CREW CENTRE OF EXPERTISE FOR WATERS

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Current policy landscape and proposed policy options to enable the implementation of eco-directed pharmaceutical prescribing in the Scottish healthcare system

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Contents

This CREW Policy Brief provides an overview of the environmental issues associated with pharmaceutical use in Scotland, focusing on pharmaceutical pollution. It presents the current policy landscape and the policy gaps related to pharmaceutical prescribing and environmental monitoring of pharmaceutical substances. This CREW Policy Brief proposes the concept of environmentally informed pharmaceutical prescribing, or the use of environmental criteria to inform the prescribing of pharmaceuticals, as one of the solutions to reducing pharmaceutical pollution in the country. Policy options on how to adopt environmentally informed pharmaceutical prescribing in the Scottish context are also presented.

Summary

The prescription of pharmaceuticals is the most commonly used healthcare intervention and indisputably has an important role to play in human health. However, pharmaceuticals can have negative effects on the environment and living organisms. Firstly, pharmaceutical use significantly contributes to the healthcare sector's carbon emissions. Secondly, pharmaceutical residues from human excretions and improper disposal of unused medicines can enter the water environment through wastewater and endanger aquatic life. Thirdly, pharmaceutical substances in the environment are thought to contribute to the global threat of antimicrobial resistance.

Often, a choice of pharmaceutical options is available to prescribers with decisions informed by therapeutic benefit, cost, and patient-related factors. To account for the environmental impacts of pharmaceuticals, environmentally informed or eco-directed prescribing proposes: 1) reducing pharmaceutical consumption as appropriate through improved rational prescribing practices; and 2) selecting medicines which have less environmental impact through the integration of environmental criteria in the development of medicine formulary[1]. This would contribute to the sustainability of the healthcare sector and safeguard both public and planetary health.

A joint analysis of policies on pharmaceutical prescribing and environmental monitoring of pharmaceutical substances in water environments was conducted to investigate whether the current policy landscape supports the adoption of eco-directed prescribing in the Scottish context. Barriers to and enablers for the policies and its implementation were also identified through a series of knowledge exchange activities with key actors[2].

Pharmaceutical pollution and the need to address this are recognised in key healthcare and environmental policies. However, barriers to the integration of environmental criteria in medicine appraisal, environmental monitoring of pharmaceutical substances, awareness of stakeholders, and coordination between key expert groups need to be resolved.

A three-pronged policy framework that should be embedded within the processes of healthcare and environmental agencies in Scotland is proposed to effectively integrate eco-directed prescribing as a joint programme of health and environmental sectors in the country. This three-pronged policy framework includes: 1) the organisation of a coordinative mechanism between key stakeholders; 2) systematic integration of environmental criteria in formulary development supported by expert evaluation of environmental risks of pharmaceuticals; and 3) improving knowledge of healthcare workers and the public on the environmental impact of medicines.

[1]The formulary guides prescribers on therapeutic options.
[2]Key actors from One Health Breakthrough Partnership (OHBP), Scottish Environment Protection Agency (SEPA), Scottish Antimicrobial Prescribing Group, and Scottish Government's Healthcare Associated Infection/Antimicrobial Resistance Policy Unit.

Background

Medicine use in Scotland

In Scotland, pharmaceutical use and expenditure have increased steadily both in primary and secondary care, accounting to a total medicine expenditure of £1.76 billion in 2019[1]. This accounts for 16.1% of the total expenses of Scotland's National Health Service (NHS) or 13.1% of the country's total health budget[2]. A large proportion of pharmaceutical prescribing comes from the primary care. For the past 10 years, the overall cost of dispensing medicines in primary care increased by 19%, with total (net) cost recorded at £1.4 billion for 2020/21 (Figure 1)[3].

The number of medicines or devices dispensed by NHS Scotland in primary care also increased, by 7.7% from 2011 to 2021 (Figure 1)[3] due to the ageing population; more people developing chronic diseases; and increased use of evidence-based clinical and prescribing guidelines by general practitioners[4]. Additionally, the top 10 items by cost in primary care were prescribed for treatment of cardiovascular, respiratory, mental health, pain, and other chronic disease conditions (e.g. diabetes and cancer) (Figure 2)[3].

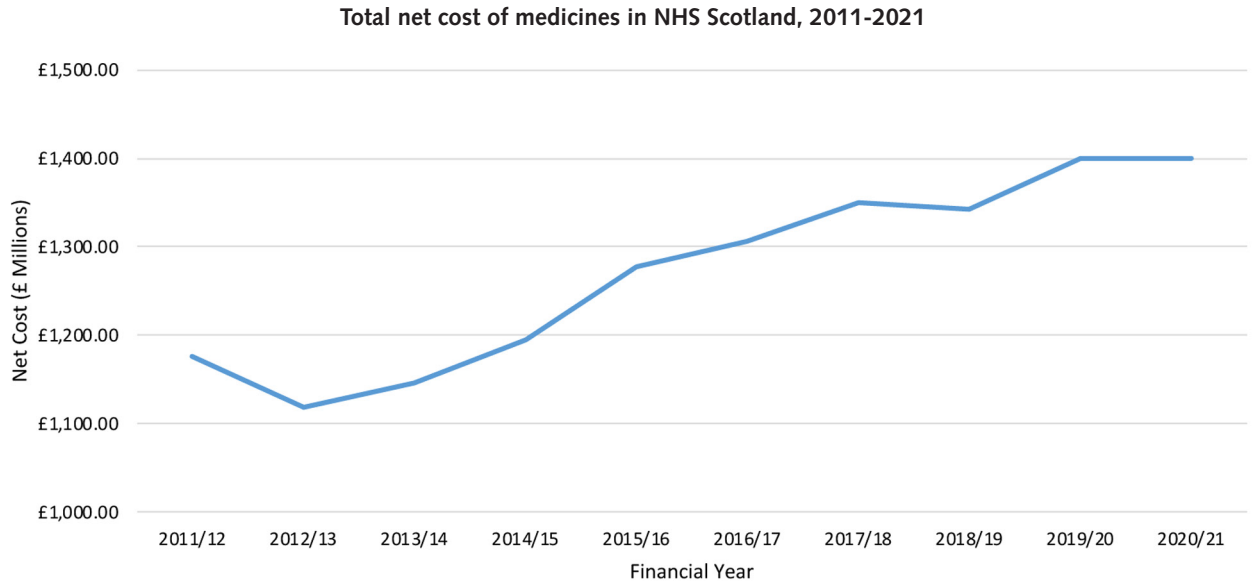

Figure 1. Total (net) cost of medicines in NHS Scotland, 2011-2021. Adopted from: Public Health Scotland, 2021.

