

The pharmacist's role in improving the treatment of erectile dysfunction and its underlying causes

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Abstract

Erectile dysfunction (ED), which worldwide is likely to affect in excess of 300 million men by 2025, is often either untreated or insufficiently treated. It can be a prelude to other serious illnesses and may be a cause or consequence of depression in affected individuals. Among men younger than 60 years of age, ED can be a robust early-stage indicator of vascular disease and type 2 diabetes. Untreated or inadequately treated ED can **also** be a sign of poor communication between health professionals and service users of all ages. Improved treatment of ED could cost-effectively prevent premature deaths and avoidable morbidity. The extension of community pharmacy-based health care would enable more men living with ED to safely access effective medications, along with appropriate diagnostic services and support for beneficial lifestyle changes such as smoking cessation in conveniently accessible settings. The task of introducing improved methods of affordably addressing problems linked to ED exemplifies the strategic challenges now facing health care systems globally. Promoting professionally supported self-care in pharmacies has the potential to meet the needs of aging populations in progressively more effective ways.

Keywords: Erectile dysfunction; Atherosclerosis; Diabetes mellitus; Community pharmacies; Online care; Professionally supported self-care

Abbreviations: cGMP, cyclic guanosine monophosphate; CVD, cardiovascular disease; ED, erectile dysfunction; GDP, gross domestic product; IT, information technology; MHRA, Medicines and Healthcare Products Regulatory Agency; MI, myocardial infarction; NCD, non-communicable disease; NICE, National Institute for **Clinical Health and Care** Excellence; OECD, Organisation for Economic Cooperation and Development; P, Pharmacy Medicine; PDE5, phosphodiesterase type 5; PoM, Prescription only Medicine; QALY, quality-adjusted life-year; DM, type 2 diabetes mellitus; WHO, World Health Organization

1 Introduction

Erectile dysfunction (ED) is defined as the inability to achieve or maintain a penile erection of sufficient firmness for satisfactory sexual intercourse.¹ In population-based models, declining levels of testosterone in aging men are associated with decreased libido.² However, clinically defined – pathological – ED is not a normal consequence of aging. It is a condition that can occur among adult men of all ages, reducing their quality of life and causing distress to both the men living with it and their partners.³⁻⁵

Epidemiological estimates of the prevalence of ED vary with the definitions employed. However, even conservative projections predict that the number of individuals living in both affluent and poorer nations who are directly affected by the condition will be in excess of 300 million in the year 2025.⁶

Vasculogenic (as opposed to psychogenic – see below) ED in men younger than 60 years of age is an independent risk factor for previously undiagnosed DM and vascular disease.⁷⁻¹⁰ There is also evidence that treatment outcomes and quality of life among men with DM and ED are worse than those among men with diabetes who retain sexual potency.¹¹ ED can also be a cause of, or risk factor for, depression.¹² In men of all ages, unreported or poorly treated ED may reflect inadequate health care and poor communication between health professionals and service users.

Improving the treatment of ED and its underlying causes is therefore an important health care objective. However, this conclusion has often been ignored or poorly understood by health policy makers. When sildenafil citrate (which by the end of 2018 will be available as an off-patent medicine in all markets) was first introduced as Viagra in 1998¹³ there were concerns about its potential cost to health service funders. Its therapeutic value was consequently challenged. In the United Kingdom, for instance, the then Secretary of State for Health claimed that “Most people in this country don’t think we should finance (sildenafil) through the health service as a sort of recreational drug at the expense of doing things which are more important.”¹⁴

This remark was made in the immediate context of preparations for the launch in 1999 of the National Institute for Clinical Excellence (NICE) initiative in the UK (now called the National Institute for Health and Care Excellence). There was a desire to avoid embarrassments like an early refusal by the new organization to recommend the use of a medication that in cost per quality-adjusted life-year (QALY) terms was – even at the time of its introduction – demonstrably more cost-effective than many other treatments already in common use.¹⁵

Twenty years later, the significance of ED as a cause of distress and a potential precursor to life-threatening events such as myocardial infarctions (MIs) and strokes is still not universally understood. Men with ED may also receive poor or insufficient care because of a combination of their reluctance to discuss their condition with health professionals and service providers' failures to foster better communication relating to sexual and reproductive

health.^{16,17} Against this background, this commentary explores issues relating to the prevention of ED-associated diseases from a public health and care quality improvement perspective.

