported data from team physicians, which may be subject to recall bias or the potential for underreporting or overreporting. Additionally, the study may not capture the full range of medication preferences and practices among team physicians in every country due to the voluntary nature of participation in the survey, and the fact that teams from some countries did not have had a physician accompanying them to the games. The survey could potentially be repeated at subsequent games with the aim to reach team physicians from more countries, and to assess whether the prescribing preferences of team physicians change over time to assess the relevance of the OPF as it is revised periodically.

The survey provided a unique understanding of the use of emergency medications which was not captured or represented by the other datasets, as the actual-use data were not collected in the context of emergency care. The survey provided validation that the existing set of PI medications used for emergency analgesia on the field of play was appropriate. The top 5 responses from 361 team physicians confirmed that the current set of emergency drugs on the OPF were what they would use for these indications (Figure 87). In essence, the survey acted as an additional international peer review to that originally conducted in 2019 during the development of the first edition, reaffirming the appropriateness of the current OPF in relation to emergency medicines for analgesia.

Despite some limitations, the survey findings provide reliable information from a large and highly relevant population of team physicians as to their prescribing preferences for the treatment of sports-related conditions. This provided robust validation as to the appropriateness and applicability of the recommended revised and optimised OPF in terms of physician preference for future games.

5.2.2 Discussion of methodology used in each phase

Phase One

For the European Games, the analysis of the results was mainly qualitative, providing a descriptive account of potential improvements to the OPF based on each of the 4 datasets separately. As described above, there were significant limitations for each dataset in terms of them being representative of the entire athlete population when taken in isolation. While the European Games approach provided some interesting observations, it was not as statistically rigorous as the quantitative approach presented in Phase Two, and it did not provide a definitive system for recommending drugs for inclusion on the OPF. Most importantly, this Phase One proof-of-concept study highlighted that a robust quantitative approach to the methodology and analysis was needed to inform the selection of PI medications, which could be reproduced for future games. Phase One was also conducted in European athletes spanning 50 countries and so was limited in terms of its generalisability to the Olympic Games.

For the European Games, all datasets were considered equally in terms of assessing potential recommendations for inclusion or deletion of drugs from the formulary. However, this pilot phase established the need to base selection of drugs on direct evidence of actual use by athletes, rather than anticipated use by team physicians. It was concluded that constructing a list of medications based on stock carried or anticipated use, would result in a set of drugs of which many will never be used, or where multiple interchangeable drugs in the same therapeutic class would co-exist. Consequently, for Phase Two, only direct evidence of actual use of medications by athletes was used to revise the OPF.

Reflecting on the initial recommendations made in Phase One, the results indicated a potential need for additional drugs in the classes of NSAIDs, COX-2 inhibitors, opioids, glucocorticoids, and skeletal muscle relaxants to be considered for inclusion for future editions of the OPF. It was interesting to note that some of these improvements were also identified in Phase Two and were actually implemented in the revised PI medication list for the OPF. These included the addition of oral ketorolac, oral etoricoxib, transdermal diclofenac, injectable betamethasone, and the deletion of rectal paracetamol and oral

hydromorphone. This shows that there was some alignment in the recommendations for improvement from Phase One with those in Phase Two.

Phase Two

The methodology used for Phase Two differed to the qualitative approach used for the European Games study previously, in that it presented a definitive quantitative measure to determine the selection of drugs for the revised formulary with a clear cut-off for inclusion or exclusion. Unlike Phase One, it provided a structured, systematic, and reproducible approach for drug selection based primarily on prevalence of drug use by athletes.

The process of data collection changed over the course of the research with new and innovative technologies in testing being introduced during the research period. For the European Games, all the doping control form declarations were hand-written, and so it was necessary to manually transcribe the declarations from 999 paper forms, which was a hugely laborious task. For the first time ever, at the Tokyo Olympics an electronic system was used for the anti-doping testing program, which was subsequently used in Beijing, meaning the doping control form data could be extracted without the manual processing. Going forward, this electronic data capture will make it more achievable for future Olympic organisers to continually reevaluate the formulary using the approach developed in this study.

The research conducted in Tokyo and Beijing demonstrated greater power to reliably demonstrate the use of PI medications in the sample population, compared to the European Games. This was due to a larger proportion of athletes included in the sample because of the more comprehensive anti-doping testing programs implemented at the Olympics compared to the European Games, and an additional source of athlete drug use data obtained through the injection declarations through the *IOC Needle Policy* process. This significantly larger study population inevitably resulted in more robust analysis and conclusive results for the second phase of the study.

However, a limitation of the study was that the data collected was not entirely representative of all drug use during the games. There were three places where drug usage was also

recorded, but which was not accessible for the purpose of this study. 1) Firstly, in the medical records of all athlete patients attending the polyclinic in the athlete village, where the patient history, which may include medication history was required to be documented. However, athletes were also required to self-report all drugs use in the last 7 days on the Doping Control Form, and so it would be expected that, in any case, this information would be documented at the time of doping control. 2) Secondly, in the medical records maintained by the team physicians through their team medical provision. But again, this information would be expected to be self-reported by the athletes at the time of doping control. 3) Thirdly, in the medical records of the emergency medical teams, and paramedics that might have attended a critical incident.

The fact that the dataset did not fully capture the use of drugs in the emergency setting was a significant limitation of this study. The drug administration records from emergency medical teams on the field of play at venues, and the ambulance service, were not included in the dataset. And if an athlete underwent emergency treatment, it was unlikely that they went on to be tested through the doping control process, and so would not have had the opportunity to self-declare any drugs they were administered. As such, the model could not be reliably used to determine the selection of drugs for emergency use. This was acknowledged in the methodology of Phase Two, where such drugs were evaluated differently to others.

It is, however, important to note that the existing OPF list of analgesic drugs for emergency treatment underwent a rigorous selection process during the initial development of the OPF in 2018-2019. This included a review of global emergency medicine protocols and included the recommendations from a number of expert emergency physicians experienced in delivery of emergency services for Olympic Games and other mass public gatherings. As such, the recommendations for inclusion of specific emergency drugs on the revised OPF were not changed as a result of this study.

The methodology employed the "% of agreement" as a cut-off threshold to select medicines for the revised OPF. This referred to the level of concordance between the PI medications on the existing OPF with those used by athletes at the games. The list of PI medications on the

existing OPF served as the baseline reference list to which the actual usage data was compared to show which medications were actually used by athletes, and which were not. The % of agreement quantified the overlap between the drugs on the OPF and the drugs athletes were using. The cut-off threshold for inclusion of a drug for the revised OPF was set as the cumulative percentage of top drugs within each OPF class and route category which maximised the percentage of agreement with the OPF. This was ideally up to 100% meaning that all the PI medications on the revised and optimised list matched those that athletes were using.

The reason for using the % of agreement method was to make the OPF as relevant to athletes in terms of the medications they take as possible. If a high proportion of athletes were using a specific medication on the OPF, then the continued inclusion was relevant. Conversely, if a drug on the OPF was rarely or never used by athletes, its continued inclusion was revaluated.

Other cut-off levels such as arbitrary frequency counts, fixed rates of prevalence, or subjective decisions might not offer the same level of consistency across different categories. The method used provided a systematic, consistent, and transparent approach to evaluate all drug classes and administration routes, based on evidence of use, rather than relying on limited historical data or personal opinion.