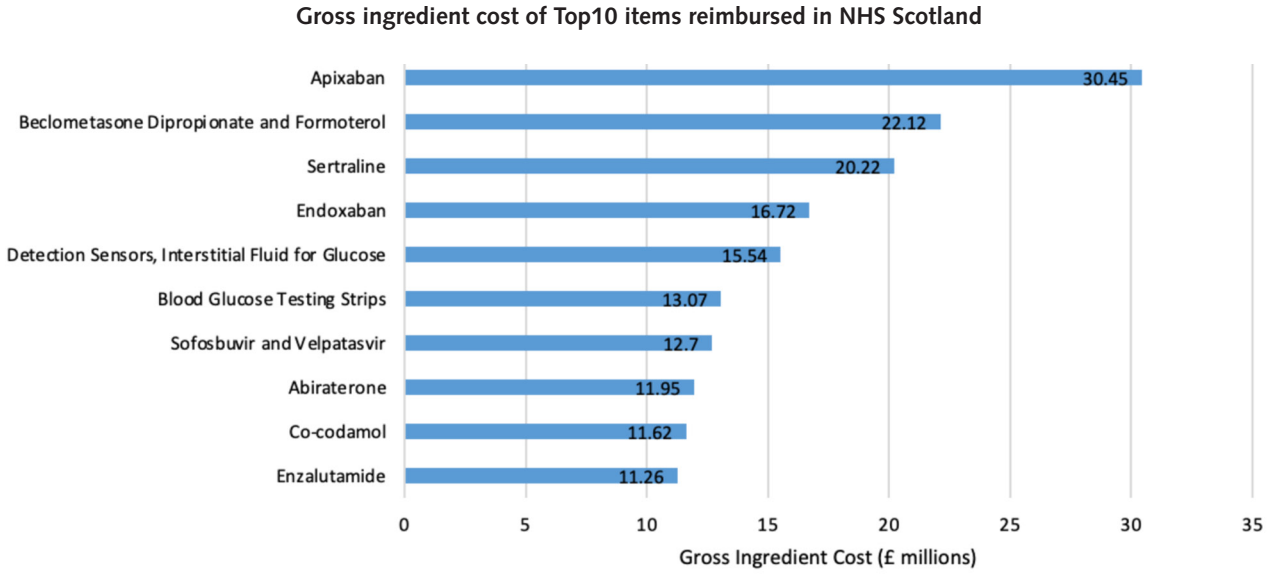

Figure 2. Top 10 items by Gross Ingredient Cost (£) reimbursed in NHS Scotland, 2011-2021. Adopted from: Public Health Scotland, 2021.

Environmental impacts of medicines: greenhouse gas emissions

The healthcare sector is one of the major emitters of greenhouse gases in Scotland. Efforts to account carbon emissions of the United Kingdom's (UK) NHS became more robust with the advent of 'sustainable healthcare'[5,6]. Greenhouse gas emissions of NHS Scotland between 1990 and 2004 accounted for 3% of total Scottish emissions, or 2.63 metric tons of CO_2[7]. Eighteen percent of this, or 0.47 metric tons, was attributed to pharmaceutical use (Figure 3)[7].

Latest estimates show that the greenhouse gas emission from pharmaceutical use further increased to 25% of the NHS's carbon emissions[5]. Aside from carbon emissions, the main environmental concern relating to pharmaceutical use is the emission of pharmaceutical substances into the water environment.

Environmental impact of medicines: pharmaceuticals in the water environment

Pharmaceutical substances or active pharmaceutical ingredients, excreted from the patient's body via urine or faeces or improperly disposed as leftover medicines, find their way into the water environment through wastewater[8]. Whilst some medicines are effectively degraded by wastewater treatment works, many are only fractionally removed[9]. Advanced treatment technologies are available, but these are cost and energy-intensive and not all technologies remove all types of substances efficiently. Scotland has nearly 2000 wastewater treatment plants, serving populations from few households to a large city, and it would not be practicable or affordable to fit all of these with advanced technologies.

Wastewater treatment works are thought to be the dominant source of pharmaceutical pollution, although manufacturing facilities, landfill sites, septic tanks, and emissions from veterinary pharmaceuticals also contribute[8]. The population density in a river catchment, the presence of hospitals (where a different range of medicines is in use), and the dilution in the river are all factors in the eventual concentration of pharmaceuticals in the water environment. Once in the aquatic environment, predicting the fate and behaviour of pharmaceuticals is complex[8]. Some degrade into harmless constituents, some disintegrate to unknown metabolites[5,6], some transfer into the sediment on the riverbed, and some persist in the water environment[8,10,11]. Even if pharmaceuticals are degraded or removed, their continual emissions has led to some pollutants being described as 'pseudo-persistent'[12].

Moreover, as new medicines are introduced to the market, the number of different pharmaceutical ingredients in use continues to rise[13], which increases the complexity

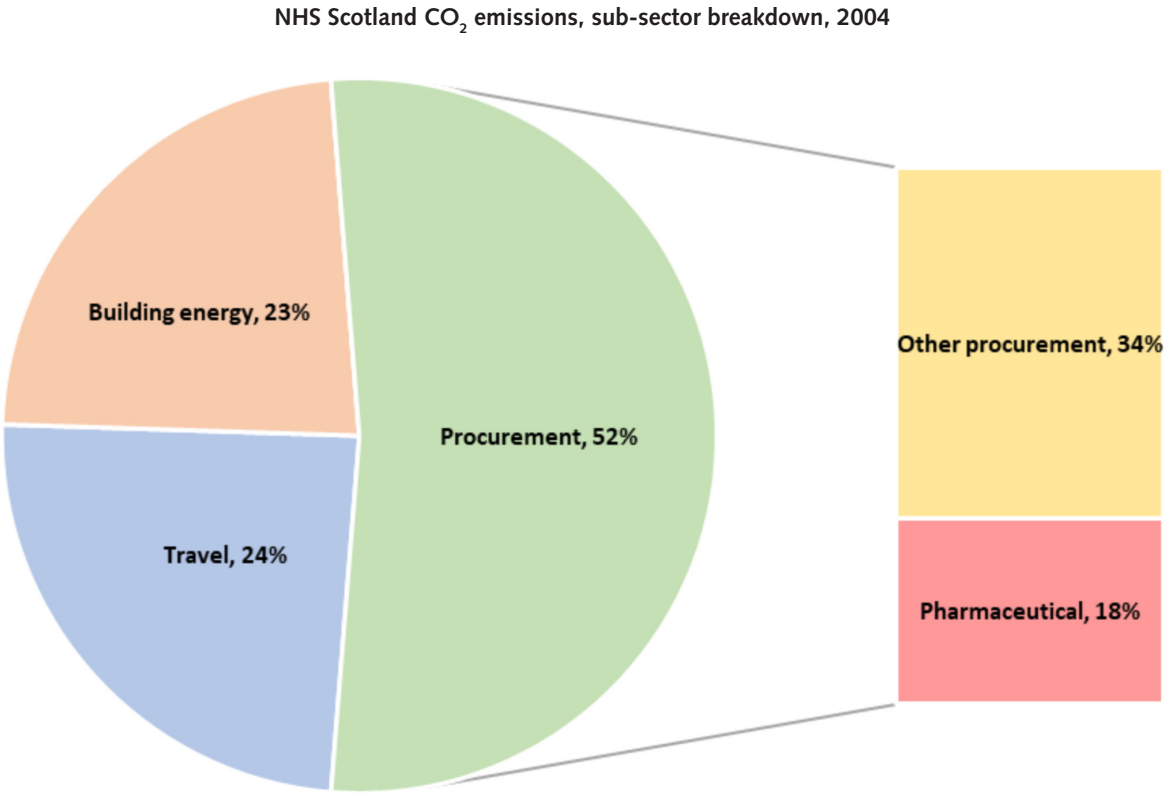

Figure 3. Carbon Footprint of NHS Scotland, sub-sector breakdown (1990-2004). Adopted from: NHS Health Facilities Scotland, 2009.

of the 'chemical cocktail' in the water environment[8]. At the moment, there are more than 3000 different compounds in use that could reach and harm the aquatic environment[14].

Effects of pharmaceutical residues in water environments

Medicines are designed to be biologically and chemically resistant to metabolic degradation and, consequently, recalcitrant to disintegration when released into the water environment[8,12,15]. Pharmaceutical substances can affect survival, reproductive ability, and behaviour of aquatic organisms and may impact birds, mammals, and other wildlife[8,16]. There are still many unknowns about the impacts of pharmaceutical pollution[8]. Ecotoxicity (the ability of substances to have negative impacts on the environment and living organisms in it) information is not available for all medicines, as the requirement for environmental information as part of marketing authorisation was only introduced in 2006[17]. Moreover, pharmaceuticals enter the environment as a complex mixture, and the interactions of different compounds with each other and with the receiving environment are not fully understood[8]. Nevertheless, harmful effects at environmentally relevant concentrations have been demonstrated for many pharmaceuticals, and they are likely to be a contributing factor to the decline of biodiversity[16].