After a brief initial overview of the changing global burden of cardiovascular disease (CVD) and the causes and treatment of ED, the analysis offered builds on recent studies of the role of community pharmacists as primary health care providers.^{18,19} It considers the viability of using their competencies in this context, along with related opportunities such as providing high-quality online product supply and support to foster professionally supported self-care among men living with ED. The significance of the UK Medicines and Healthcare Products Regulatory Agency's (MHRA) decision in late 2017 to reclassify Viagra (as distinct from generic sildenafil) as a Pharmacy (P) **medicine** as opposed to a Prescription only Medicine (PoM) is also discussed, along with issues relating to resulting availability of Viagra Connect beginning in March 2018.^{20,21}

Some advocates of extended pharmacy-led care argue that a significant proportion of the medicines used for treating long-term conditions that are currently available only via medically-controlled processes should be made accessible via information technology (IT)-enabled pharmacies. An especially strong case for this approach can be made in relation to CVD and the control of conditions like hypertension. Yet, even in circumstances in which it serves only as an access point to care provided by doctors and nurses, enhanced pharmacist-led support could help save and improve lives.

The primary methodology used in the development of this commentary involved cycles of iterative feedback between the authors, who between them have extensive experience and knowledge of the issues covered. Their shared understanding of the field and the available literature was complemented by a literature review based on an interrogation of PubMed. Further methodological details are available on request.

2 The evolving cardiovascular disease burden

Average global life expectancy at birth has risen from under 40 years in the early 1900s to over 70 today.²² In Western Europe and North America it is now around 80 years. This progress has primarily stemmed from the prevention and treatment of infectious diseases, followed by CVD-related advances. However, improved survival has led to a rise in the prevalence of later-life disorders of many types. Today, about 70% of all deaths worldwide are caused by non-communicable diseases.²³ In the relatively wealthy Organisation for Economic Co-operation and Development (OECD) countries, CVD and associated events alone still account for about a third of all deaths,^{24,25} together with a growing disability burden.

The World Health Organization (WHO) considers reducing the burden of mortality and morbidity associated with CVD a priority in all regions.²⁶ This view is shared by national agencies ranging from the American Heart Association to NHS England.^{27,28}

Phenomena that typically occur alongside life expectancy increases, such as dietary transitions, bring with them a complex mix of health-related benefits and costs. As societies grow more affluent individuals can typically afford to eat increased amounts of meat and processed foods, drink more sugary beverages and buy more items like cigarettes. At the same time, physical exercise rates tend to decrease in line with changes in patterns of work and transport. During the population ageing-linked process of epidemiological transition, such shifts contribute to trends like community-wide weight gains and increases in the prevalence of diseases such as DM. Age-standardized mortality from strokes and MIs also rises during “middle-stage” socio-economic development.²⁹

However, communities and the people living in them eventually acquire defenses against the unwanted consequences of “living with plenty.” When this happens, smoking levels decline and age-standardized CVD mortality drops. This is in part due to better health care and the impacts of public health initiatives and changed behavioral norms.

In the richest regions of the world, age-standardized CVD death rates presently stand at around half of those recorded in the 1950s.²⁹ This means that the age-specific risk of death from strokes or MIs is today higher in parts of India and sub-Saharan Africa than it is in Germany or the United States. CVD case fatality rates in middle and low income countries are now 2 to 3 times greater than those seen in the most economically advanced nations.³⁰

Yet, to date, the reduced levels of cardiovascular mortality enjoyed in affluent nations have been gained at the price of increased morbidity among surviving individuals and a high overall burden of vascular disease-associated disabilities,^{27,31} including ED. This highlights the universal importance of stopping tobacco smoking, encouraging protective dietary habits, promoting exercise, and improving access to effective medications for reducing CVD risks. In regions such as Europe, North America, and Australasia, there are still major health gains to be made from preventing or delaying the disabling consequences of atherosclerosis and related lifestyle-linked disorders. Improved outcomes can be achieved by promoting “healthy living” and intervening pharmacologically as soon as possible after, or before, disease processes become identifiable.