It is important to note that the methodology did incorporate additional considerations and exceptions to ensure that essential or emergency drugs were not excluded, and that drugs with known safety risks were excluded, even if they met the % agreement threshold. The approach therefore combined the systematic rigor of the % of agreement threshold with these other exceptions to create a revised set of PI medications for the OPF that was practical for the games setting.

The other major shift in methodology that was implemented for Phase Two was the role of the team stock importation data and team physician survey results. In this phase, these data sources were repositioned as a method of validation of the revised OPF, rather than being a deciding factor in the selection of drugs. This approach was effective in being able to show

that the revised list of PI medications also served the anticipated drug prescribing needs of the majority of team physicians.

5.3 Athlete safety risks identified

Across all three of the games in this research, we have uncovered the use of a number of drugs still in use but documented to have significant safety concerns and which may present a risk to athlete health, including, during the Olympics, metazimole (0.54% athletes, n=33), piroxicam (0.28% athletes, n=17), nimesulide (0.68% athletes, n=42) and rofecoxib (carried by 1 team as stock). This research has shown that these drugs continue to be used by athletes and remain the preferred choice in their class by some physicians, despite strong clinical safety warnings issued by global regulatory agencies regarding their use for musculoskeletal injury. This finding is one of the most important discoveries of this research, which will be acted upon immediately and proactively through information and education to team physicians and athletes across the sports community, including at the Paris 2024 Olympic Games, and actively discouraged through specific warnings in future updates of the OPF regarding their inappropriate use in athletes.

5.4 Generalisability of the OPF to summer and winter games

The OPF was originally conceived to standardise the delivery of pharmacological needs for athletes participating in both summer and winter Olympic and Paralympic Games. At the time of writing the first edition of the OPF in 2019, it was uncertain if there were significant differences between the needs of winter sport athletes and summer sport athletes, and the compilation and peer review for the original OPF took a very general approach, based on previous published formularies at other games and best clinical evidence, rather than prevalence of medication use at the games.

A direct comparison of PI medication usage between the summer and winter Games was not possible during Phase One. However, the Phase Two of the research enabled such a comparison. The results showed no significant difference in the use of PI medications

between the Tokyo and Beijing Games, with the exception of glucocorticoid injections, where the reduction in use in Beijing compared with Tokyo could be explained by the prohibition by WADA of local injections from 1 January 2022. Consequently, we can confidently recommend the publication of a single list of PI inflammation medications that meet the needs of athletes at both summer and winter games.

5.5 Generalisability of the OPF to the Paralympic Games

For every edition of the Olympic and Paralympic Games, the medical and pharmacy service for each is developed in synergy, even though the respective oversight of medical services for each lies separately with either the IOC or IPC. The same organising committee in the host country is responsible for the operations of both games, and the games formulary is also always applied to both games. Because of this, the OPF was intended as a collaboration between the IOC and IPC for the application across both events. As such, the development of the first version, closely involved the medical experts of the IPC who were involved in the peer review process and ratification of the original OPF.

It is essential to note that the scope of this research has only focussed on evidence of actual use drug records of Olympic athletes during Tokyo and Beijing. The analysis does not directly compare the original OPF to the actual drug usage by Paralympic athletes. However, some general observations can be made about the generalisability and potential differences in medication use between these two groups of athletes.

Olympic and Paralympic athletes may have distinct types of injuries and medical conditions due to differences in the nature of their sports and the physical differences they present with, including the impact of any specific impairments that Paralympic athletes may have. In comparison with Olympic athletes, Paralympic athletes are more likely to compete with pre-existing disabilities or medical conditions, which may require additional or specialised medications for management.[25] In terms of the treatment of pain and inflammation for Olympic athletes compared with Paralympic athletes, the same principles of clinical management apply, as do the range of drugs prescribed for the treatment of acute sports

injury. However, in general, Paralympic athletes may often experience more pain than Olympic athletes, potentially due to an increased incidence of injuries in their sports, or the nature of the specific impairment.[205 206] The use of pain medications, particularly those used to treat chronic neuropathic pain, is therefore likely to be higher in Paralympic athletes than in non-disabled athletes.[25]

The primary scope of the OPF is to provide treatments for newly acquired conditions, and immediate and necessary care during the Games.[1] As such, is less focussed on the treatment of long-term conditions such as chronic pain, which may present in either group of athletes but potentially more common in Paralympic athletes due to underlying conditions.[25] Although the treatment of chronic pain can often be managed by the drugs provided on the OPF, some specific formulations that have not been identified through looking at the prevalence of drug use in Olympic athletes might potentially be observed if the same study was done at the Paralympic Games. These might include, for example, oral opioid drugs formulated in a long-acting slow-release formulations, and opioid drugs formulated as transdermal patches, also for the longer-acting effect. However, if an individual athlete is on long-term treatment for chronic pain, it is likely, and advised, that they bring their own medications to the games to cover for the duration they are in the host country, particularly if they are not specifically provided for on the games formulary.[1 7]

In any case, at every games there is a process for accessing non-formulary medications for athletes who require them for continuation of essential treatment of a specific condition, should they run out or forget to bring enough of their own stock to the games. This system is always in place at both the Olympic and Paralympic Games, and so providing that the drug is licensed for use and available in the host country, it can be prescribed by the physicians working in the polyclinic and is usually obtained through the designated local hospital for the games.[7 182] There is, however, usually a policy in place that requires any non-formulary drug dispensed to be paid for by the patient, or their team; usually all other formulary medications are dispensed free of charge during the games.[7 182]

The OPF category relating to skeletal muscle relaxation may potentially have differences in terms of prevalence of use between Olympic and Paralympic athletes. Paralympic athletes with specific disabilities, such as spinal cord injuries, cerebral palsy or other neurological conditions, may require medications for muscle relaxation and spasticity management which can be painful and can result in reduced mobility.[207] These conditions are far less likely to be seen in Olympic athletes and so a thorough peer review of this specific section, along with the benzodiazepine section in the context of pain management, should be conducted in light of the potential requirements for some Paralympic athletes, before the revised OPF is implemented for the Paralympic Games.

Similarly, the OPF category relating to medicines for the treatment of neuropathic pain should be reviewed in light of the potential requirements of Paralympic athletes. Paralympic athletes with nerve-related injuries or similar conditions may have a higher prevalence of neuropathic pain, necessitating medications such as gabapentin or amitriptyline, which might be less common among Olympic athletes. The prevalence of use by Olympic athletes for all examples of medicines for neuropathic pain listed in the current OPF was very low (0.26%; see Table 24). The resulting revisions to the OPF include the omission of the anticonvulsant drug, pregabalin, but the inclusion of the serotonin-noradrenaline reuptake inhibitor (SNRI), duloxetine. Gabapentin and amitriptyline continue to be listed on the revised OPF. Gabapentin and pregabalin are both anticonvulsant-type drugs considered first-line treatments for various neuropathic pain syndromes,[150 152] and so just one option is likely to be acceptable for the OPF. However, given the potentially greater need for these medications in Paralympic athletes, this change should be verified by experts before the OPF is implemented for the Paralympic Games.

In highlighting these potential differences in application of the OPF between the Olympic and Paralympic Games, it should be noted that the validation process of the revised OPF included a comparison with the results of the team physician survey. This survey was conducted across both the Olympic and Paralympic Games, and so included physicians working with Olympic and Paralympic athletes. The survey did not differentiate between athletes with or without disabilities or impairments, but rather focussed on asking what physicians prescribe for types

of pain in general, and was based on the clinical indications covered by the scope of the OPF relevant to both Olympic and Paralympic athletes. The responses to the survey do, however, also support the recommended revisions to the OPF, with no additional drugs being identified through the survey that warranted further consideration for inclusion. Based on this, it is unlikely that further significant changes might be required for the Paralympic Games context.