The presence of pharmaceuticals in the environment, particularly antimicrobials, has also been associated with the development of antimicrobial resistance in bacteria, fungi and other microorganisms[8,18]. Whilst there is very limited understanding on the contribution of environmental antimicrobial resistance on population health, this is nevertheless an area of serious concern, since antimicrobial resistance is a major global health problem which accounted to 4.5 million deaths in 2019[19].

Lastly, even though pharmaceutical contaminants are found in the water environment[8], they are rarely detected in drinking waters[10,20,21].

Scale of pharmaceutical pollution in Scotland

A recent study collated environmental monitoring data from the Scottish Environment Protection Agency (SEPA), Scottish Water (SW), and academic sources[22]. Sixty substances in 11 distinct environmental matrices (including raw sewage, treated effluent, rivers, lakes, and coastal waters) were entered into a database of over 3000 data points, providing a comprehensive baseline for Scotland. Eight substances – ibuprofen, clarithromycin, erythromycin, diclofenac, EE2, metformin, ranitidine, and propranolol – emerged as posing a higher ecotoxicological risk in inland surface waters. Three substances – clarithromycin, erythromycin, and ciprofloxacin – were identified as posing a higher risk in terms of antimicrobial resistance. Data gaps were recognised in terms of the spatial coverage of monitoring efforts and pharmaceuticals investigated[22].

Initiatives for sustainable healthcare in Scotland

Scotland has made significant progress in transforming its healthcare system to a more sustainable one as part of its Net Zero ambition. The latest report of Scotland's Chief Medical Officer emphasised the need for a more 'realistic healthcare'[23]. Realistic medicine means focusing on personalised and equitable healthcare and putting a premium on providing healthcare services that do not harm patients and the environment.

First, health and environmental agencies in Scotland (e.g. NatureScot, Scottish Forestry, NHS Scotland, Public Health Scotland, Transport Scotland) worked together to establish the 'Our Natural Health Service Programme'[23]. As part of this programme, the NHS Greenspace Demonstration Project and the Green Health Partnership promote connection with nature to improve public health and the health of individuals with health conditions. On-site greenspace was created on NHS outdoor estates, and green space activities were developed for service users. The programme resulted in improvements in health, nature, and climate outcomes. There are also movements to sustainably utilise 'blue spaces' or water environments due to the increasing evidence for the positive impacts of water environments on physical and mental health[24]. Studies suggest that 'bluespace prescription programmes', like other nature-based social prescribing interventions, are associated with patient improvement in terms of their physical, social, and mental health, as well as the development of patients' pro-environmental behaviours[24]. As Scotland is abundant in natural surface waters, it is appropriate to protect these blue spaces from pollution and to sustainably utilise the ecosystem services of water environments for public health improvement.

Second, the Scottish Environmental Anaesthesia Group (SEA-G) advocated for the manufacturers' declaration of medical products' environmental information during procurement; for ecological choice in drug and product procurement; re-appraisal of single-use culture in healthcare; and theatre waste segregation[23]. The SEA-G also created the 'Green Theatre Project' that resulted in banning disposable cups and desflurane as an anaesthetic gas in Raigmore Hospital[23].

Third, the Scottish One Health Antimicrobial Resistance (AMR) Register (SOHAR) provided an overview of the

research landscape on antimicrobial resistance in the Scottish context within the scope of One Health approach and the UK National Action Plans[25]. It highlighted gaps in the development of end-user applications to tackle antimicrobial resistance.

Finally, the One Health Breakthrough Partnership (OHBP), a regional initiative based in Highland region advocates for the reduction of pharmaceuticals pollution in the environment[23]. OHBP includes SEPA, SW, NHS Highland, and the University of Highlands and Islands (UHI); with other partners such as Forrit, The James Hutton Institute (JHI), Talking Medicines, Glasgow Caledonian University (GCU), University of Strathclyde, and The University of Edinburgh. The partnership implemented projects and research to help reduce pharmaceutical pollution and is a driving force of strategic interventions on the issue in Scotland. For instance, an initiative for reducing pharmaceutical pollution in Caithness General Hospital was awarded certification by the Alliance for Water Stewardship (AWS) Standard[23]. The OHBP's approach is based on cross-sectoral engagement, research, innovation, and advocating for policy change. The OHBP has been advocating for the adoption of a 'green formulary' that will guide environmentally informed prescribing in primary care and hospital settings[23].

The concept of environmentally informed prescribing of pharmaceuticals

Environmentally informed or eco-directed pharmaceutical prescribing refers to a combination of two approaches: 1) reducing pharmaceutical consumption as appropriate through improved rational prescribing practices; and 2) prescribing medicines which have less environmental impact based on environmental risk assessment data reflected by biodegradability (or persistence), bioaccumulation potential, toxicity, and excretion profile of pharmaceutical substances[26–28]. It can contribute to reducing environmental footprint of medicine (e.g. pharmaceutical pollution, and possibly, carbon emissions due to reduced demand and use for medicines); and reducing medical cost due to reduced dose and consumption of medicines[26–28].

Eco-directed prescribing requires behavioural and systemic changes both in the healthcare and environmental sectors[29]. These include the development of and adherence to a strategy for the reduction of the environmental risks of pharmaceuticals through an environmental classification system of medicines[30] as well as modifications to pharmaceutical selection criteria and prescribing practices[26].

Several examples of eco-directed prescribing, with different programmatic elements, have been piloted elsewhere (e.g. targeted ecopharmacovigilance in rural China, the Stockholm's Wise List in Sweden)[31,32]. Generally, prescribers have had high adherence to these changes[32], but knowledge and awareness of patients are low[33]. In some cases, a reduction on pharmaceutical concentration in the water environment has been achieved[31], but questions remain about the optimal design of an environmentally informed formulary[34].

Immediate enabling actions needed to adopt eco-directed pharmaceutical prescribing in Scotland

The One Health concept emphasises the importance of a healthy environment to human health. The climate crisis, environmental degradation, and biodiversity loss negatively impact human health and wellbeing. Sustainability is therefore consistent with the remit of the healthcare sector. Whilst the Scottish healthcare system is transitioning into a more sustainable one where human and planetary health are protected, some aspects of this transition require further development such as the adoption of an eco-directed prescribing strategy for pharmaceuticals. For instance, policy recommendations on standardised monitoring of emerging contaminants have been suggested[35], but there are still gaps in monitoring of pharmaceutical substances. Baseline data on pharmaceuticals in the environment are available[22]; however, clarification on their usability to inform changes in formulary development and in prescribing practices is needed.

Transforming to a sustainable healthcare system requires multi- and intersectoral policy change, especially in the health and environment sectors. The readiness of these sectors should be assessed to understand the current policy landscape, barriers, and leverage points for policy change. Doing so will enable the holistic integration and bridging of perspectives from public health, medicine, environmental protection, and water management, to address a complex problem such as pharmaceuticals in the environment. Co-created policy options by representatives from health and environmental sectors can help the transition of Scotland's healthcare system to an environmentally sustainable one through the prevention of pharmaceutical pollution in its waters that would further contribute to the achievement of the NHS and Scotland's Net Zero ambition.

The subsequent sections of this policy brief discuss the policy landscape for prescribing and environmental monitoring of pharmaceuticals; policy and implementation barriers consulted with key stakeholders; and co-created policy options to support the adoption of eco-directed prescribing as vital element for sustainable healthcare transition in Scotland.