3 Erectile dysfunction and vascular damage

Erectile dysfunction has multiple causes linked to both lifestyle and environmental factors. It has been estimated that 70% of cases of ED are primarily due to organic as opposed to psychological variables.³² The most important underlying physiological cause of ED is damage to the endothelial cells that line arteries, including the small vessels of the penis.³³ This reduces their capacity to produce nitric oxide (NO), which is crucial for cavernosal smooth muscle facilitated vaso-relaxation needed to achieve and maintain erections.³⁴

Endothelial dysfunction is associated with tobacco smoking, elevated blood pressure, and plaque deposition.³⁵⁻³⁸ Other causes of ED include neurological lesions and diseases, the most prevalent of which are neural damage as a result of pelvic surgery or radiotherapy for cancer especially prostate cancer, multiple sclerosis and spinal cord injury.^{39,40} Depression is another cause of ED.³⁵

In many cases, pathophysiological and psychological factors act in tandem. As experiencing ED can itself promote depression and psychological distress,⁴¹ there is a danger of feedback cycles that – in the absence of appropriate support and effective treatment – perpetuate “psychogenic impotence.”⁴² The diagnosis of psychogenic ED is facilitated by signs such as nocturnal erections being of normal quality. This is not the case in ED resulting from endothelial dysfunction.³⁵ A diagnosis of vasculogenic ED should prompt monitoring for, and when appropriate, the treatment of, conditions such as hypertension, atherosclerosis and DM. Because the prevalence of diagnosed CVD and allied conditions increases markedly with age, the utility of ED as an indicator of unidentified forms of early-stage disease exists primarily if not exclusively in men aged younger than 60 years.^{10,43-45}

The onset of vasculogenic ED typically offers between 2 and 5 years' warning before potentially life-threatening events such as MIs occur. Its identification can therefore permit the initiation of protective therapies and lifestyle changes in a timely manner.⁴⁶⁻⁴⁸ In addition to being intrinsic to vasculogenic ED, endothelial dysfunction is a central component of atherosclerotic disease and an important element in the pathological consequences of DM.⁴⁹ Middle-aged men with ED are at an increased risk of not only having undiagnosed DM but also of developing it later in their lives, after the onset of ED.⁹

Erectile dysfunction provides early warnings of CVD partly because of the narrowness of the arteries supplying blood to the penis. At 1 to 2 mm in width, they are about half the size of the average coronary artery.⁴⁷ This means that even a limited thickening of the walls of the penile arteries due to the formation of plaque leads to a proportionally significant narrowing of the lumen and blood flow restrictions sufficient to impede erection. Over and above this, the penile arteries must dilate by about 80% to permit sexual intercourse. This is approximately 5 times more than larger arteries widen during vigorous exercise. The fact that plaque deposition inhibits the dilatory capacity of penile as well as other arteries provides a second reason why vasculogenic ED can serve as an early indicator of CVD.³³

3.1 Prevention opportunities

The long-term consequences of atherosclerosis may include up to half of all broadly defined dementia cases⁵⁰ in addition to life-threatening conditions like heart failure. Preventing ED-causal CVD might also prevent occurrence of ED. However, there is evidence that many men are embarrassed to talk about their erection problems and do not know that ED is often caused by the same factors as events like heart attacks and strokes.^{51,52}

This can be taken to represent a significant health education failing. From a health policy perspective such observations underscore the potential importance of promoting greater “health literacy” in this arena. Providing more men in their teens, twenties, and beyond with access to information about the causes of impaired erectile ability/function could, if complemented by other effective forms of public health intervention and personal support, be a valuable means of contributing to the achievement of goals such as smoking cessation and obesity avoidance and also of maintaining cardiovascular health throughout life.

In countries like the United States and the UK, most men and women aged 50 and older could benefit from interventions that reduce their CVD-related risks.^{53,54} There is evidence favoring the use of combinations of blood pressure and lipid-lowering drugs for disease avoidance (in addition to actions such as cutting salt intake).^{54,55} Yet, in practice there is still considerable resistance to the concept of using medicines for primary prevention, especially for individuals and groups judged to be at or below average risk levels. The result is that people may only be offered effective therapies after an initial MI or stroke, despite the fact that such events can be fatal.