It should also be noted that the original OPF did undergo a comprehensive international peer review involving experts in Paralympic medicine during the development phase in 2019. Fundamentally, the revised OPF still covers all the same pharmacological categories, and routes of administration as before, with the only changes being the example of a drug within a class being presented. The spectrum of clinical indications covered by the OPF has not changed and so we would therefore not expect to see major revisions being required for the Paralympic Games, but rather a check would be recommended to see that the most commonly used drugs within a class are represented for the Paralympic athlete population.

A full review of actual prevalence of drug use in Paralympic athletes and using the selection model applied for this study is, however, still warranted and should be considered as future research. The approval from the IPC Medical Committee to undertake this research has already been granted. This work could form the basis of subsequent post-doctoral research.

5.6 Impact of Covid-19 on the results during Tokyo and Beijing

Both the Tokyo 2020 and Beijing 2022 Olympic Games were staged in unprecedented circumstances during the global Covid-19 pandemic, which resulted in the Tokyo Olympics being postponed to 2021. The postponement of the Tokyo Games also had a huge impact on this research by delaying the data collection by one year. Because of this, there was only around 7 months between the data collection at Tokyo and Beijing. With this smaller time between data collection, the data was potentially less likely to be influenced by general changes or advances in relation to new drugs, or global prescribing trends that might otherwise have been seen with a longer 19-month window as originally anticipated.

The public health measures in place within the athlete village of both games had an effect on how the pharmacy services within the polyclinic were accessed. In general there was less reliance on the pharmacy services in Tokyo and Beijing than previous games, likely due to the fact that many teams operated in a more isolated way so as to reduce the contact of their athletes to potential risks of Covid-19 transmission in the public areas of the village, including the polyclinic. The NOC teams also tended to import larger volumes and a wider range of stock than previous games, and so their reliance on polyclinic pharmacy stock was reduced for the main reason of keeping a tight bubble around their delegation to prevent Covid-19 infection.[196 197]

The number of prescriptions issued during the Tokyo 2020 Games was 59% less than during the London 2012 Games (Tokyo 2020: 1648 prescriptions; London 2012: 5216 prescriptions).[14 196] This was due to a number of reasons. Firstly, there was a notable reduction in demand for drugs for infectious illness, such as gastrointestinal illness and general respiratory infections which was attributed to the wearing of masks, social distancing, and generally better infection control processes in place in place in the Olympic Village. Secondly, the population of the village was much lower than previous games as athletes were restricted to staying only for the few days after their competition. And finally, the greater reliance on team stock medicines due to more self-sufficient systems for care the teams had in place.[208] A very similar effect was seen in Beijing, again with significantly lower volume of pharmacy items dispensed compared to previous Olympic Winter Games (Beijing 2022: 626; PyeongChang 2018: 3621; Sochi 2014: 1405).[197]

However, the impact of this shift in access of medicines during is unlikely to have had any significant effect on this research, as the data collection involved the self-reported use of medicines by the athletes, which was not dependant on where the medicines were sourced. The anti-doping testing program undertaken by the ITA was unaffected in terms of the numbers of athletes that were tested at each games, with the expected testing targets being achieved,[209 210] and so the size of the sample population for this study was largely unaffected.

There may indeed have been less drugs for pain and inflammation dispensed by the pharmacy than previous games, with more issued to athletes from team stock, however this would also not change the reporting of drugs actually used by the athletes on the doping control forms. The use of the imported team stock lists to validate the revised OPF was also a reliable reference to check for any potential discrepancies as a result of teams carrying different types of stock in light of the Covid-19 restrictions, but there was no indication of such differences found, with the types of drugs stocked broadly matching the types of drugs used by athletes. Finally, it should also be noted that the declarations made for injections administered by team physicians through the *IOC Needle Policy* were all done via remote reporting and so their submission would not be affected by any potential hesitations or restrictions in terms of polyclinic access in relation to Covid-19.

5.7 Considerations relating to prohibited substances in sport

Unlike a standard medicines formulary in the community setting, an Olympic formulary must be developed with full considerations of the regulations of WADA with regard to substances and methods prohibited in sport. The *WADA List of Prohibited Substances and Methods*[145] has a significant influence on the use of some PI medications, with the regulations being tightened in recent years with some drug categories.

Since January 2022 all injectable routes of administration have been prohibited for glucocorticoids during the in-competition period.[201] Oral, intramuscular, rectal and intravenous routes have been prohibited for some time due to evidence that the systemic effects could potentially enhance performance and be harmful to health. In 2021, sufficient data became available to show that the same systemic concentrations as existing prohibited routes could be achieved after administration by local injection at licensed therapeutic doses,[211] and so the prohibition was extended to include local injections. The impact on medical practice of this regulation is evident, as can be seen through data collected in this research showing a significant reduction in the prevalence of glucocorticoid use in Beijing compared to Tokyo (Tokyo: 3.5%; Beijing: 1.4%; $p<0.05$).

At the same time, WADA issued guidance for physicians relating to washout periods following administration of glucocorticoids which presented a time after administration of a glucocorticoid by which the drug would be excreted to a level that would not result in a positive doping test, which ranged from 3-60 days depending on which drug and which route was used.[191]

Through the data collected in this study, the shift in medical practice can be observed. Notably, the use of the triamcinolone by local injection with the longest washout period of 10 days, has reduced, in favour of drugs with a shorter washout period such as betamethasone and dexamethasone, both with 3 days washout time.[191] During Tokyo 2020, triamcinolone accounted for 42% (n=26) of declared injections of glucocorticoids, compared to 20% (n=1) during Beijing 2022. The difference of 3 days compared to 10 days during the Olympic Games will determine whether a TUE needs to be applied for mid-games.

Inevitably physicians will choose drugs with the shortest washout in the games setting and so this choice must be reflected by the OPF. The revised OPF was developed using data from Tokyo, at a time when triamcinolone was still the most common drug. As a result, for the revised OPF, triamcinolone is still included, but 2 options with shorter washout times are now listed too. Only after Paris 2024 will we be able to determine whether the use of triamcinolone becomes completely redundant in the Olympic setting, in which case could be omitted from future editions of the OPF.

The other future major change to the Prohibited List is the prohibition of tramadol in-competition for all sports from 1 January 2024.[146] The impact of this change on medical practice will likely be significant as tramadol was the drug of choice for many team physicians for the treatment of moderate to severe pain, as also shown through the team physician survey (Figure 73). At every Olympic Games in the last decade,[12-14 196 212] tramadol has been available at every sport venue on the field of play for emergency treatment of severe pain, and also routinely carried by team physicians at events for the same reason. One of the reasons tramadol has been the drug of choice is that it has not been regulated in the same way as other strong opioids such as morphine, which are considered “controlled drugs” by

law and require strict storage and recording at venues. Tramadol has always offered a suitable substitute to morphine that did not require it to be stored in the same highly secure way.

