Improving guideline adherence in urology

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Abstract

Context: Clinical Practice Guidelines (CPG) distil an evidence base into recommendations. CPG adherence is associated with improved patient outcomes. However, preparing and disseminating CPG is a costly task involving multiple skilled personnel. Furthermore, dissemination alone does not ensure CPG adherence. The reasons for non-adherence are often complex but understanding practice variation and reasons for non-adherence is key to improving CPG adherence, harmonising clinically-appropriate and cost-effective care.

Objective To overview approaches to improving guideline adherence, provide urology specific examples of knowledge-practice gaps, and highlight potential solutions informed by implementation science.

Evidence Acquisition Three common approaches to implementation science (the Knowledge-To-Action framework, the Consolidated Framework for Implementation Research, and the Behaviour Change Wheel), are summarised.

Evidence Synthesis Three implementation problems in urology are illustrated (underuse of single instillation of intravesical chemotherapy in non-muscle invasive bladder cancer, overuse of androgen deprivation therapy in localised prostate cancer, and guideline discordant imaging in prostate cancer). Research using implementation science approaches to address these implementation problems is discussed.

Conclusion: Urologists, patients, healthcare providers, funders, and other key stakeholders must commit to reliably capturing and reporting data on patient outcomes, practice variations, guideline

adherence, and the impact of adherence on outcomes. Leveraging implementation science frameworks is a sound next step towards improving guideline adherence and the associated benefits of evidence-based care.

Patient Summary: Clinical practice guidelines documents are created by expert panels. These documents provide overviews of the evidence for the tests and treatments used in patient care. They also provide recommendations and it is expected that in most circumstances clinicians will follow these recommendations. Sometimes, healthcare professionals can't or don't follow these recommendations and it is not always clear why. In this review article we look at some examples of research approaches to addressing this problem of 'non-adherence', and we provide some urology specific examples.

INTRODUCTION

What are clinical guidelines and why are they important?

Clinical Practice Guidelines (CPG) distil an evidence base into recommendations. These recommendations typically carry a 'strength' rating (strong or weak) and an indication of the 'certainty of evidence' (high, moderate, low, or very low).[1] A judicious systematic review process based on transparent and reproducible methodology ideally underpins these recommendations.[2] However, expert opinion and consensus are also used to guide clinical recommendations where evidence is lacking or weak. CPGs are important because they promote standardisation and use of clinically-appropriate and cost-effective care, as well as mitigate against overuse and other harmful practices. Ultimately, CPG adherence is associated with improved patient outcomes.[3]

Many guidelines for urological practice exist, but the most comprehensive and widely used are those developed by the European Association of Urology's (EAU) Guidelines Office (GO); which are endorsed by 75 national urological and medical societies worldwide. The EAU GO's guideline recommendations focus on the clinical effectiveness of various tests, treatments and follow-up, and traditionally do not include cost-effectiveness evaluation because of the variety of healthcare payment systems across Europe. The EAU GO guidelines are organised across 21 panels each focussing on a specific urological speciality (e.g., prostate cancer, urolithiasis, chronic pelvic pain) and these guidelines are updated annually. Within each guideline there are numerous recommendations. Each recommendation requires a summary of the evidence base and a justified strength rating. There are approximately 300 clinical members of the EAU GO's panels (panel members and guideline associates), all have been trained in systematic review methodology and guideline production by the EAU's Methodology Committee. [2] The systematic review programme is supported by both the Methodology Committee and a group of trained guidelines associates (mostly consisting of research-active young urologists). As evidenced by this extensive effort, CPGs are costly to develop and maintain requiring constant work from many highly skilled personnel with clinical and methodological expertise, engaged patients, project and panel coordination and administrative support, with further costs for meetings, publication/printing, and dissemination.

Why should patients be involved in guideline development?