Policy landscape on pharmaceutical prescribing and pharmaceutical pollution in Scotland

Ideally, prescribing policies need to support eco-directed prescribing, whilst environmental monitoring policies need to guide the development of environmentally informed formularies and evaluation of the strategy's success. Key policies related to pharmaceutical prescribing and environmental monitoring were identified, consulted with key stakeholders, and analysed, to understand the policy landscape and the policy gaps that could hinder eco-directed prescribing of pharmaceuticals in the Scottish healthcare system. Analysis of the current policy landscape shows a clear difference on the 'policy readiness' between health and environmental sectors.

In general, the current healthcare policy landscape has the necessary policy frameworks to consider environmental sustainability in selecting, prescribing, using, and disposing of medicines. These policies promote a patient-centred approach to public health promotion; prevention of diseases; optimising pharmaceutical use and prescription; reduction of pharmaceutical wastes; and reducing variations in clinical practice. These measures are cognisant of the need to reduce pharmaceutical contamination in the environment; however, there are gaps in the integration of environmental criteria in medicine selection and prescribing.

Moreover, current environmental monitoring policies offer limited opportunities for a full and regular evaluation of the success of a changed prescribing strategy. The regular monitoring of pharmaceutical pollution is restricted to a small number of pharmaceuticals only, selected by a risk-based approach driven primarily by the European Water Framework Directive (WFD) and its translation into Scottish policies.

Key healthcare polices related to pharmaceutical prescribing

Overarching policy frameworks to achieve excellence in pharmaceutical prescribing

The National Clinical Strategy for Scotland provides a framework for the development and improvement of health service[36]. It set outs the direction to achieve a coherent, comprehensive, and sustainable high-quality healthcare. It recognises the problem of harm and wastes resulting from medical interventions and the need for a new clinical paradigm to address this. Realistic Medicine[23], proposed as the new clinical paradigm, is designed to do so, whilst also addressing variations in clinical practice, promoting quality, and cost-effectiveness. Realistic Medicine emphasises proportionate and realistic care to knowledgeable patients through lifestyle modification, medical intervention, self-management, and resilience building[23]. It sets out commitments to support the development of an environmentally sustainable healthcare in Scotland and recognises the contribution of the NHS to the climate emergency through carbon emissions and waste. More specifically, it recognises that the prescription of medicines, albeit the most common intervention in healthcare, also has negative impacts on the environment, and recognises the complexity of removing pharmaceutical substances in wastewater treatment plants.

The Realistic Medicine approach also provides recommendations on how to adopt green practice behaviours in healthcare[23]. The first one is by 'fostering a culture of stewardship for greener, sustainable healthcare' through communication and engagement with all actors[23]. Shifting the focus from a traditional medical model to lifestyle changes could also benefit the health and social care system. Realistic Medicine is also considered in Scotland's Health and Social Care Delivery Plan[37].

To ensure the realisation of the priorities and goals of Realistic Medicine and the National Clinical Strategy, the Effective Prescribing and Therapeutics Division[38] developed tools and guidance for specific disease conditions such as diabetes[39], respiratory diseases[40], and chronic pain[41]; and provides recommendations for the safe and effective prescribing and use of medicines[38]. One key theme in these guidelines is the reduction of pharmaceutical wastes by reducing variations in clinical practice, delivering patient education on treatment, and promotion of non-pharmacological interventions (e.g. lifestyle changes) through a patient-centred approach.

Linked to Realistic Medicine is Achieving Excellence in Pharmaceutical Care – A Strategy for Scotland[42]. Key components of this strategy are safe, effective, and person-centred pharmaceutical care and safer use of medicines through improved and enabled service provision, delivered through healthcare partnerships between the patient and the healthcare worker. The strategic actions on delivering safe use of medicines include data measurement and monitoring systems, ensuring awareness of pharmacy roles, and quality improvement in community pharmacy, which could be extended to promote environmental sustainability in pharmaceutical prescribing.

The accompanying Prescription for Excellence – A Vision and Action Plan provides key actions to create models of pharmaceutical care that are safe, effective, person-centred, and provide long-term sustainability[43]. It designs an environment for pharmacists to engage with other

health and social care professionals through integrated partnerships and innovation. The overall vision of the plan is the provision of high-quality pharmaceutical care to all, by clinical pharmacists and independent prescribers, in collaboration with the patient, carer, other professional representatives from health, social care, and third sector, so that patients get the best possible outcome from medicines with minimal (or without) waste and harm. It is hoped that this will contribute to the realisation of a person-centred care in all aspects of medical intervention.

The plan also recognises the need to address medicine wastage (with an estimated potential saving of £15 million) and to better manage polypharmacy[43]. It proposes the use of new and existing medicines and technologies; review of prescribing guidelines and practices; and development of partnerships between general practitioners and pharmacists. For instance, the Polypharmacy Guidance Realistic Prescribing provides the knowledge, structure, and tools for the management of polypharmacy[44]. It sets out a 7-step patient-centred medicine review that helps in assessing the health and therapeutic goals of the patient, the essential and unnecessary medicines that the patient takes, as well as the effectiveness, safety, and efficiency of the therapeutic intervention. Moreover, therapeutic partnerships and good communication between general practitioners and pharmacists are also identified as cost-effective measures in resolving the problem on prescribing and medicine wastage.

The healthcare sector in Scotland is also guided by the UK's 20-year Vision for Antimicrobial Resistance[45]. This strategic vision aims to contain, control, and mitigate antimicrobial resistance. Its ambition for change focuses on global partnership; innovation; minimisation of infection; provision of safe and effective care; protection of animal health and welfare; minimisation of environmental spread; supporting sustainable supply and access; appropriate use of antimicrobials; and public engagement on antimicrobial resistance. Providing safe and effective care to patients is proposed to be achieved through strong antimicrobial stewardship and using data and appropriate tools to administer evidence-based diagnostic tests and clinical interventions on infections. Moreover, effective waste and wastewater treatment; environmental stewardship; and modernisation of the manufacturing of medicines are also recommended to minimise environmental antimicrobial resistance and sustainable supply and access to antimicrobials.

Policies on selecting and licensing of medicines in Scotland

In terms of decision-making on pharmaceutical selection and licensing, the guidelines on the Introduction and Availability of Newly Licensed Medicines in the NHS in Scotland emphasises that the NHS boards are in charge of deciding which medicines to prescribe, but must follow the three criteria on safety, effectiveness, and value for money[46]. Together with the Guidance to Further Strengthen the Safe and Effective Use of New Medicines across the NHS in Scotland[47], this guideline outlines systems at national and local NHS boards to ensure that cost-effective treatments are made available to patients and to assist the rationalisation of prescribing given the large numbers of medicines available in the market. The guidance provides a framework within which NHS boards are expected to align their local policies to ensure a consistent and standard approach for access to newly licensed medicines.

The marketing authorisation for new medicines (licensing) is reserved to the UK Government. The Medicines and Healthcare Products Regulatory Agency (MHRA) and the European Medicines Agency (EMA) (for European Member States) have the remit to ensure that newly licensed (human) pharmaceuticals undergo a robust process of evaluation, using the criteria on safety, quality, and efficacy. In Scotland, the Scottish Medicines Consortium (SMC) acts as a single point advisory group for the selection of medicines that guides Area Drug Therapeutic Committees (ADTCs)[48]. The Consortium conducts horizon scanning of pharmaceuticals and provides advice to NHS Scotland about the value for patients of every new medicine that receives a licence from the MHRA or EMA. The SMC also reviews new formulations and new ways to use established medicines. This process is illustrated in Figure 4.