Like glucocorticoids, it is likely that we will see a shift from tramadol to other analgesic drugs, such as injectable NSAIDs, or other oral opioids that remain permitted, such as codeine. With the Prohibited List already listing 12 strong opioid analgesics in the "Narcotics" section,[145] the choice of permitted drugs for strong analgesia will be further limited. It must, however, be noted that prohibited drugs can always be used when required for emergency treatment and should not be withheld if legitimately required for essential treatment. In the case of emergency use, a Retroactive TUE can be submitted to exempt the use of that drug for the athlete in that situation.[213] In future application of the model for selection of drugs using the new Formulary Medication Match Website presented developed for this research, any future shift as a result of changes to the Prohibited List will be able to be identified, with appropriate changes to the OPF made to accommodate the changing patterns of use that may result.

A secondary purpose of the data collected using the methodology in this research is for the detection of potential new doping substances. The data provides a unique snapshot of every substance athletes are taking, which can be searched to see if there are any emerging trends in supplement use, which may be an indication that they are being used with the intention to improve performance. Over the course of the 4 years of this research, and during the time of the Tokyo and Beijing Games when the data was being collected daily, the data were also used to undertake such real-time searches, in collaboration with the ITA.

The ITA's anti-doping drug surveillance initiative for Tokyo 2020 and Beijing 2022 involved daily, real-time reporting in relation to drug-use declarations made by athletes on the doping control form. During these games, the ITA observed any indication of potential misuse of prohibited drugs by athletes that may warrant additional targeted testing or investigation. In addition, they identified any new or suspicious drugs or supplements that could potentially be taken with the intention of enhancing performance, and any substance that was under investigation by WADA through the official WADA Monitoring Program; these were then reported to the WADA Prohibited List Expert Group for further consideration for potential

inclusion on the Prohibited List. During Tokyo 2020, through the review of 5008 Doping Control Forms, 124 notifications were made, and in Beijing, through the review of 2232 Doping Control Forms, 23 notifications were made to the ITA's Intelligence and Investigations, and Testing Departments to consider potential further action, possible target testing, and notification to WADA.[209 210]

5.8 Translational impact of the research

This research was undertaken with the intention to apply the results to the real-life setting of the Olympic Games to improve the pharmacy services for athletes competing at the games in the future. The first Olympic Games that these OPF revisions can be applied to are the Paris 2024 Olympic Games which will be held from 26 July–11 August 2024, followed by the Milano-Cortina Olympic Winter Games in February 2026, the Los Angeles 2028 Olympic Games, and the Brisbane 2032 Olympic Games. The implementation of the revised sections of the OPF, relating to PI medications, will lead to several enhancements in the OPF application at these upcoming games.

Firstly, the revised OPF offers improved relevance and applicability to the athlete population of the Olympic Games. It caters more effectively to the clinical needs of the athlete population and the better reflects the unique medication demands of athletes in the Olympic Games setting in relation to PI medications. It provides a wider selection of the medicines most commonly used by athletes, enabling greater reassurance that the drugs they need will be available in the host country, and provision for the continuity of treatment for their medical conditions while away from home.

The revised OPF also provides an improved selection of medicines for team physicians, better matched to their prescribing preferences and anticipated drug usage, as validated through the team physician survey and the review of imported team stock medications. As shown through this research, the revised OPF now covers the vast majority of PI medications that team physicians prescribe, and that medical teams import to the games.

As indicated by the team physician survey, most teams carry a significant amount of stock to the Olympic Games, with only a small number of teams relying fully on the pharmacy supply. Importing medicines to the games is costly, results in medicines wastage, is resource heavy and often logistically challenging due to the importation laws and customs checks, plus environmental impacts associated with transporting large volumes of stock internationally. The revised OPF will improve the list of drugs available at each games to better meet the prescribing preferences of the team physicians, enabling medical teams to have greater reliance on this stock for the treatment of their athletes while in the athlete village. In order for this to occur, clear communication to all NOCs regarding what medicines are available to them during the games and how to access them is required.

5.9 Immediate implementation of the research findings

The research conducted at the Tokyo 2020 and Beijing 2022 Olympics provided the first major opportunity to review the very first implementation of the OPF following its initial development. With the conclusion of this study, there are a number of steps that will be undertaken immediately after, and in the runup to the Paris 2024 Olympic and Paralympic Games.

The OPF will be updated with the new sections relating to medicines for the treatment of pain and inflammation and sent for both a peer review to include the members of the IOC Medical and Scientific Commission Games Group, and IPC Medical Committee. The final version will then be requested to be ratified by the IOC and IPC medical departments for use at the games, as was the process for the original edition, and the formulary for Paris 2024 will reflect these changes.

In addition, recommendations to potential expected volumes of prescribing of these drugs will be provided to the Paris 2024 Organising Committee to better plan the procurement for pharmacy stock for the Games. Based on the direct results of this research, lower levels of stock can be planned for drugs with known low prevalence of use, with higher volumes in place for drugs with high prevalence of use, this will inevitably lead to less wastage of unused

stock at the end of the Games and will enable the pharmacy drug costs to be kept to a minimum.

The resulting OPF will be published by the IOC and will replace the existing 2019 version. At this time, there will be other editorial updates to the OPF made, including some changes to the status of the drugs in accordance with the *WADA List of Prohibited Substances and Methods* that have changed since 2019, namely the status of glucocorticoid injections and Tramadol from 1 January 2024.

5.10 Future research

Over the course of this work, an incredibly rich and comprehensive set of data has been collected on the use of both drugs and supplements by athletes. Although the research focussed solely on the use of drugs for the treatment of pain and inflammation, the dataset collected covers every medication and nutritional supplement taken by athletes over the course of the games. There is huge opportunity to dive further into this data in a number of ways as part of subsequent research related to both drugs and supplement use at the Olympics.

The main priority for further post-doctoral research is to extend the current model of selection of drugs, utilising the new Formulary Medication Match Website, to every other pharmacological class and category on the OPF in order to revise the entire OPF to better meet the needs of athletes. Already, through the implementation of the OPF at Tokyo and Beijing, and in initial review of the pharmacy dispensing reports for all drug categories, it is clear that some redundancies may be warranted due to very low actual use of some types of medicines. It is likely that efficiencies in other OPF classes can be made too.

Review of supplement use by athletes

The use of supplements by athletes is widespread, with the research conducted at the European Games showing that 71.6% athletes were taking one or more supplements, despite the doping risks of supplements being well documented.[26] The data collected for the Olympic Games will potentially provide a valuable opportunity to undertake future research to fully understand the extent and types of supplements being used by Olympic athletes, and to potentially inform future education initiatives promoting safe use.

Evaluation of prevalence of drug use for medical conditions

There are a number of other ways the data collected can be used for further post-doctoral research, including potentially a focus on specific medical conditions, particularly those which are more prevalent in the athlete population or have a particular impact on sport performance. Such medical conditions might include asthma, sleep disturbances, mental health, or depression, where the range of drugs being used to treat such conditions in athletes could be evaluated. The data could also be applied to public health research to get an understanding of the use of drugs by athletes for infectious or communicable diseases in the Olympic Games setting, such as antibiotics or treatments for infections.

Evaluation of whether sex affects the selection of PI medications in athletes

This research revealed notable differences between males and females with use of some medication classes, with the most significant differences observed for NSAIDs and non-opioid analgesics, which were used more frequently by female athletes. These results also reflect the higher use of analgesic medications by females than males in the general population as reported by a number of studies,[199 200] however research in the athlete population is lacking. As such, the exploration of sex as a determinant in the selection of PI medications in athletes is certainly warranted for future research. Such research could focus on potential underlying factors relating to pain and inflammation such as physiological or pain perception differences, and physician attitudes and influences on prescribing for male athletes compared to female athletes.