Recognising the important role patients can play in both guideline development and implementation, the EAU recently created a Patient Office within its organisational structure. The Patient Office, in collaboration with the Guidelines Office and European School of Urology, will help ensure patient engagement is meaningful through patient training and skill-building to enable effective contributions to all activities of the EAU including guideline production. Appropriate training and education facilitate proper patient representation in the guideline production process, as well as during subsequent steps. For example, patient engagement is critical to translating technical guideline documents into easy-to-understand patient summaries, as well as across European languages. Taken together, proper patient representation helps ensure high-quality CPGs are trustworthy and supports their effective implementation. Furthermore, the Patient Office envisions playing a critical role in more effective

dissemination and implementation of CPGs. As a related example, the EVOLVE (giving patients a m**E**aningful **VO**ice in the design and de**LiV**ery of car**E)** research project is supported by the EAU GO and aims to provide an evidence-based framework for patient involvement in guidelines. [4, 5] (and see editorial by Bjorkqvist and colleagues in current volume).

EVIDENCE AQUISITION

What are key challenges to effective guideline development?

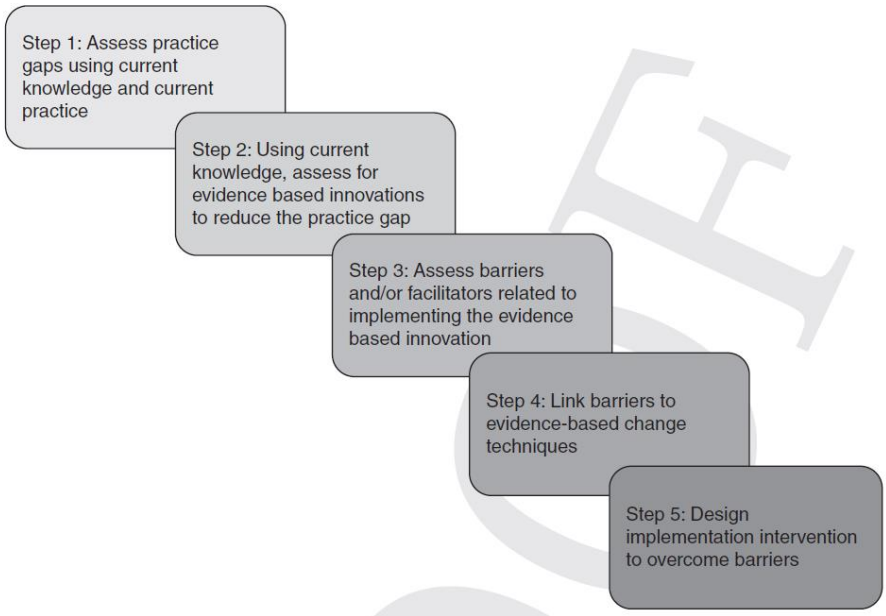
Despite the promise of patient engagement and robust CPG processes, guideline developers face a variety of challenges. First, regardless of the rigour of the systematic review processes, the results are only as reliable as the studies on which they are based. For instance, randomized clinical trial (RCT) results may disagree, [6] observational studies subject to selection bias may lead to exaggerated effect sizes, [7-9] and scant studies with weak designs may fail to adequately inform decision-making and recommendations. [10] Where there is a lack of conclusive evidence, the EAU GO have created robust and transparent expertise-based consensus projects on which to base guidance. [11, 12] Furthermore, where published primary research is deficient, there is increasing interest in the use of real-world evidence to fill evidence gaps. The European Commission IMI funded PIONEER (**P**rostate Cancer D**i**agn**o**sis and Treatment E**n**hancement Through th**e** Pow**e**r of Big Data in **E**u**r**ope) project coordinated by the EAU aims to make best use of the real-world data available in the prostate cancer arena and use Big Data analytics to answer prioritised research questions. [13]

What are the key challenges for guideline adherence?