Medical products initially undergo rapid appraisal by the New Drugs Committee (NDC), a subgroup of the SMC[49]. Criteria for considering and selecting new medicines

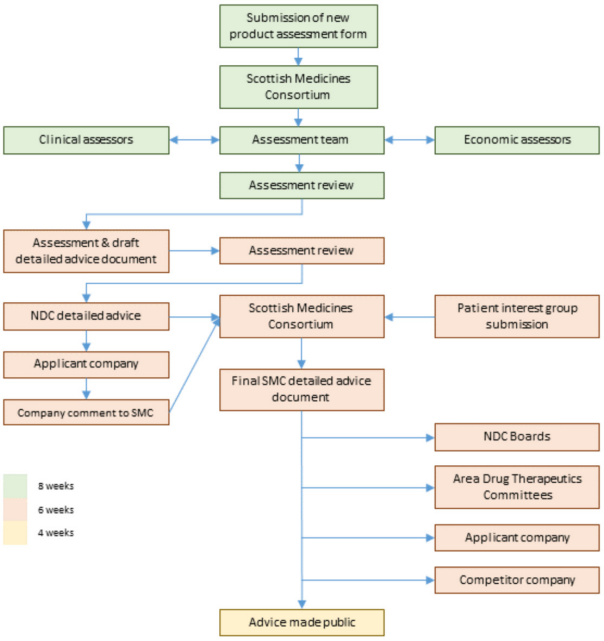

Figure 4. SMC assessment process for health technology (medicines) appraisal. Adopted from: New Medicines Review, The Scottish Government, 2013.

include effectiveness (as compared to existing medicines currently used in the NHS), benefit to patients, and value for money. In some instances, the SMC also considers additional factors or 'modifiers' that allow flexibility in accepting certain pharmaceuticals, especially those with higher cost per quality-adjusted life year. These modifiers could be: evidence of substantial improvement in life expectancy and/or quality of life, evidence that a sub-group of patients could have a specific or targeted benefit, an absence of therapeutic options, bridging to another therapy, and providing an alternative to an unlicensed medicine currently in use in NHS Scotland. Aside from licensing of medicines, SMC also works with the Scottish Antimicrobial Prescribing Group (SAPG) on the rational, safe, and effective use of antimicrobials.

SMC and NDC are composed of clinicians (medical and pharmacy) from the Area Drug Therapeutic Committees of local NHS boards; representatives from the Association of British Pharmaceutical Industries; the pharmaceutical industry; and representatives from the public. The SMC is also supported by an executive group of pharmacists and health economists. The Consortium has published the Guide to the Scottish Medicines Consortium[48] which outlines key processes in selecting medicines.

Policies on environmental sustainability in pharmacy services and good prescribing practices

The Royal Pharmaceutical Society (RPS) published the Competency Framework for all Prescribers, which guides prescribers on 'good prescribing'[50]. The competencies are split into two domains: 1) consultation; and 2) prescribing governance. Consultation competencies take the principle of shared-decision making and patient-centred approach. Specific competencies for consultation include the consideration of alternative medical options or interventions such as providing non-pharmacological approaches and appropriate cessation of treatment (de-prescribing). It also highlights the importance of prescribing medicine with adequate and updated information (on actions, indications, dose, contraindications, interactions, cautions, and adverse effects) through relevant frameworks for medicine use (local formularies, care pathways, protocols, and guidelines). Prescribing governance include prescribing safely, by identifying potential risks, minimising identified risks, and remaining updated with emerging safety concerns. The competency framework also provides recommendations on how to improve prescribing practice by using available tools such as prescribing data analysis and audit and feedback.

RPS also published its Sustainability Policies that set out how pharmaceutical services could help tackle the climate and ecological emergency by focusing on reducing environmental harm from medicines[51]. The policy recognises the environmental impacts of medicines, including the environmental risks posed by active pharmaceutical ingredients, the carbon footprint of the whole medicinal supply chain, and pharmaceutical waste. It proposes four strategies to tackle environmental degradation and the climate emergency: disease prevention, medicine use optimisation, pharmaceutical waste reduction, and improving supportive infrastructure.

Key environmental policies related to pharmaceutical pollution

Overarching sectoral policies related to pharmaceuticals in the environment

A Fairer and Greener Scotland is a policy framework that outlines the recovery of the Scottish health and social care systems after the COVID-19 pandemic[52]. It sets out the ways to achieve a green economic recovery in the context of the opportunity to address crucial problems, such as inequalities and drug deaths. It also discusses the restoration of the environment, improvement of the healthcare system, and the need for a Net Zero nation. Moreover, the One Planet Prosperity – Our Regulatory Strategy recalls the challenges of the 21st century that need to be tackled, such as diffuse sources of pollution, over-use of natural resources, and climate change, with an eye towards the social and the economic success of the society[53]. It sets actions that will regulate businesses to reduce the use of water, carbon-based energy and materials, and to prevent all forms of waste and pollution beyond compliance standards in ways that improve business profitability and long-term viability.

For the water environment, the Water Supply and Waste Water Sector Plan focuses on how SEPA supports operators and other actors in tackling the global pressures on freshwater resources[54]. It mentions how society manages the provision of its water supply and its wastewater services, as well as how to reduce the use of natural resources and the creation of waste. One of the aspirations set in this sectoral plan is to minimise the quantities of toxic chemicals and other pollutants that enter the water environment via wastewater. To accomplish this, SEPA aims to encourage manufacturers to reduce or eliminate environmentally toxic substances in everyday products that end up in the sewer system.

Policies related to prevention, control, and monitoring of pharmaceutical pollution

The Water Environment (Controlled Activities) (Scotland) Regulations provide a regulatory framework for controlling activities that could adversely affect Scotland's water environments, such as abstraction, impoundments,

engineering, dredging, surface water drainage, and pollution[55]. These regulations are the basis of discharge licenses, including for wastewater treatment plants, manufacturing, landfill, and private systems (septic tanks). A tiered, risk-based approach is applied, with General Binding Rules for low risk activities and registrations or license requirements for higher risk activities. The discharge licenses provided in this policy contain geospatial information that could help map and could potentially be used to estimate pollution by using standard emissions figures. The license and registration records could also be optimised for easier analysis and estimation of sewage-derived pollutants.

The European Water Framework Directive (WFD), Directive 2000/60/EC, is an umbrella directive for water management in Europe and establishes a framework for the protection of inland surface waters, transitional waters, coastal waters, and groundwaters[56]. Amongst many other provisions, this Directive mandates European Member States to implement necessary measures to progressively reduce pollution from priority substances and cease or phase out emissions, discharges, and losses of priority hazardous substances. It also mandates the European Commission to identify the priority substances for monitoring. In doing so, the European Commission considers the selection of substances of concern undertaken in relevant legislations regarding hazardous substances or relevant international agreements. The Environmental Quality Standards Directive (2008/105/EC) specifies the monitoring requirements and establishes maximum allowable concentrations as well as maximum annual average concentrations for the substances identified under the WFD[57]. In 2013, the Priority Substances Directive (2013/39/EU) identified 12 additional priority substances (45 in total), with six designated as priority hazardous substances[58]. It set out stricter environmental quality standards (EQS) for four existing priority substances and slightly revised EQS for three others. It also introduced biota standards for several substances and outlined strategic actions to improve the efficiency of monitoring and the clarity of reporting, with regard to certain substances behaving as ubiquitous, persistent, bioaccumulative, and toxic. A provision for a Watch List mechanism was made to allow targeted, EU-wide monitoring of substances of possible concern, to support the prioritisation process in future reviews of the priority substance list. The first Watch List included the painkiller diclofenac as well the hormones 17-Alpha-ethinylestradiol (EE2) and 17-Beta-estradiol (E2). When reviewed in 2018, diclofenac was removed. Another hormone, estrone (E1) was added, as well as the antibiotics amoxicillin, ciprofloxacin, and the macrolides (erythromycin, clarithromycin, azithromycin). The 2018 review also summarised analytical methods and the reliability of the predicted no-effect concentration (PNEC) values for the potential Watch List-candidate substances.