Longitudinal studies

With the medication declarations now being collected electronically from the doping control forms, the potential exists to develop a longitudinal study over the course of a number of future events. Such research could be conducted to follow the patterns of use by athletes over time, to identify trends in drug use and any global shifts in prescribing patterns. A similar longitudinal study has been running since 2008 as undertaken by the IOC looking at the incidence of illness and injury in sport over multiple Olympic Games[214 215].

Understanding emergency drug use at the Olympics

As the research did not include data on drug usage in emergency settings or through ambulance services, future studies could focus on collecting and analysing such data to better understand the selection of drugs for emergency use during the Olympic Games. Such a study could conceivably be done in collaboration with the official designated hospitals that serve the athlete population, and the city-wide ambulance service that is required to be in place as a requirement of the IOC Host City Contract.[216] In addition, the records of drug administration to athletes for immediate or urgent treatment by the field-of-play and competition and training venue medical teams could also be included to provide a comprehensive assessment of urgent and pre-hospital care of athletes at the Olympic Games.

5.11 CONCLUSION

The OPF plays an important role in ensuring the availability of essential medications to meet the specific needs of the world's best athletes participating in the Olympic Games. This research undertook a comprehensive exploration of the alignment between the PI medications listed on the first edition of the OPF and the actual pharmacological requirements of athletes.

By applying a quantitative and systematic approach to revising the OPF based on direct evidence of actual medication use by athletes at the Tokyo 2020 and Beijing 2022 Olympic Games, this study resulted in the recommendation of a revised and optimal set of 48 different medicines to be available for the treatment of pain and inflammation in athletes competing at the Olympic Games.

Several key insights emerged from this study. Firstly, that there was a high prevalence of PI medication use among athletes compared with the general population, with NSAIDs as the most widely used category. In addition, sex, and age-based differences, as well as sport-specific variations, were apparent in the use of PI medication by athletes. The study also uncovered the use of a number of medications with potential harmful risks to athlete health, which warrant further warnings and education regarding their use and prescribing in this population.

While achieving perfect alignment between the OPF and actual drug use is a complex challenge due to factors such as global variances in clinical practice, athlete choice, team physician prescribing preferences, anti-doping regulations and local medicines availability, this study presented a robust, structured, and systematic methodology for selecting and revising the PI medications included on the OPF. The development of the online Formulary Medication Match Website as part of this study offers a resource for future games organisers to regularly update the OPF to ensure it continues to remain relevant to the changing medication requirements of athletes over time.

APPENDICES

Appendix 1. Olympic and Paralympic Model Formulary

The 2019 Olympic and Paralympic Model Formulary can be viewed online HERE

Appendix 2. Participant Information Sheet: Team Physician Survey

Note. *The following participant information sheet and subsequent survey questions are the version used at the Tokyo 2020 Olympic & Paralympic Games. These were updated with a number of additional questions and the choices since the 2019 European Games version. The forms were slightly modified for the Beijing 2022 Olympic & Paralympic Games, but only in terms of reference to the games it was used in where mentioned in the participant information sheet.*

Team Physician Survey on Medicines Use at the Tokyo 2020 Olympic and Paralympic Games

PARTICIPANT INFORMATION SHEET

As a physician working at the Tokyo 2020 Olympic and Paralympic Games, you are invited to take part in a survey to evaluate the effectiveness of the Tokyo 2020 Medicines Formulary in providing an appropriate choice of medicines for physicians to prescribe in this setting. It also aims to evaluate whether the medicines available specifically for the treatment of musculoskeletal injury in athletes:

- Meets the clinical need of the athletes you treat
- Represents your preferred selection of medicines for sports injury
- Could be improved for future Olympic Games

By taking part in this survey, you will contribute to research that will inform the optimum selection medicines for future Olympic and Paralympic Games.

When completing this survey refer to the **Tokyo 2020 Pharmacy Guide** which lists the medicines available for prescribing at the Games. We kindly request team physicians to complete the online survey before the end of the Games. The link to the survey can be found here [*refer to survey below*].

Eligibility to participate

Only physicians accredited to work at the Olympic or Paralympic Games, either with a NOC or National Paralympic Committee (NPC), or the Tokyo 2020 Organising Committee are eligible to complete the survey.

Completing the survey

This information is being collected anonymously and involves completing an online survey. The survey covers demographic details, professional background, views on the medicines available at the Games and your clinical practice regarding their use. Most of the questions can be answered by selecting the most appropriate answer from a drop-down menu. A number of questions ask for you to add comments. The survey should take around 10 minutes to complete. If you do not want to answer a particular question, you can just leave it blank.

About the survey

This survey is being led by Mark Stuart, IOC Medical Commission Games Group Pharmacist, and University College London (UCL) in collaboration with the International Olympic Committee Medical and Scientific Department and the International Paralympic Committee Medical Committee. It has been reviewed and approved by the UCL Research Ethics Committee. If you have questions regarding the survey, please contact Mark Stuart (pharmacy@olympic.org).

Participation in this survey is completely voluntary and you reserve the right to discontinue at any stage without any explanation or penalty. Whether you participate in this survey or not will have no effect on your participation at the Olympic or Paralympic Games. There are no anticipated risks in taking part in the survey.

Your answers will only be used for research purposes. Your identity will remain confidential and anonymous at all times during the research project. If you have any complaints or concerns relating to this research, please contact UCL via Dr Mohamed-Ali (v.mohamed-ali@ucl.ac.uk). If you are still not satisfied, contact the UCL Research and Ethics Committee at ethics@ucl.ac.uk.

Once all the results are collected, the research team will write up these findings for publication in a peer reviewed medical journal. No part of the research that is written up and published will have any personally identifiable data included.

Appendix 3. Team Physician Survey Questions

CONSENT TO PARTICIPATE

I confirm that I have read and understand the participant information above regarding the study exploring team physician use of medicines at the Tokyo 2020 Olympic and Paralympic Games, including the inclusion criteria. I understand the benefits of participating and have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask any questions which have been answered to my satisfaction.

I understand that my responses to the survey will remain confidential and will be stored anonymously and securely and that it will not be possible to identify me in any resulting reports or publications. I agree that the anonymised data collected in this survey may be used by others for future research.

I understand that the anonymised data from the survey will be made available to the IOC Medical and Scientific Department and the IPC Medical Committee and may be subject to review by University College London for monitoring and audit purposes.

I confirm that I am a physician and consent to participate in this survey.