All these initiatives highlight the importance of a well-organised clinical speciality community and professional society, such as the EAU, and the centrality of a function like the GO to administer these various initiatives. However, even where cumulative evidence clearly supports a clinically-effective practice, passive dissemination through publication of guidelines alone is rarely enough to effect widespread guideline adherence. [14] Guidance may not be accepted by all, nor possible to implement as intended in all circumstances, and the reasons for this are complex. Consequences of not adhering to guidelines include failing to provide optimal care, potential for patient harm, unnecessary healthcare system expenditure, and research waste necessitating a better understanding of barriers to and proven facilitators of guideline adherence.

Fortunately, the evolving field of implementation science has a wealth of resources and evidence-based frameworks to guide investigations, strategies and intervention development to support improved CPG adherence in our urology communities. A stepwise approach is often used when addressing implementation gaps between real-world practice and CPG recommendations. As illustrated in Figure 1, practice gaps are typically identified and further examined to better understand the reasons for mismatches between evidence and practice, identifying barriers and facilitators to guideline adherence as well as strategies to address gaps in care. In turn, evidence-based strategies and interventions are designed and implemented to support behaviour change leading to improved practice (i.e., decreasing practice gaps).

Figure 1. Steps to systematic intervention design for implementation of evidence-based practices



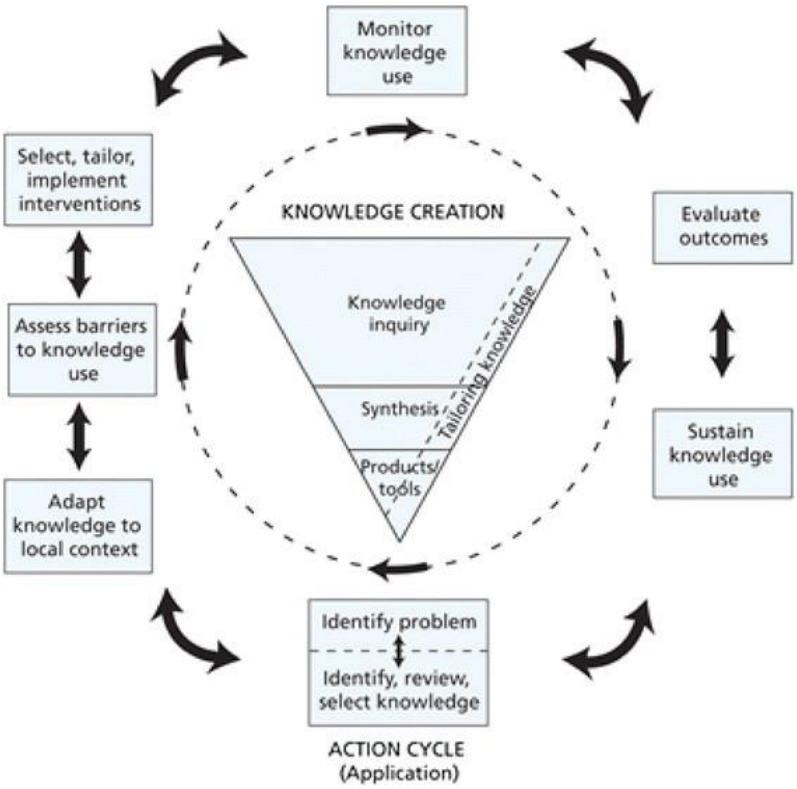
From: Skolarus TA, Sales AE: "Implementation issues: towards a systematic and stepwise approach". Complex Interventions in Heath Care: a Research Handbook, Richards, Hallberg (eds) Richards, Hallberg (eds), 2014.