In 2019, the European Commission published the Strategic Approach to Pharmaceuticals in the Environment which states that although there is no clear evidence that pharmaceutical substances in the environment have impacts on human health, the possibility of long-term exposure of vulnerable populations remains, and the problem cannot be ignored[59]. It also references the risk of antimicrobial resistance and the One Health approach. The document commits the European Commission to (inter alia) 'promote the development of guidelines for healthcare professionals on the prudent use of pharmaceuticals posing a risk to or via the environment [and] foster best-practice exchanges between European Member States on how environmental considerations are taken into account in the advertising and prescription of medicinal products and the choice of therapy more generally, where appropriate' and to stimulate the development of 'greener' (more easily degradable) pharmaceuticals by the pharmaceutical industry. The document also commits to adding further pharmaceuticals to the Priority Substances and Watch List; including pharmaceuticals as part of the Best Available Techniques Reference Documents; improving the level of expertise in the European Commission's committees on environmental risk assessment of pharmaceuticals; increasing public access to risk assessment and environmental information; and fostering various commitments in relation to pharmaceutical wastage and wastewater.

SEPA's Control of Priority and Dangerous Substances and Specific Pollutants in the Water Environment implements the WFD and related directives (Priority Substances, EQS) in the Scottish context[60]. It outlines that substances on the priority lists can be controlled via discharge licenses. Following the introduction of the WFD, SEPA revised its aquatic monitoring strategy, which was laid out in the WFD Aquatic Monitoring Strategy – Scotland River Basin and its equivalent for the Solway Tweed Basin[61]. Three types of monitoring are distinguished: surveillance monitoring (at 60 sites throughout Scotland, mainly to understand long term trends), investigative monitoring (used when the source of pollution is not well understood), and operational monitoring (driven by risk assessments and compliance). The documents do not cover Watch List monitoring and the chemicals investigated do not include pharmaceuticals.

The Regulatory Method (WAT-RM-40) Assessment of Numeric Discharge Quality Conditions (for Controlled Activities Regulations, Urban Waste Water Treatment Directive, and Pollution Prevention and Control Compliance) provides guidance for determining compliance with conditions to protect the water environment. It specifies details of sampling requirements (e.g. sampling frequency, planned SEPA and operator samples, or SEPA response samples, such as following incidents)[62]. The current guideline is strongly focused on compliance monitoring.

Future perspectives on eco-directed pharmaceutical prescribing in Scotland focusing on key issues in the policy landscape

Policy gaps and implementation barriers were identified through rapid policy analysis and knowledge exchange engagements with key stakeholders from the water industry, health, and environmental sectors. Barriers were related to: 1) limited strategic approaches in integrating environmental information in pharmaceutical prescribing; 2) lack of a well-represented organisational body for national and high-level policy advocacy; 3) low level of knowledge and awareness on the environmental impact of pharmaceuticals amongst prescribers and the public; and 4) limitations on monitoring practices for pharmaceutical substances. These identified barriers could direct future research perspectives that will contribute to the knowledge base for eco-directed pharmaceutical prescribing in the Scottish context.

Limited strategic approaches in integrating environmental information in pharmaceutical prescribing

Detailed operational guidelines and specific interventions in how to achieve environmental sustainability in pharmaceutical prescribing in NHS Scotland are limited. Decision-making tools for prescribers are not available to support environmentally sustainable pharmaceutical prescribing. There is no protocol that prescribers can follow if they want to swap two medicines with similar clinical effects but different ecotoxicity values. Environmental risk assessment of human pharmaceuticals has become a mandatory requirement for marketing authorisations in Europe as provided by Directive 2001/83/EC[63]. This has been updated recently to have more consistent and holistic approach to environmental risk assessment[64] by harmonising with the WFD[65]. Results of environmental risk assessment of pharmaceuticals are submitted together with data on quality, safety, and efficacy of pharmaceuticals. Information from environmental risk assessment serves as the basis for appropriate evaluation and minimisation interventions on the concentration of pharmaceuticals in the environment. It also provides necessary and appropriate precautionary measures in the form of clearer labelling to promote proper disposal of medicinal products by patients and healthcare professionals. This information is included in the patient information leaflet of pharmaceutical products but this seems to have low impact as reflected by weak adherence to pharmacy take-back schemes[66].

Even though environmental risk assessment reports are available for marketing authorisation of medicines, these are not transparent and some actors highlighted that these reports are not taken into consideration when licensing new pharmaceuticals in the UK by the MHRA and SMC, since these bodies only consider safety, effectiveness, and cost information of pharmaceuticals when awarding marketing authorisation. It was suggested that decisions on granting market authorisation of medicines in Scotland should not be based on costs and benefits alone. Social and other factors are also considered, which is reflected in the list of additional factors or modifier for pharmaceutical licensings[49]; however, these only include clinical reasons and no environmental considerations.

Although the UK has left the European Union, Scottish policymakers have indicated their intention to remain aligned with European Union's environmental policies. Several European Member States have taken steps towards eco-directed prescribing, and collaboration on developing robust frameworks would save duplication of efforts. The European Strategy on Pharmaceuticals in the Environment[59] supports this direction; the introduction of eco-directed formularies contained within it could support development of 'greener' pharmaceuticals by creating markets. Other elements of the strategy, such as addressing advertising of pharmaceuticals and providing accessible information to the public, further support a patient-focused, eco-directed approach[59].

Lack of a well-represented national body that coordinates high-level advocacy measures to adopt eco-directed pharmaceutical prescribing

The SMC, SAPG, OHBP, and the SEA-G advocate for the reduction of the carbon and environmental footprint of the NHS at national and regional levels. These groups have expertise on the subject; however, consulted stakeholders highlighted that the initiatives of these groups on reducing the environmental impact of pharmaceuticals are not well-coordinated, which could result in duplication of initiatives and missed opportunities for a stronger and more collective approach for policy change at a national scale.

Ecotoxicity specialists who are trained and have the technical expertise to assess and evaluate environmental risk assessment reports of pharmaceuticals for market authorisation are not part of the decision-making working groups of the SMC and Area Drug Therapeutic

Committees. This is in line with other health technology appraisal bodies in the UK such as the MHRA, National Institute for Health and Care Excellence, and the All Wales Medicines Strategy Group and reflects the current criteria for authorisation. Similar to these health technology appraisal bodies, the SMC is composed of medical specialists, pharmacists, health economists, NHS board representatives, pharmaceutical industry, representatives from the public, and members providing administrative support.

According to a review on medicine licensing[49], this current membership is 'appropriate and representative of those groups which should be expected to have influence in the appraisal process'. However, with the changing climate and sustainability directions of the NHS and the Scottish Government[6], this representation might not be sufficient anymore. Without the expertise of ecotoxicity specialists in the SMC, it might be difficult to push forward changes, specifically the integration of environmental criteria in the medicine appraisal standards and processes.

Low level of awareness and knowledge on the environmental impacts of pharmaceutical prescribing, consumption, and disposal amongst prescribers and the public

There is low level of awareness and knowledge amongst healthcare professionals and the public about the negative impacts of pharmaceuticals on the environment. There is low public awareness of the environmental impact of pharmaceuticals beyond a limited awareness of good disposal practices such as take-back schemes[9]. There is an appetite to reduce pharmaceutical use and pollution; however, interventions to address this low knowledge and awareness level are limited[9].