[ ] Yes
[ ] No

SURVEY QUESTIONS

1. Which country or team are you working with at the Games?

Afghanistan	American Samoa	Antigua and Barbuda	Aruba	Bahamas
Albania	Andorra	Argentina	Australia	Bahrain
Algeria	Angola	Armenia	Austria	Bangladesh
			Azerbaijan	Barbados

Belarus
Belgium
Belize
Benin
Bermuda
Bhutan
Bolivia
Bosnia and Herzegovina
Botswana
Brazil
Brunei Darussalam
Bulgaria
Burkina Faso
Burundi
Cambodia
Cameroon
Canada
Cape Verde
Cayman Islands
Central African Republic
Chad
Chile
Chinese Taipei
Colombia
Comoros
Congo
Cook Islands
Costa Rica
Côte d'Ivoire
Croatia
Cuba
Cyprus
Czech Republic
Democratic People's Republic of Korea
Democratic Republic of The Congo
Denmark
Djibouti
Dominican Republic
Dominique
Ecuador
Egypt
El Salvador
Equatorial Guinea
Eritrea
Estonia
Eswatini
Ethiopia
Federated States of Micronesia
Fiji
Finland
France
Gabon
Gambia
Georgia
Germany
Ghana
Great Britain
Greece
Grenada
Guam
Guatemala
Guinea
Guinea-Bissau
Guyana
Haiti
Honduras
Hong Kong, China
Hungary
Iceland
India
Indonesia
Refugee
Olympic Team (IOC)
Refugee Paralympic Team (IPC)
Iraq
Ireland
Islamic Republic of Iran
Israel
Italy
Jamaica
Japan
Jordan
Kazakhstan
Kenya
Kiribati
Kosovo
Kuwait
Kyrgyzstan
Lao People's Democratic Republic
Latvia
Lebanon
Lesotho
Liberia
Libya
Liechtenstein
Lithuania
Luxembourg
Madagascar
Malawi
Malaysia
Maldives
Mali
Malta
Marshall Islands
Mauritania
Mauritius
Mexico
Monaco
Mongolia
Montenegro
Morocco
Mozambique
Myanmar
Namibia
Nauru
Nepal
Netherlands
New Zealand
Nicaragua
Niger
Nigeria
North Macedonia
Norway
Oman
Pakistan
Palau
Palestine
Panama
Papua New Guinea
Paraguay
People's Republic of China
Peru
Philippines
Poland
Portugal
Puerto Rico
Qatar
Republic of Korea
Republic of Moldova
Romania
Russian Federation
Rwanda
Saint Kitts and Nevis
Saint Lucia
Samoa
San Marino
Sao Tome and Principe
Saudi Arabia
Senegal
Serbia
Seychelles
Sierra Leone
Singapore
Slovakia
Slovenia
Solomon Islands
Somalia
South Africa
South Sudan

Spain	Syrian Arab	Tunisia	United	Vietnam
Sri Lanka	Republic	Turkey	Republic of	Virgin Islands,
St Vincent and	Tajikistan	Turkmenistan	Tanzania	British
the Grenadines	Thailand	Tuvalu	United States	Virgin Islands,
Sudan	Timor-Leste	Uganda	of America	US
Suriname	Togo	Ukraine	Uruguay	Yemen
Sweden	Tonga	United Arab	Uzbekistan	Zambia
Switzerland	Trinidad and	Emirates	Vanuatu	Zimbabwe
	Tobago		Venezuela	

2. Approximately how many athletes are under your care while at the Games?

- ⇒ Less than 5
- ⇒ 6-50
- ⇒ 51-100
- ⇒ 101 - 150
- ⇒ 151 - 200
- ⇒ 201 - 250
- ⇒ 251 - 300
- ⇒ 301 - 350
- ⇒ More than 350

3. What is your main clinical specialty?

- ⇒ General practice - primary or community care
- ⇒ Emergency medicine
- ⇒ Sports medicine primary care
- ⇒ Sports medicine surgery
- ⇒ Neurology
- ⇒ Orthopaedics
- ⇒ Rheumatology
- ⇒ Psychiatry
- ⇒ Other (please state)

4. Approximately what proportion of your prescriptions can be covered by the medicines in the Tokyo 2020 Pharmacy Guide for the athletes under your care?

- ⇒ All of my prescriptions
- ⇒ Most of my prescriptions (>75%)
- ⇒ Some of my prescriptions (25-75%)
- ⇒ Few of my prescriptions (<25%)
- ⇒ None of my prescriptions

5. What proportion of your prescriptions can be covered by your <u>own team's stock</u> of medicines you brought to the Games for the athletes under your care?

- ⇒ All of my prescriptions
- ⇒ Most of my prescriptions (>75%)
- ⇒ Some of my prescriptions (25-75%)
- ⇒ Few of my prescriptions (<25%)
- ⇒ None of my prescriptions

6. What proportion of the medicines you prescribe for athletes will be obtained from the Tokyo 2020 Polyclinic Pharmacy?

- ⇒ All
- ⇒ Most (>75%)
- ⇒ Some (25-75%)
- ⇒ Few (<25%)
- ⇒ None

7. Approximately what percentage of your athlete patients do you expect to require ANALGESIC or ANTI-INFLAMMATORY medicines for sports-related conditions during the Games?

- ⇒ 0 - 10%
- ⇒ 11 - 20%
- ⇒ 21 - 30%
- ⇒ 31 - 40%
- ⇒ 41 - 50%
- ⇒ 51 - 60%
- ⇒ 61 - 70%
- ⇒ 71 - 80%
- ⇒ 81 - 90%
- ⇒ 91 - 100%

8. What proportion of your expected ANALGESIC and ANTI-INFLAMMATORY prescriptions for sports-related conditions can be covered by the medicines in the Tokyo 2020 Pharmacy Guide for the athletes under your care?

- ⇒ All of my prescriptions
- ⇒ Most of my prescriptions (>75%)
- ⇒ Some of my prescriptions (25-75%)
- ⇒ Few of my prescriptions (<25%)
- ⇒ None of my prescriptions

ORAL MEDICINES

This section relates to medicines for oral use.

9. Which ORAL non-opioid or non-steroidal anti-inflammatory drugs (NSAIDs) have you prescribed in the last 12 months to athletes for sports-related conditions (check all that apply)

- ⇒ Acetaminophen (paracetamol)
- ⇒ Aspirin
- ⇒ Celecoxib
- ⇒ Diclofenac
- ⇒ Diflunisal
- ⇒ Etodolac
- ⇒ Etoricoxib
- ⇒ Fenoprofen
- ⇒ Flurbiprofen
- ⇒ Ibuprofen
- ⇒ Indometacin
- ⇒ Ketoprofen
- ⇒ Ketorolac
- ⇒ Mefenamic Acid
- ⇒ Meloxicam
- ⇒ Metamizole (dipyrone)

⇒ Nabumetone
⇒ Naproxen
⇒ Nimesulide
⇒ Oxaprozin
⇒ Paracetamol
⇒ Parecoxib
⇒ Piroxicam
⇒ Sulindac
⇒ Tenoxicam
⇒ Tolmetin
⇒ Other (please list)

10. Which, if any, of the following ORAL OPIOID ANALGESIC DRUGS have you prescribed in the last 12 months to athletes for sports-related conditions? (check all that apply)

⇒ Buprenorphine
⇒ Codeine
⇒ Dihydrocodeine
⇒ Dipipanone
⇒ Fentanyl
⇒ Hydromorphone
⇒ Meptazinol
⇒ Methadone
⇒ Morphine
⇒ Oxycodone
⇒ Papaveretum
⇒ Pentazocine
⇒ Pethidine
⇒ Sufentanil
⇒ Tapentadol
⇒ Tramadol
⇒ Other (please state)

Which ORAL medicine would you most frequently prescribe for the following clinical indications in athletes? (check all that apply)

11. Mild to moderate pain WITHOUT INFLAMMATION for sports-related conditions (ORAL)

⇒ Acetaminophen (paracetamol)
⇒ Aspirin
⇒ Celecoxib
⇒ Codeine
⇒ Codeine + paracetamol combination
⇒ Diclofenac
⇒ Diflunisal
⇒ Etodolac
⇒ Etoricoxib
⇒ Fenoprofen
⇒ Flurbiprofen
⇒ Ibuprofen
⇒ Indometacin
⇒ Ketoprofen
⇒ Ketorolac
⇒ Mefenamic Acid
⇒ Meloxicam
⇒ Metamizole (dipyrone)
⇒ Nabumetone
⇒ Naproxen
⇒ Nimesulide
⇒ Oxaprozin
⇒ Paracetamol
⇒ Parecoxib
⇒ Piroxicam
⇒ Sulindac
⇒ Tenoxicam
⇒ Tolmetin
⇒ Other (please list)