As illustrated in Step 1 of Figure 1, the initial step to any implementation/de-implementation project is to estimate practice variation. This may be estimated from pre-existing sources such as claims databases or institutional registries, but often reliable, current estimates do not exist raising significant barriers for improvement efforts. To address this issue and informed by the Knowledge-to-action (KTA) approach outlined in Box 1, the **IM**pact **A**ssessment of **G**uidelines **I**mplementation a**n**d **E**ducation (**IMAGINE**) group have created a bespoke online data collection platform and in collaborati with national urology societies are currently auditing ADT practices in European countries. The aim of this audit is to describe practice variation, to identify sites with high and low adherence, and then target these sites to understand the barriers and facilitators to practicing in accordance with the EAU guidelines. [15]

There are several commonly used frameworks to guide implementation efforts, [16] including the KTA described above, highlighted in Box 1. The advantages of using these and other frameworks include systematic characterization of barriers and facilitators to practice gaps and change, as well as links to evidence-based strategies to support behaviour and practice change efforts. In other words, implementation researchers and practitioners looking to address gaps between real-world practice and CPG recommendations resulting from poor adherence can look to these resources as guideposts for developing effective improvement interventions.

Box 1 – The Knowledge to Action Framework

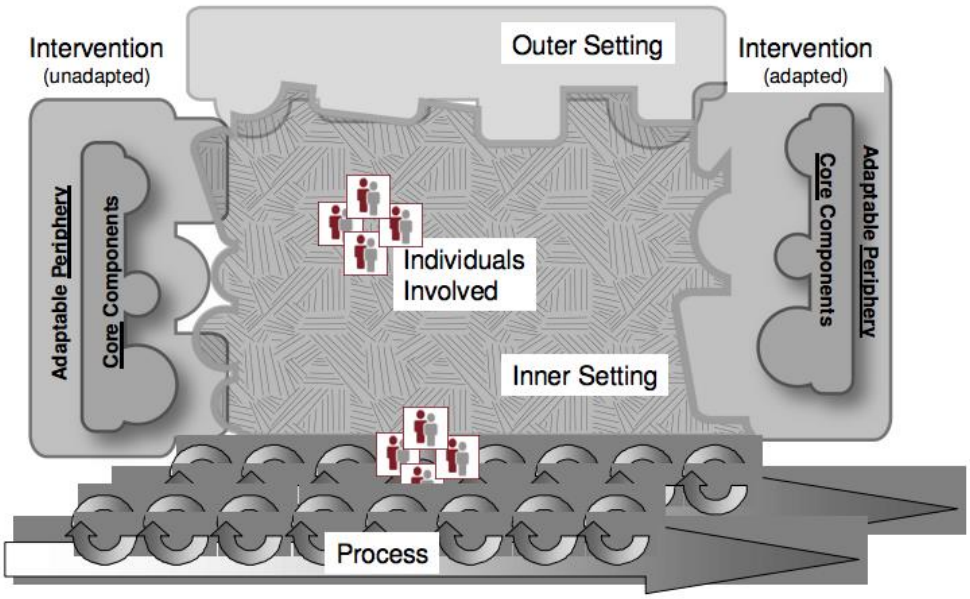
The knowledge-to-action (KTA) framework was developed by Graham and colleagues to offer conceptual clarity and guide implementation processes. [17] The KTA framework outlines two key processes, 'knowledge creation', and the 'action cycle'. Knowledge creation is a process of tailoring knowledge, moving from primary research to evidence synthesis and guideline recommendations. Whereas the action cycle describes application activities whereby the knowledge is adapted to local contexts, barriers to use assessed, implementation interventions developed, practice monitored and evaluated, and repeated as necessary.



From: Graham et al [17]