3.2 Therapeutic options

Secondary prevention involves intervening in established pathological processes as early as possible to reduce the likelihood of future harm and to reverse, stop, or delay disease progression. Responding early to ED offers opportunities to recover sexual function, reduce death rates and avoid other disabilities. There is evidence that if ED becomes well established it may – perhaps partly for psychological reasons – become harder to treat than if medications like phosphodiesterase type 5 (PDE5) inhibitors are used promptly.⁵⁶

Along with encouraging lifestyle changes, potential treatments for ED may involve alprostadil local delivery, including intraurethral and most commonly intracavernosal injections.^{57,58} Some men find vacuum pumps useful. However, the most widely recommended and prescribed drugs for this indication are PDE5 inhibitors, of which there are now at least 7 molecular variants available on the world market. They work by slowing the breakdown of cyclic guanosine monophosphate (cGMP) by the enzyme PDE5⁵⁷; cGMP plays a central role in promoting the smooth muscle relaxation involved in the erectile response to sexual stimulation.

Recent studies provide evidence that, although they are not currently licensed for this purpose, taking PDE5 inhibitors to treat ED may directly reduce CVD-related morbidity and mortality.⁵⁹⁻⁶¹ Such observations point to the conclusion that enhancing the accessibility of PDE5 inhibitors could generate increased health benefits, provided that safe and appropriate supply arrangements are assured. While PDE5 inhibitors are well tolerated, there are contraindications and molecule-specific adverse events to be guarded against.⁶² For example, PDE5 inhibitors should not be taken by men who are using nitrates to alleviate angina. Also, sildenafil may affect retinal function because of variations in drug selectivity for different forms of the phosphodiesterase enzyme found in the eye.⁶² Those who experience sight-related side effects should seek alternative PDE5 inhibitor-based medicines or alternative ED therapies.

Men and women are more likely to take medications that they believe are necessary for their continuing survival and well-being or which offer immediate rewards as compared with those medications which cause unwanted

side effects, provide “silent” benefits, or are seen as non-essential. Treatments for ED are unusual because, despite their capacity to improve sexual performance, many men are reluctant to seek effective care via traditional routes.⁵² This is due to factors like embarrassment and denial. Innovative approaches to promoting the appropriate use of PDE5 inhibitors should address all barriers to their acceptance as necessary and beneficial.

4 Policy challenges

There is extensive public debate regarding the affordability of health and social care, not only in Europe and North America but also in emergent economies such as Brazil, India, and China. Concerns range from assertions that new pharmaceutical treatments are too costly to fears that increased life expectancy is driving up service costs to unsustainable levels. However, there is evidence to the contrary that preventing deaths and disabilities caused by disorders like CVD can be achieved in ways that are cost-effective and – in part because of their role in reducing health inequalities – are necessary for strengthening the economic performance and social well-being of modern populations.^{63,64}

Average spending on health services in the richer countries of the world has remained relatively stable in the last 10 to 20 years, at about 10% of gross domestic product (GDP).⁶⁵ Even in the US, which reportedly spends approximately 17% of its GDP on health care, there is no evidence that this level could not be sustained if the US public and its governmental representatives believe it to offer value for money.

Regarding pharmaceutical costs, when medicines and allied products are priced at manufacturers' return levels (ie, allowing for factors like price discounting) they are likely to account for about 1% of GDP in the average OECD nation.⁶⁵ Despite the introduction of new therapies, this proportion has also been relatively stable in recent decades, mainly because pharmaceutical prices typically fall after the intellectual property rights required for financing ongoing investment in research and development expire. Generic PDE5 inhibitors are, for example, now available for 10% or less of the amount charged when such medicines were first marketed as branded products.

The available evidence to date indicates that extending life expectancy has not been a dominant driver of health care spending in nations like the United States and United Kingdom.⁶⁶ In the context of preventing events such as strokes and MIs, major costs are often postponed rather than increased as survival is extended, ~~which should~~ This could save money and enhance productivity.^{67,68} However, health services across the globe are struggling with raising adequate funds, necessitating difficult decisions regarding supporting alternative forms of health service development. Similar challenges exist as far as ensuring quality and economic purchase and use of medications for indications such as ED.

4.1 The cost-effectiveness of comprehensive ED treatment

The value for money obtained from helping men to overcome or live well with ED depends on the circumstances in which their condition is identified and treated. This is because of variations in diagnostic practice, service mix, labor cost, and pharmaceutical and other prices, as well as differences in the health service-related preferences of people living in contrasting communities.

In many areas of ED care the extent and quality of the health economics data available are poor. Yet in the case of PDE5 inhibitors, studies have shown that the average cost per QALY gained as a result of their use has been around \$10,000 (approximately €8000) during periods in which innovators have enjoyed exclusive supply rights.⁶⁹⁻⁷¹ This is a modest figure compared with the QALY cost equivalents for many other forms of treatment. Seen from this viewpoint there is little doubt as to the cost-effectiveness of medicines such as sildenafil when they are used appropriately, especially after relevant intellectual property rights have expired.