12. Mild to moderate pain WITH INFLAMMATION for sports-related conditions (ORAL)

⇒ Acetaminophen (paracetamol)
⇒ Aspirin
⇒ Celecoxib
⇒ Codeine

⇒ Codeine + paracetamol combination
⇒ Diclofenac
⇒ Diflunisal
⇒ Etodolac
⇒ Etoricoxib
⇒ Fenoprofen
⇒ Flurbiprofen
⇒ Ibuprofen
⇒ Indometacin
⇒ Ketoprofen
⇒ Ketorolac
⇒ Mefenamic Acid
⇒ Meloxicam
⇒ Metamizole (dipyrone)
⇒ Nabumetone
⇒ Naproxen
⇒ Nimesulide
⇒ Oxaprozin
⇒ Paracetamol
⇒ Parecoxib
⇒ Piroxicam
⇒ Sulindac
⇒ Tenoxicam
⇒ Tolmetin
⇒ Other (please list)

13. Moderate to severe pain for sports-related musculoskeletal conditions WITHOUT INFLAMMATION (ORAL)

⇒ Acetaminophen (paracetamol)
⇒ Alfentanil
⇒ Buprenorphine
⇒ Celecoxib
⇒ Codeine + paracetamol (acetaminophen)
⇒ Dexamethasone
⇒ Diamorphine
⇒ Diclofenac
⇒ Diflunisal
⇒ Dihydrocodeine
⇒ Dipipanone
⇒ Etodolac
⇒ Etoricoxib
⇒ Fenoprofen
⇒ Fentanyl
⇒ Flurbirofen
⇒ Hydromorphone
⇒ Ibuprofen
⇒ Indometacin
⇒ Ketoprofen
⇒ Ketorolac
⇒ Mefenamic Acid
⇒ Meloxicam
⇒ Meptazinol
⇒ Methadone
⇒ Morphine
⇒ Nabumetone
⇒ Naproxen
⇒ Oxaprozin
⇒ Oxycodone
⇒ Papaveretum
⇒ Paracetamol
⇒ Parecoxib
⇒ Pentazocine
⇒ Pethidine Hydrochloride
⇒ Piroxicam
⇒ Remifentanil
⇒ Sufentanil
⇒ Sulindac
⇒ Tapentadol
⇒ Tenoxicam
⇒ Tolmetin
⇒ Tramadol
⇒ Other (please state)

14. Moderate to severe pain for sports-related conditions WITH INFLAMMATION (ORAL)

⇒ Acetaminophen (paracetamol)
⇒ Alfentanil
⇒ Betamethasone
⇒ Budesonide
⇒ Buprenorphine
⇒ Celecoxib
⇒ Codeine + paracetamol (acetaminophen)
⇒ Dexamethasone

⇒ Dexamethasone
⇒ Diamorphine
⇒ Diclofenac
⇒ Diflunisal
⇒ Dihydrocodeine
⇒ Dipipanone
⇒ Etodolac
⇒ Etoricoxib
⇒ Fenoprofen
⇒ Fentanyl
⇒ Fluocortelone
⇒ Flurbirofen
⇒ Hydrocortisone
⇒ Hydromorphone
⇒ Ibuprofen
⇒ Indometacin
⇒ Ketoprofen
⇒ Ketorolac
⇒ Ketroprofen
⇒ Mefenamic Acid
⇒ Meloxicam
⇒ Meptazinol
⇒ Methadone
⇒ Methylprednisolone
⇒ Morphine
⇒ Nabumetone
⇒ Naproxen
⇒ Oxaprozin
⇒ Oxycodone
⇒ Papaveretum
⇒ Paracetamol
⇒ Parecoxib
⇒ Pentazocine
⇒ Pethidine Hydrochloride
⇒ Piroxicam
⇒ Prednisolone
⇒ Remifentanil
⇒ Sufentanil
⇒ Sulindac
⇒ Tapentadol
⇒ Tenoxicam
⇒ Tolmetin
⇒ Tramadol
⇒ Triamcinolone
⇒ Other (please state)

15. Neuropathic pain in athletes (ORAL)

⇒ Amitriptyline
⇒ Baclofen
⇒ Bretylium
⇒ Codeine
⇒ Codeine + paracetamol (acetaminophen) combination
⇒ Gabapentin
⇒ Hydromorphone
⇒ Nortriptyline
⇒ NSAID (non-steroidal anti-inflammatory drug)
⇒ Oxycodone
⇒ Pregabalin
⇒ Tramadol
⇒ Other (please state)

16. Which, if any, of the following SKELETAL MUSCLE RELAXANTS have you prescribed in the last 12 months to athletes for sports-related conditions (check all that apply)

⇒ Baclofen
⇒ Carisoprodol
⇒ Chlorzoxazone
⇒ Cyclobenzaprine
⇒ Dantrolene
⇒ Diazepam
⇒ Mephenoxalone
⇒ Metaxalone
⇒ Methocarbamol
⇒ Orphenadrine
⇒ Thiocolchicoside
⇒ Tizanidine
⇒ Other (please state)

INJECTABLE MEDICINES

This section relates to medicines for injection.

17. Which, if any, of the following INJECTABLE non-opioid and non-steroidal anti-inflammatory drugs (NSAIDs) have you prescribed in the last 12 months to athletes for sports-related conditions (check all that apply)

- ⇒ Acetaminophen (paracetamol)
- ⇒ Diclofenac
- ⇒ Etodolac
- ⇒ Etoricoxib
- ⇒ Flurbiprofen
- ⇒ Ibuprofen
- ⇒ Indometacin
- ⇒ Ketoprofen
- ⇒ Ketorolac
- ⇒ Meloxicam
- ⇒ Metamizole
- ⇒ Nabumetone
- ⇒ Naproxen
- ⇒ Nimesulide
- ⇒ Oxaprozin
- ⇒ Paracetamol
- ⇒ Parecoxib
- ⇒ Piroxicam
- ⇒ Sulindac
- ⇒ Tenoxicam
- ⇒ Other (please list)

18. Which, if any, of the following INJECTABLE OPIOID ANALGESIC DRUGS have you prescribed in the last 12 months to athletes for pain from sports-related conditions? (check all that apply)

- ⇒ Alfentanil
- ⇒ Fentanyl
- ⇒ Buprenorphine
- ⇒ Codeine
- ⇒ Diamorphine
- ⇒ Dihydrocodeine
- ⇒ Dipipanone
- ⇒ Fentanyl
- ⇒ Hydromorphone
- ⇒ Meptazinol
- ⇒ Methadone
- ⇒ Morphine
- ⇒ Oxycodone
- ⇒ Papaveretum
- ⇒ Pentazocine
- ⇒ Pethidine
- ⇒ Remifentanil
- ⇒ Sufentanil
- ⇒ Tapentadol
- ⇒ Tramadol
- ⇒ Other (please state)

Which INJECTABLE medicine would you most frequently prescribe to athletes for the following clinical indications? (check all that apply)