Limitations on monitoring standards for pharmaceutical substances

Environmental policies in Scotland, especially on the prevention and control of pollutants, are generally robust. However, due to the current risk-based approach, key policies have some gaps in the identification and recognition of emerging micropollutants such as pharmaceutical substances; and do not provide comprehensive monitoring requirements for pharmaceutical substances. For instance, the Pollution Prevention and Control (Scotland) Regulations 2012[67] outlined monitoring activities of pollutants but does not provide a definite distinction regarding the use of the term 'water'. This could lead to some opacities in policy implementation since different aquatic environments require specific emission limits due to differences in their stress resistance. The current guidelines on Regulatory Method on the Assessment of Numeric Discharge Quality Conditions (WAR-RM-40)[62] focuses on compliance monitoring. An eco-directed formulary should be based on sound scientific evaluations of hazard and risk. Monitoring to support interventions that 'go beyond compliance' would help to evaluate the impact of eco-directed prescribing; however, this would require discussion on who should bear the cost of sampling and analysis, as well as the appropriate feedback mechanism in sharing and utilising results of analysis for pharmaceutical selection and prescribing decisions.

Efforts to improve environmental monitoring activities for pharmaceutical substances to support an eco-directed prescribing strategy are also hindered by other factors. These include knowledge gaps on ecotoxicity, chronic toxicity, long-term biological effects, and complex mixture interactions of pharmaceutical substances. Moreover, since both human and veterinary pharmaceutical substances are emitted to the water environment, the relative contribution of human pharmaceuticals – and therefore the potential risk mitigation achievable through their reduction – is locally specific and not always clear. Whilst more research is needed on these issues, monitoring activities could already support evaluation of the effectiveness of an adherence to formulary changes.

Policy recommendations

Eco-directed pharmaceutical prescribing requires multi- and intersectoral policy change[8]. A strategic approach to improving the capability and motivation of prescribers to adopt eco-directed prescribing whilst removing barriers to its full implementation, is vital. An immediate action is to lay the foundations of an eco-directed prescribing strategy within Scotland's health and environment sectors. These foundations should foster high- and grassroots-level policy advocacies that will push for the institutionalisation of the strategy in key Scottish Government agencies (e.g., NHS, PHS, SEPA) whilst addressing identified barriers.

There is a need to improve the capability of prescribers and the public, especially their awareness and knowledge on the impact of pharmaceuticals on the environment. This could be done by equipping them with tools and skills for proper disposal and for selecting less environmentally harmful medicines. Opportunities where prescribers can practise these knowledge and skills should be created by removing the barriers that make it difficult for prescribers not to implement the strategy in healthcare settings. This could be done by optimising essential enablers, such as the development of an environmentally informed formulary based on robust evidence, including data obtained by the environmental monitoring of pharmaceuticals. Prescribers should also be motivated to implement eco-directed prescribing and this could be inspired by putting in place social structures such as a well-represented national multi- and intersectoral working group that advocates and advise for the adoption and implementation of the strategy. Details of this approach are outlined in the proposed three-pronged policy framework for eco-directed prescribing in Scotland (Figure 5).

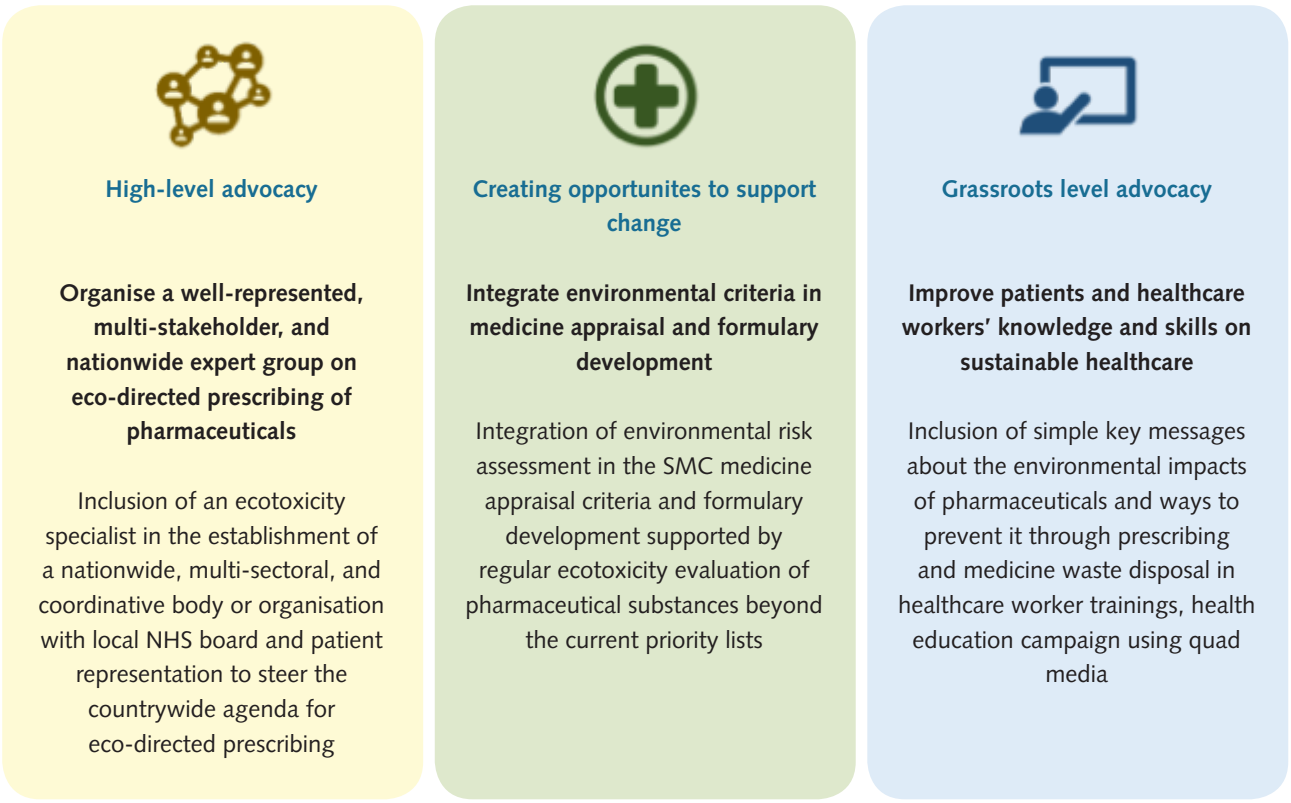

Figure 5. A three-pronged policy approach to initiate the adoption of eco-directed prescribing in Scotland.

Organise a well-represented, multi-stakeholder, and nationwide expert group on eco-directed prescribing of pharmaceuticals

A multi-stakeholder approach is needed to reduce the environmental impacts of pharmaceuticals[68], focusing on risk reduction; knowledge creation; awareness and capacity building; governance; and international cooperation[69,70] (see Case Study 1).

Case Study 1:
Multi-stakeholder collaborative group to implement eco-directed prescribing in The Netherlands[71]

Collaboration with other sectors (healthcare, environment, and water industry) and support from other stakeholders (e.g., physicians, pharmacists, and members of the water board) contributed to reduced prescription of diclofenac and increased prescription of naproxen as suggested.