Box 2 – The Consolidated Framework for Implementation Research

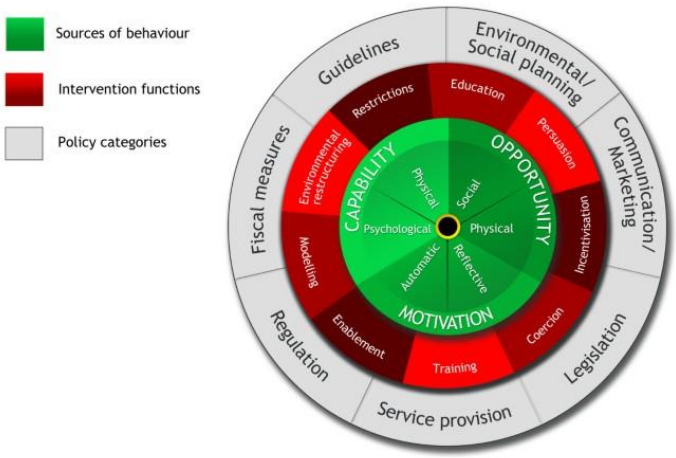
The Consolidated Framework for Implementation Research provides a comprehensive overview of constructs associated with effective implementation [18]. It is arranged across five domains and can be used to systematically assess barriers and facilitators to prepare for implementation. These include intervention characteristics (such as evidence strength, intervention complexity, cost, and adaptability), outer setting (such as patient needs and resources, external policies and incentives), inner setting (such as organisational culture, networks and communication, and readiness for change) characteristics of individuals (knowledge and beliefs, and self-efficacy), and process (such as planning, engagement, leadership, and evaluation).



Source: Damschroder et al [18]

Box 3 - The Behaviour Change Wheel

The Behaviour Change Wheel (BCW) is a theory and empirically informed guide to behaviour change intervention development and evaluation. [19] The BCW synthesises 19 frameworks of behaviour change and proposes three essential conditions for behaviour: capability, opportunity, and motivation. This BCW is a broad guide to behaviour change, and a more implementation science specific conceptualisation, the Theoretical Domains Framework (TDF) has further specified 14 domains which reflect barriers and facilitators to behaviours – domain examples include 'social influences', 'beliefs about consequences' and 'intentions'. [20] Guideline implementation depends on individuals and organisations changing their behaviours and behaviour change theories are therefore highly relevant. The BCW and TDF provides a comprehensive framework of behaviour change theory to 1. investigate what needs to be done differently by whom, when and where for successful implementation to occur, and 2. design implementation interventions to support this to happen.



Source: Michie et al [19]

The clinical relevance of the implementation science approaches outlined in boxes 1,2 and 3, is that where evidence-based recommended practices are not followed, the local context and barriers to practice need to be understood to improve adherence. This requires clinical experts to contribute to the design of implementation initiatives, because they may have insight in to how feasible any implementation interventions are. Clinical experts should also be participants in implementation science research because they have the experiential knowledge of why it may be difficult to follow recommendations in their sites. Patients may also play a role in influencing barriers and facilitators to practice so, depending on the context, it may also be appropriate to involve them as research participants in implementation projects. It is important to note that 100% adherence may not be realistic, but what is important is that variation and the reasons for non-adherence are documented so that justifiable reasons for non-adherence can be factored into performance targets in feedback, which is a common implementation intervention. Ultimately, the aim of using implementation science in evidence-based medicine is to ensure high-certainty evidence is implemented in routine clinical practice.

EVIDENCE SYNTHESIS

We now provide three urology implementation problems (one in bladder cancer and two in prostate cancer) as exemplars illustrating how guideline adherence in urology can be more effectively improved and to highlight initiatives using implementation science to design solutions.

The EAU NMIBC guidelines strongly recommend giving a single instillation of intravesical chemotherapy (SI-IVC) to eligible patients with low/intermediate grade tumours. This is based on high-certainty evidence, the NMIBC guidelines have included this recommendation since their inaugural edition 20 years ago. Adherence to this guidance is suboptimal internationally. For instance, estimates range from 0.33% to 50% in the Unites States, [21-23] a mean of 43% was estimated across five European countries (France, 22%, Germany, 39%, Italy, 38%, Spain, 41%), [24] UK mean adherence was estimated at 61%, [25] and Scottish estimates ranged from 21% to 85%. [26]