19. MODERATE TO SEVERE PAIN without inflammation due to sports-related injury (INJECTION)

- ⇒ Acetaminophen (paracetamol)
- ⇒ Alfentanil
- ⇒ Bupivicaine
- ⇒ Buprenorphine
- ⇒ Celecoxib
- ⇒ Diamorphine
- ⇒ Diclofenac
- ⇒ Diflunisal

⇒ Dihydrocodeine
⇒ Dipipanone
⇒ Etodolac
⇒ Etoricoxib
⇒ Fenoprofen
⇒ Fentanyl
⇒ Flurbirofen
⇒ Hydromorphone
⇒ Ibuprofen
⇒ Indometacin
⇒ Ketamine
⇒ Ketoprofen
⇒ Ketorolac
⇒ Mefenamic Acid
⇒ Meloxicam
⇒ Meptazinol
⇒ Methadone
⇒ Morphine
⇒ Nabumetone
⇒ Naproxen
⇒ Oxaprozin
⇒ Oxycodone
⇒ Papaveretum
⇒ Paracetamol
⇒ Parecoxib
⇒ Pentazocine
⇒ Pethidine
⇒ Piroxicam
⇒ Remifentanil
⇒ Sufentanil
⇒ Sulindac
⇒ Tapentadol
⇒ Tenoxicam
⇒ Tolmetin
⇒ Tramadol
⇒ Other (please state)

20. MODERATE TO SEVERE PAIN with INFLAMMATION due to sports-related injury (INJECTION)

⇒ Acetaminophen (paracetamol)
⇒ Alfentanil
⇒ Betamethasone
⇒ Bupivicaine
⇒ Buprenorphine
⇒ Celecoxib
⇒ Dexamethasone
⇒ Diamorphine
⇒ Diclofenac
⇒ Diflunisal
⇒ Dihydrocodeine
⇒ Dipipanone
⇒ Etodolac
⇒ Etoricoxib
⇒ Fenoprofen
⇒ Fentanyl
⇒ Flurbirofen
⇒ Hydrocortisone
⇒ Hydromorphone
⇒ Ibuprofen
⇒ Indometacin
⇒ Ketamine
⇒ Ketoprofen
⇒ Ketorolac
⇒ Mefenamic Acid
⇒ Meloxicam
⇒ Meptazinol
⇒ Methadone
⇒ Methylprednisolone
⇒ Morphine
⇒ Nabumetone
⇒ Naproxen
⇒ Oxaprozin
⇒ Oxycodone
⇒ Papaveretum
⇒ Paracetamol
⇒ Parecoxib
⇒ Pentazocine
⇒ Pethidine
⇒ Piroxicam
⇒ Prednisolone
⇒ Prednisone
⇒ Remifentanil
⇒ Sufentanil
⇒ Sulindac
⇒ Tapentadol
⇒ Tenoxicam
⇒ Tolmetin
⇒ Triamcinolone
⇒ Other (please state)

21. Which GLUCOCORTICOID would you most frequently administer to athletes by LOCAL INJECTION (e.g. intra-articular) for inflammation due to sports injury?

⇒ Triamcinolone
⇒ Methylprednisolone
⇒ Betamethasone

⇒ Hydrocortisone
⇒ Prednisolone
⇒ Prednisone
⇒ Dexamethasone
⇒ Other (please state)

22. Which ANAESTHETIC would you most frequently administer to athletes by LOCAL INJECTION (e.g. intra-articular) for pain due to sports injury?

⇒ Lidocaine
⇒ Bupivacaine
⇒ Ropivacaine
⇒ Levobupivacaine
⇒ Prilocaine
⇒ Other (please state)

URGENT OR EMERGENCY TREATMENT

This section relates to acute urgent or emergency treatment of athletes.

23. Which medicine would you use for EMERGENCY ANALGESIA for SEVERE PAIN due to serious injury on the FIELD OF PLAY

⇒ Alfentanil
⇒ Diamorphine
⇒ Dihydrocodeine
⇒ Dipipanone
⇒ Fentanyl
⇒ Hydromorphone
⇒ Ketamine
⇒ Methadone
⇒ Methoxyflurane inhalation
⇒ Morphine
⇒ Nitric oxide
⇒ Oxycodone
⇒ Papaveretum
⇒ Pentazocine
⇒ Pethidine
⇒ Remifentanil
⇒ Sufentanil
⇒ Tapentadol
⇒ Tramadol
⇒ Other (please state)

24. Which medicine would you use for ANALGESIA with SEDATION requiring RAPID ONSET on the FIELD OF PLAY (INJECTION)

⇒ Alfentanil
⇒ Diamorphine
⇒ Dihydrocodeine
⇒ Dipipanone
⇒ Fentanyl
⇒ Hydromorphone
⇒ Ketamine
⇒ Methadone
⇒ Methoxyflurane inhalation
⇒ Morphine
⇒ Nitric oxide inhalation
⇒ Oxycodone
⇒ Papaveretum
⇒ Pentazocine
⇒ Pethidine
⇒ Remifentanil
⇒ Sufentanil
⇒ Tapentadol
⇒ Tramadol
⇒ Other (please state)

TOPICAL MEDICINES

This section relates to medicines for topical application.

25. Which TOPICAL medicine would you most frequently prescribe for PAIN AND INFLAMMATION due to sports-related musculoskeletal conditions (check all that apply)

⇒ Capsaicin

⇒ Diclofenac

⇒ Felbinac

⇒ Ibuprofen

⇒ Indometacin

⇒ Ketoprofen

⇒ Lidocaine

⇒ Menthol or camphor preparations (cooling)

⇒ Methylsalicylate

⇒ Naproxen

⇒ Piroxicam

⇒ Prilocaine

⇒ Other (please state)

Appendix 4. The Formulary Medication Match Website

The Formulary Medication Match Website was an online tool developed as part of this research to generate the resulting list of drugs after applying the cut-off threshold (%) to each class and route category.

This tool was designed to assist in the review of any pharmacy medicines formulary by comparing the actual use of medications in a given population, with the list of medications on the organisation's current pharmacy medicines formulary. The reports generated by the tool can be used to visualise the comparison to inform decisions as to whether to include or omit a medication from subsequent editions of any pharmacy medicines formulary, based on actual patient usage, or lack of use, in a population.

The tool generates a report showing the patient usage of a medication as a proportion (%) of all medications in a particular category (defined by the therapeutic class and route of administration). A cut-off level for inclusion of a medication on the report can be set based on the desired proportion (%) of use of a medication within therapeutic class and route categories.

The tool generates a list of drugs that is colour-coded to enable comparisons between actual usage of medications in the population, with the list of medications on the existing pharmacy medicines formulary in the following way:

GREEN: Drugs used by athletes that are already on the formulary

ORANGE: Drugs used by athletes but not currently on the formulary

RED: Drugs currently on the OPF but not used by athletes

The online tool was built using a combination of technologies. Firstly, *Python*®, which is a programming language, along with *Flask*®, a web development framework was used to build the functional backend of the website. For the data manipulation functionality, *Pandas*®

software was used. The front-end interactive interface was designed with HTML, *Bootstrap*®, and *JavaScript* to create the formatted and responsive layout for the web page.

One of the key features of the website is the ability to upload files, and so a validation system was integrated to ensure that only Excel files are accepted, also a session management system so that uploaded files remain available for 10 minutes before automatically deleting from the server. This helps to maintain data privacy and optimise server resources.

The Formulary Medication Match Website, including the instructions for using it can be viewed here:

https://formularycheck.herokuapp.com/

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