The organisation of a coordinative mechanism linking SMC, SAPG, OHBP, and SEA-G, under a nationwide umbrella group that could be co-led by Public Health Scotland and SEPA, under the remit of Scottish Government's Realistic Medicine strategy would be helpful in implementing high-level advocacy for the institutionalisation of an eco-directed prescribing strategy in Scotland. These groups have unique expertise and remits (SMC – medicines appraisal; SAPG – antimicrobial resistance; SEA-G – reducing carbon footprint of inhalational anaesthetic gases; and OHBP – reducing pharmaceutical pollution in the environment) that need to be brought together for a more coordinated nationwide approach in integrating environmental criteria on pharmaceutical selection, licensing, prescribing, and development of regional and national formularies.

The inclusion of an ecotoxicity specialist in the group is important for advocating, assessing, and providing evidence-based recommendations on pharmaceuticals that have lesser or higher environmental impact alongside other expert advice on safety, clinical benefits, and economic value of medicines. Representation from Area Drug Therapeutic Committees in this national body should also be ensured to safeguard potential concerns on the local usability of a consistent, comprehensive, and environmentally informed formulary. Ad-hoc committees for specific disease conditions (e.g. infections, diabetes, mental health, etc.) could be formed within the group to inform proper integration of the environmental criteria on the prescription of pharmaceuticals for specific therapeutic pathways.

Integrate environmental criteria in medicine appraisal and formulary development

A systematic and stepwise approach to integrating environmental information in pharmaceutical selection and prescribing is a key component of an eco-directed prescribing programme. This approach should focus on three policy actions:

1. Integrate environmental risk criteria in SMC's medicine appraisal process and in the development of consistent and environmentally informed formularies by utilising all available relevant environmental data on pharmaceuticals.
2. Invest in environmental monitoring beyond compliance and explore public-private partnership with pharmaceutical industry for potential funding of monitoring activities and ecotoxicity data sharing.
3. Collaborate internationally for the creation of a definite, enhanced, and transparent ecotoxicity database.

A critical step for developing an eco-directed prescribing strategy is the recognition and inclusion of environmental criteria when licensing medicines (see Case Study 2). The SMC only considers safety, effectiveness, and cost when awarding market authorisation to new pharmaceuticals.

Case Study 2:
Stockholm's Wise List[72]

Stockholm Region's Drug Therapeutic Committee considers five criteria in the systematic introduction of new medicines in their formulary.

These are **efficacy, safety, cost-effectiveness, medical and pharmaceutical suitability, and environmental impact**.

The RPS recommends the improvement of prescribing guidelines to include environmental criteria to promote environmentally sustainable selection and prescription of medicines. That is, 'where medicines have equivalent clinical efficacy, the medicine with the lowest environmental impact should be the first choice'[51]. Environmental criteria in SMC's medicine appraisal process and the development of regional and national formularies should be integrated by utilising available ecotoxicity data of pharmaceuticals[22]. A new prescribing guideline and the inclusion of environmental criteria would result in changes in therapeutic regime of some patients. A patient-centred approach through consultation, education, and shared-decision making should be followed to appropriately prescribe medicines in alignment with the choices and the health goals of patients[49].

There are 11 formularies used across 14 health boards in Scotland and the development of consistent, comprehensive, and environmentally informed

formulary could reduce variations in pharmaceutical prescribing and medicines waste[73]. The updating of NHS health boards' formularies into a more consistent and comprehensive regional formulary presents an opportunity to utilise the available ecotoxicity data of some pharmaceuticals in Scotland[22]. A pragmatic, stepwise, and regional development of a new formulary in Lothian has already started for some therapeutic areas (e.g. skin, gastrointestinal, or infections)[74]. By doing so, an environmentally informed Lothian Joint Formulary (East Region) could be used as a template for the North and West regions' formulary, and eventually leading to a consistent and environmentally informed approach to formulary development across Scotland.

To support the development of an environmentally informed formulary, environmental monitoring beyond compliance is desirable (see Case Study 3). However, this would require discussion on sustained investment for sampling and analysis.

Case Study 3:
Targeted ecopharmacovigilance in China[31]

Reduced prescription of antibiotic of concern in rural China was associated with environmentally informed prescribing of antibiotics supported by **regular monthly monitoring of antibiotic residues in pond water**.

A spatial-based pharmaceutical ranking approach could inform decision making on pharmaceutical prescriptions and the development of an environmental classification of pharmaceuticals[67]. Increased monitoring of effluents, in particular of hospital and wastewater treatment plants, and surface waters, would better inform the understanding on the extent and severity of pharmaceutical pollution and the risk it poses, which in turn could inform appropriate interventions. Given that many pharmaceuticals are discharged to the environment as a mixture, the assessment of the risk posed by mixtures of pharmaceutical substances into the environment is an essential parameter that should also be considered[75]. Another option that could be considered is to leverage existing partnership with pharmaceutical companies who are members of the SMC's Users Group Forum (composed of pharmaceutical industry representatives). This private-public collaboration could be used in sharing environmental data on pharmaceutical substances which could support the development of a definite, enhanced, and transparent ecotoxicity database; and possibly, funding of environmental monitoring activities for more pharmaceuticals. Modelling based on local prescription data could also be an alternative or complementary way to measure the success of the strategy. Formulary design based solely on inherent characteristics of medicines would eliminate the need for monitoring; monitoring capacity should therefore be considered in the design of the formulary.

Improve patients and healthcare workers' knowledge and skills on sustainable healthcare through capability-building activities

An integrated and comprehensive communications and advocacy strategy aimed at prescribers and the public, to improve awareness, knowledge, and skills on pharmaceutical pollution and ways to prevent it, should be implemented alongside other health campaigns of the NHS (see Case Study 4). This will socially prepare patients and healthcare workers on the potential changes in medicine prescription.

Case Study 4:
Sweden's educational and instructional booklet on environmental classification of pharmaceuticals[76]

Distribution of easy-to-understand booklets with instructions on how to interpret environmental classification of pharmaceuticals increased prescribers' adherence to the Wise List.

To be cost-efficient, key messages on pharmaceutical pollution and ways to prevent this through prescribing and medicine disposal should be embedded in existing health education and campaigns such as the antimicrobial stewardship programme and pharmacy take-back scheme.

Community pharmacy services could also play an important role in widespread and consistent public messaging about the environmental impacts of pharmaceuticals (see Case Study 5). Pharmacists are key implementers of clinical advice provision, prescribing guideline development, and capacity-building which are essential components of an antimicrobial stewardship programme[49]. However, messaging would need to be carefully constructed to avoid blaming the patient and additional resources needed by community pharmacies should be provided.

Case Study 5:
Germany's educational programme on sustainable consumption and disposal of medicines[9]

Training and educational campaign on sustainable consumption and responsible consumption of pharmaceuticals implemented in schools and sports clubs involving pharmacists and doctors resulted to increased environmental awareness, proper disposal, and reduction on the use of painkillers.

Lastly, there is a need to invest in a research agenda that would address knowledge gaps to evidence the need for policy change as the Scottish Government moves to the institutionalisation of eco-directed prescribing in the NHS[6]. In addition to evaluation of environmental gains (e.g. gaps in toxicity data, complex mixture interactions, long-term biological effects), research on the adherence to prescribing changes, health outcomes, and patient satisfaction will be needed.

In conclusion, pharmaceutical pollution is a health and environmental concern in Scotland. Eco-directed pharmaceutical prescribing has co-benefits both on preventing pharmaceutical pollution and reducing medicine expenditure through reduced use of medicines and integration of environmental criteria in pharmaceutical selection. There are opportunities through policy change to adopt eco-directed prescribing in Scotland. These opportunities could be meaningfully utilised through robust, comprehensive, and coordinated strategic actions fostered by multi- and intersectoral collaboration, especially between the health and environmental sectors. The full implementation of eco-directed prescribing is a long process, although eminently suitable for step-wise introduction. Thus, implementation of these key strategic actions will require sustained long-term investment.

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