If PDE5 inhibitors can definitively be shown to confer benefit as direct CVD treatments, the cost-effectiveness of their use in the ED context will increase further. Nevertheless, even without allowing for this possibility there is robust evidence that treating ED comprehensively, with not only appropriate medications but also effective lifestyle change support, offers good value for money.

In the past there have been failures to provide ED therapies because they have been considered “medically unnecessary” and/or because treating impaired sexual performance was regarded as a matter of “individual responsibility.”¹⁵ However, the view offered here is that this approach should no longer be regarded as ethically acceptable or economically rational. Emphasis ought to be given to the importance of treating ED as a condition amenable to intervention.

Some guidelines accept this interpretation.^{72,73} Yet, ~~this~~ this is not consistently the case. There is a strong argument in favor of more coherent national policy and professional approaches to recognizing the benefits that high-quality ED care generates for individuals and communities. The full advantages of improving access to such treatment include indirect benefits such as promoting increased use of medicines that (like anti-hypertensives – see below) some men inadvisably avoid taking because of ED-related concerns.

Economic evaluations of service models that address ED as both an immediate problem and a risk factor for CVD should take into account costs like those of testing for and treating CVD in men presenting with ED, as well as the full range of gains generated. Recent US research has found that the benefits of optimal ED identification and treatment outweigh the costs by in excess of 10:1.⁷⁴ Although the absolute cost of health service provision in the United States is many instances higher than that incurred elsewhere, this 10:1 benefit:cost ratio is likely broadly applicable across regions such as Europe.

4.2 Assuring the integrity of the drug supply

“Aphrodisiac” foods and drugs such as ginkgo biloba extract have been consumed throughout recorded history to treat ED, despite the reality that these substances are normally ineffective or only mildly efficacious for this use.⁷⁵ The use of illicit products such as (medicinally inert) rhinoceros horn has seriously impacted animal populations, while pharmacologically active herbal remedies are no less likely to have contraindications and side effects than conventional medications. Non-allopathic treatments may in addition be adulterated or counterfeited.^{76,77}

There are currently concerns that men using “natural” alternatives are sometimes receiving unknown doses of PDE5 inhibitors, putting them at risk of problems such as drug-drug interactions.⁷⁸ Given the effectiveness and convenience of PDE5 inhibitor use, it is not surprising that significant volumes of medicines containing them have been falsified or sold illegally via the internet and in settings such as night clubs and sports facilities.⁷⁹ The increased availability of legitimate generic versions of products like sildenafil might reduce falsification risks. But it has not eliminated them, and fake or substandard ED treatments can carry significant safety risks.^{78,80}

Some critics of agencies like the WHO have argued that the hazards posed by fake or substandard medicines have sometimes been exaggerated, in part to discourage the use of low-cost alternatives.⁸¹ Nonetheless, even if the use of lowest possible cost medicines is in principle desirable, particularly in poorer communities, men with ED should be encouraged to take authentic products that have been manufactured and supplied in a well-regulated manner.

The extent of illicitly obtained PDE5 inhibitor use is not accurately known; however, an observational study undertaken in Germany, Italy, and the United Kingdom in 2010 found that about one-third of men using such medicines had bypassed medical prescription.⁸² The authors estimated that up to 6 million European men were using ED treatments supplied via unauthorized sources. Similarly, a study of PDE5 inhibitor users in Japan found that only 55% of men there obtained their ED medicines via health professionals.⁸³ Of the remainder, about half purchased their medication from “friends,” and half purchased via the internet. Although there have been few recorded deaths as a direct result of such drug use,⁸⁴ there is a certainty of lost health gain and a strong possibility of significant indirect mortality. Another survey found that among UK resident men obtaining treatments like sildenafil independently of health professionals, approximately two-thirds had clinically defined ED,⁷⁸ which also indicates lost health improvement opportunities.

5 Towards new solutions: professionally supported self-care

Following the in large part successful control of infectious diseases in more affluent regions, important public health improvement opportunities relate to reducing the extent of CVD and diabetes-linked disabilities among individuals in middle and later life. The measures needed to achieve this end should also help to prevent significant numbers of cancers, dementias, and depressive illness episodes. They require both the adoption of healthier lifestyles and using medicines more effectively for primary as well as secondary disease prevention.