Dunsmore et al [27] interviewed urology consultants, nurses and urology specialist trainees in the UK to understand what helps or hinders urology teams to give SI-IVC. They used the TDF [20] (see Box 3) to organise their investigation and analysis. They found that barriers to SI-IVC were present at different organisational levels and professional roles. For instance, in some hospitals there was a policy to not instil SI-IVC in theatre. Some staff reported delays in MMC ordering and/or local storage. Gaps in training, skills and perceived workload affected motivation. Facilitators included access to modern instilling devices and incorporating reminders operation pro-forma. Differences in coordinated leadership, sharing best practices, and disliking being perceived as underperforming, were evident in Scotland. [27] Based on these results, Dunsmore et al suggest that SI-IVC adherence could be improved by modifying policies around giving SI-IVC in theatre, the delivery and storage of IVC and improving staff training, and TURBT documentation. Addressing gaps in knowledge about guidelines and confidence in the evidence base as well as beliefs about consequences of SI-IVC (e.g., adverse effects if there is a bladder perforation) were also identified as barriers in a systematic review. [28] Auditing practice against national performance targets may have led to improvements in SI-IVC rates in Scotland, [29] thus demonstrating a possible implementation intervention. However, audit and feedback should ideally be compared to controls or another intervention to provide evidence of effectiveness. [30] The findings from these various studies have informed the design of an audit with an embedded RCT aiming to improve sites' SI-IVC rates and other TURBT performance indicators: the Transurethral **RE**section and **S**ingle instillation intra-vesical chemotherapy **E**valuation in bladder **C**ancer **T**reatment (RESECT) RCT. [31]The RESECT intervention arm was developed using the BCW [19] (see box 3 for an outline of the BCW) which facilitated mapping the TDF to intervention functions and

behaviour changes techniques. The RESECT intervention involves audit and feedback of four quality indicators, one being related to SI-IVC. The feedback involves peer comparison accompanied by behaviour change statements plus an educational video highlighting good practice. The study is recruiting now (protocol publication in preparation) and sites in the study will be randomised to the intervention arm or to audit participation only during the study period.

Just as the underuse of clinically effective practice is undesirable, overuse of treatments too is problematic, and may need different considerations in tackling it. [32] The drive to reduce low value care has crystallised in the international 'Choose Wisely' initiative – a clinician-led campaign which identifies tests, treatments and procedures with strong scientific evidence of overuse and significant potential harm or cost. [33] The central goal of this initiative is to change the culture of medical care that has historically supported overuse of unnecessary or low-value interventions. A uro-oncology example of treatment overuse is androgen deprivation therapy (ADT) in circumstances with little evidence of benefit leading to low-value care. For example, both European and American guidance recommends against giving ADT as monotherapy to men with localized prostate cancer. An Italian study showed that guideline discordant ADT use ranged from 20% to 60% across the country. [34] Studies of US patients receiving fee-for-service or integrated health system care show that ADT is used in patients who are unlikely to benefit and may experience harm, [35, 36]. One US study estimated that around 50% of low- or intermediate-risk patients (inappropriately) received ADT, [37] whereas another notes that around one in eight men received ADT in discordance with guidance, at an estimated cost of $42,000,000 per year. [38] What is clear from these estimates is that ADT overuse is variable and problematic.

Along these lines, Skolarus and colleagues are researching ways to de-implement inappropriate ADT prescribing in the US setting. [39] They used qualitative methods (manuscript under review), informed by the TDF (see box 3), to understand patient and urologist barriers and facilitators to ADT de-implementation. [40] Aiming to prioritise which barriers and facilitators to target in creating de-implementation strategies, the interview results were used to inform an innovative (in this setting) discrete choice experiment (DCE). Informed by the DCE survey, de-implementation interventions with different underlying behaviour change approaches, hypotheses, and operating at different levels of the health system will be developed and eventually compared in a cluster RCT. In brief, an informed decision-making intervention as a patient-provider dyad strategy will be compared to a formulary restriction intervention as an organisational-level strategy to understand which is more effective in decreasing low-value ADT as this is currently unknown. The informed decision-making model is two-way dialogue whilst formulary restrictions are top-down and enforceable, leaving little room for judgement though may also result in significant provider resistance or gaming. Rigorous pilot testing prior the full de-implementation comparative effectiveness trial will help ensure successful study completion to better understand optimal approaches to de-implementing low value cancer care.