During the last century, the practice of medicine has become more specialized in hospitals and more complex in the community. In parallel with these trends, pharmacies have moved from making medications to supplying them. It has also, at least in some contexts, shifted more towards the active delivery of health care in the community. For example, pharmacists and pharmacy staff members have in a number of settings become involved in areas such as stopping smoking, controlling weight, and supplying contraception and pharmaceutical care more broadly.⁸⁵⁻⁹⁰

As advances in computer and information science continue, further community pharmacy developments will occur. Health care delivery systems are even now facing a choice between dispensing being undertaken in large automated centers backed by home delivery systems versus enabling community pharmacies to evolve further in the direction of delivering preventive health care and treatments for long-term conditions. Fig. 1 illustrates aspects of the opportunities available.

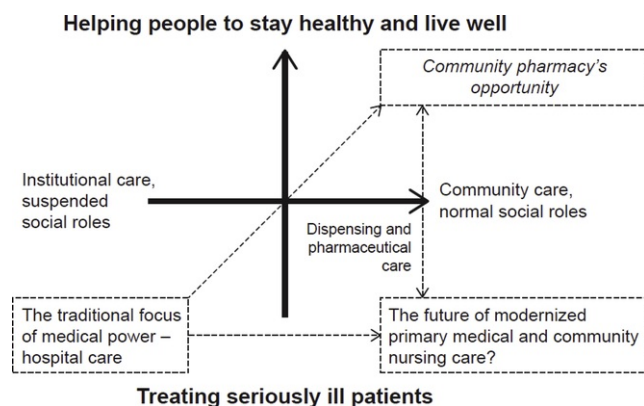


Fig. 1 The direction of health care development?

alt-text: Fig. 1

5.1 Pharmacy-based care

In the context of encouraging men to present early with ED and accept comprehensive lifestyle change and treatment packages, there can be no one cure-all solution. Progress is required throughout primary care and in every national setting. Improvements in medical and nursing practices will be needed in addition to pharmacy developments. The latter will take place when policymakers, service users, and pharmacists themselves prove sufficiently motivated to pursue them.

Community pharmacists have often been regarded as an underused clinical care resource. If they, along with other pharmacy staff members, can effectively interact with not only men who choose to consult them but also other primary and secondary care professionals, they should be able to improve ED treatment standards and CVD outcomes. This is in essence because, as outlined in [Table 1](#), the number of pathways available for accessing effective therapies in an affordable and sustainable manner will be increased.

Table 1 Current and future ED treatment access routes – an illustrative outline.

alt-text: Table 1

Current Routes	Process	Comments
Visit to a Primary Care Practitioner	Service user–initiated contact.	Primary care medical practices vary within and across countries and regions. Patients' underlying conditions may not be addressed, although good practice requires comprehensive care.
	Clinical discussion about ED followed by professional decision to investigate and/or treat.	Men may be reluctant to visit their doctor to discuss ED and when they do decide to act may have to wait for access.
Visit to an online service, if available	Service user initiated. Men are typically required to answer a number of standard questions.	It may be easier for men without ED to obtain drugs such as PDE5Is online than via face-to-face consultations. However, if accredited (as opposed to unregulated/illicit) online service providers are used, this risk is limited.
	Decision made by online physician as to suitability for treatment.	The extent of clinician/patient interaction is likely to be very restricted. Patients' underlying conditions are not necessarily addressed.
Specialist Pharmacist or Nurse Prescriber Supply, if available	Service user initiated, and/or accessed via an initial medical referral. Patient may go through a structured questionnaire with a pharmacist or another health professional in a clinic setting.	Questionnaires may take in excess of 20 minutes to complete. Non-medical prescribers (who can also include physician's assistants) are often required to undergo approved training in order to treat specific indications.
	Depending on the regulations in place, a treatment decision is made or a doctor consulted.	Patients' underlying conditions will be addressed if a well-designed protocol is employed.
Secondary Care	Patient is referred by a primary care doctor to a secondary care practitioner such as a urologist or a specialist in sexual medicine.	Usually for ED classified as severe. It may take time to get an appointment. This option offers alternatives to oral therapy alone.
Future Routes		
Visit to a Community Pharmacy	Service user initiated. Depending on the regulatory environment, the pharmacist (or another suitably qualified professional) could take men through a structured questionnaire or conduct a semi-structured consultation to determine treatment suitability.	User choice and convenience of service access would be enhanced. Primary care system capacity would be extended.
	Information could also be provided 'at shelf' and with product. All men with ED would be referred for additional treatment to address their underlying condition(s).	Access to treatment will be enhanced and health outcomes for individuals and populations will be improved if illicit use of treatments is reduced and if comprehensive preventive approaches to underlying CVD and type 2 diabetes are safely instituted.
Visit to an optimally configured Online Pharmacy	Service user initiated. Sites will take each visitor through a series of questions to determine suitability.	All questions must be answered to obtain treatment.
	All those identified as having ED would be directed to their primary care providers for follow-up and comprehensive preventive care.	Validated patient contact details will be required in order to facilitate appropriate primary care referrals. Health outcomes will again be improved

The same applies to the potential for well-designed, suitably regulated, ehealth and mhealth services supplied under the control of pharmacists or other qualified health professionals to enhance access to effective ED care. To the extent that online service contacts obviate problems associated with embarrassment, they may prove particularly valuable to those groups of men most difficult to engage, provided safety and other aspects of care quality are assured.

In many countries there is more reserve capacity available in community pharmacy than in other areas of primary care. In part because of this, pharmacists are actively seeking extended public health improvement and health care delivery roles.⁸⁹ This is the case in economies ranging from the United States, England, Scotland, and Australia to, for instance, the Netherlands, Spain and Brazil.^{18,90-93} There is also evidence that community pharmacies and the professionals working in them can offer acceptable points of first contact for men with ED, including those who have not previously discussed their condition with their doctors or any other health professional.⁹⁴

Recent developments also illustrate the possibilities that exist for extending pharmacy-based primary health care provision. There is evidence that such approaches can be cost-effective. For example, hypertension management in community pharmacies in Canadian provinces like Alberta has been shown to deliver sustained reductions in blood pressure and reduce service outlays.^{95,96} In the United States, a report of pharmacist-led interventions based in a local barbershop led to significant reductions in blood pressure and improved control for those with previously uncontrolled blood pressure.⁹⁷ In the United Kingdom, the recent decision of the Medicines and Healthcare Regulatory Agency to permit Viagra (as distinct from generic or alternative branded versions of sildenafil citrate) to be supplied under pharmacist supervision without medical prescription²¹ marks another important step towards what might be termed pharmacy-supported self-care. In New Zealand, a comparable change occurred even earlier, in 2014, although ~~it~~ **it-in this case medicine supply** was limited to men 35-70 years of age.⁹⁸

As already described, the rationale for extending access to PDE5 inhibitor-based ED treatments via additional pharmacist-controlled routes is partly based on research indicating this should enhance health outcomes by encouraging a greater proportion of the men using PDE5 inhibitors to address the systemic causes of their reduced potency. The use of illicitly supplied products, whether or not they contain the correct amounts of pharmaceutical-quality active ingredient and are free of contaminants, normally precludes such opportunities.⁷⁸

Lack of professional advice and support can also deprive men who are living with ED of the opportunity to use treatments like antihypertensive medicines containing angiotensin-receptor blockers in an optimal manner. These medications protect the endothelial cells of blood vessels and can reduce the risk of ED while also lowering blood pressure.⁹⁹ Such considerations, coupled with the reality that drugs such as sildenafil are already widely available without prescription via unregulated channels, underpin the case for extending community pharmacy supply in ways that an increasing proportion of men will find accessible and consistent with their needs and preferences.

5.2 Barriers to overcome

The degree to which pharmacy-led initiatives like those now underway in England and other UK nations (like, for instance, Scotland¹⁰⁰) will prove successful deserves monitoring from both a global pharmaceutical care development and public health improvement perspective. There is reason to hope that it will be possible for pharmacists working in both traditional community and IT-supported community service settings to play increasingly significant health care roles in constructive collaboration with doctors, nurses and other clinical professionals.

However, the rate of change achieved to date has been slow world-wide. Furthermore, the scale of the remaining barriers to progress should not be under-estimated. In the United States, for example, challenges to pharmacists being classified as health care providers at the Federal level have proved difficult to overcome.¹⁰¹ Arguably, outdated regulations governing which medications can be supplied by pharmacists without medical prescription have blocked desirable developments and failed to protect public interests, as too have professional inflexibilities associated with concerns about maintaining incomes. There are also important questions to be resolved regarding the extent to which pharmacists will in differing health care environments be able to access health records and whether or not they have the communication skills needed to engage groups such as men with ED.