In another example, studies on imaging for men with prostate cancer estimated that around 50% of men in the US received guideline discordant imaging [41], and up to 70% received guideline discordant imaging in Italy. [42] Makarov et al. investigated the reasons for guideline discordant use of imaging to stage incident prostate cancer using a qualitative study design grounded in behavioural theory and implementation science. [43] One barrier to guideline adherence was that although some physicians felt they knew and trusted the guidelines, they felt their experience, knowledge, and intuition should take precedence. Others noted they worried about missing clinically significant cancers, and feared litigation associated with this, and felt the trade-off for radiation-associated with imaging was minimal. Other barriers to imaging guideline adherence were departmental norms and practicing in-line with more senior colleagues despite guidelines. Furthermore, there were differences in these opinions related to the seniority of the physicians and the types of institutions they were practicing in (university vs. non-university affiliated). [43] This rigorous study, grounded in the TDF, enabled a

subsequent pilot study and an ongoing randomized trial of strategies to improve imaging guideline adherence [44] not only advancing implementation science but also quality of clinical care and generalizable knowledge.

The examples featured above highlight ambitious studies using implementation science approaches to tackle practice gaps in urology where real-world practices differ from CPG recommendations. It is exciting to see robust research of this nature in urology and the results are eagerly awaited.

What is the future of guideline implementation in urology?

If implementation strategies and interventions (e.g., audit and feedback, order checks, informed decision-making) are to show evidence of success, they should not only include outcomes relating to clinician behaviour changes (e.g., increase in guideline adherent practice); but also capture other relevant outcomes such as patient clinical outcomes (e.g., cancer recurrence or quality of life) to be more meaningful to our urology field (see the editorial by Beyer and colleagues in this volume on the importance of including patients in developing core outcome sets). Only then can we provide compelling evidence that guideline adherence improves patient outcomes, reduces harms, and reduces costs. This is one of the main reasons for including 'early recurrence' as a secondary outcome in the RESECT study example outlined previously. However, often patient outcomes take a long time to accrue thereby increasing the complexity and cost of implementation trials. The potential for mass guideline adherence surveillance in the European urology setting is possible by engaging the national societies networks to collaborate such as the IMAGINE project that went live in 2020. [15]

There are other various solutions being developed in projects coordinated by the EAU GO, such as PIONEER [13] and OPTIMA (**Op**timal **t**reatment for pat**i**ents with solid tu**m**ours in Europe through **A**rtificial Intelligence – another big data for better outcomes project funded by the European Commission's Innovative Medicines Initiative focussing on Prostate, Breast and Lung cancers). One of OPTIMA's aims is to embed computer interpretable guidelines within Electronic Health Records (EHR) and to also test the effectiveness of implementation interventions such as computerised decision support and audit and feedback. The innovative tools that such projects offer gives the urological community the opportunity to further standardise practice based on high quality CPGs and importantly demonstrate the impact of such standardisation through continuous monitoring of improvement of patient outcomes, reduction in harms, and improvements in healthcare efficiency.

CONCLUSIONS

Urologists, patients, healthcare providers, funders, and other key stakeholders must commit to reliably capturing and reporting data on patient outcomes, practice variations, guideline adherence, and the impact of adherence & non-adherence on outcomes. Including patients in these endeavours will be critical for CPG development and downstream implementation as empowering patients with knowledge about their condition and relevant guideline recommendations in patient-friendly language will help ensure understanding and confidence in their healthcare providers and support informed and shared decision-making. Leveraging implementation science and its frameworks, as well as the innovative efforts described above, appears as sound next steps towards improving guideline adherence and the associated benefits of evidence-based care.

TAKE HOME MESSAGE

There are evidence-practice gaps in urology. Implementation science approaches should be used to improve adherence to clinical practice guidelines. This will require a concerted effort from multiple stakeholders to describe practice variations, understand reasons for non-adherence, and design implementation interventions.

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