To the extent that enhanced pharmacy-based support for women and men with needs in spheres such as sexual and reproductive health care will involve out-of-pocket payments as opposed to tax or insurance funding, there are equity issues to be addressed. In economically developed communities those men most at risk of inadequately treated ED and associated conditions tend to be less socially and materially advantaged than their peers.⁴³

Yet such challenges are not insurmountable. With the informed support of policymakers, regulators, professional bodies and others in authority in health care, it should be possible to make treatments such as those for ED and its causes conveniently and affordably available via, for example, pharmacies acting as “healthy living centres.”^{102,103} As communities and the people living in them become more oriented towards disease prevention rather than seeking remedies after symptoms have started impairing their lives, demand for affordable forms of easily accessible, professionally informed, self-care support is likely to rise. Reforms centered on improving the treatment of ED could prove an important step along the path towards meeting evolving service user requirements.

6 Conclusion

A key twenty-first century health policy objective is to reduce rates of disability and improve quality of life among men and women as they live into their 80s and beyond. Finding better ways of addressing the mental and physical health problems linked to ED exemplifies the strategic challenges now facing health care providers and policymakers as they seek to meet the needs of aging populations as cost-effectively as possible.

Erectile dysfunction is a significant source of avoidable distress among **affected** men and their partners, and there is strong evidence of it being a robust indicator of early-stage CVD and DM in men younger than 60 years of age. Effectively applied, modern diagnostic and treatment approaches could further decrease male mortality and morbidity rates and improve the quality of life of both men living with ED and – indirectly – their partners.

There are important opportunities to improve access to treatment and support via community pharmacies and well-designed, appropriately accredited online services. The evidence reviewed for this commentary indicates that this could be achieved safely. To the extent that it will reduce the use of illicitly-supplied medicines, progress towards providing enhanced pharmacy-based sexual and reproductive health care for conditions like ED will reduce risks of harm.

Enabling this vision to become reality will involve investing in public education about both the physical and mental health aspects of ED. In many settings, it may also require regulatory reforms permitting pharmacists greater freedom to supply medications used in ED therapy, CVD prevention, and diabetes care without medical prescription.

Professional guidelines should incorporate up-to-date biomedical knowledge and psycho-social insight into the factors that inhibit the uptake of beneficial advice and treatment. They should seek to ensure that men presenting with ED receive care characterized by careful attention to their individual concerns and which enables the fundamental causes of their condition to be competently addressed in convenient settings.

Some policymakers have in the past said that improving the treatment of men living with ED is not an important health care priority. However, this is no longer an acceptable position. The treatment of ED and its underlying causes should be recognized as twenty-first century tasks that demand serious attention. Failing to enable pharmacists to act as more effective primary health care providers could in the future impose costs well in excess of the investments needed to enhance their current roles.

Conflicts of interest

David G. Taylor has received funding from Pfizer Ltd relating to work on issues such as sexual and reproductive health policy and has worked with other pharmaceutical sector companies and organizations on a range of other matters.

Francois Giuliano is a speaker for Recordati, Menarini, and Lilly and an advisory board member for Ixchelsis, Pfizer, Recordati, and Sanofi.

Geoff Hackett is an occasional speaker for Bayer and Besins and advisory board member for Pfizer.

Evelyn Hermes-DeSantis has served as an advisory board member for Heron Pharmaceuticals.

Michael G. Kirby has received funding for research, conference attendance, lecturing, and advice from Astellas, Pfizer, Takeda, Bayer, Merck Sharp & Dohme, Boehringer Ingelheim, Eli Lilly, GlaxoSmithKline, AstraZeneca, and Menarini; is an editor for the *Primary Care Cardiovascular Journal*; and has served on several NHS advisory boards including the Prostate Cancer Risk Management Programme and the Prostate Cancer Advisory Group.

Robert A. Kloner is a consultant for Pfizer, Bayer, and Sanofi.

Terry Maguire acts as a consultant on community pharmacy related matters to Reckitt Benckiser, Pfizer, and GSK.

Vera Stecher is an employee of Pfizer, Inc.

Paul Goggin is an employee of Pfizer Ltd, Sandwich, UK.

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