CREW CENTRE OF EXPERTISE FOR WATERS

Policy Note

Eco-directed pharmaceutical prescribing in Scotland

Julius Cesar Alejandre*, Gabriele Frascaroli*, Ania Escudero*, Ole Pahl*, Lesley Price*, Sharon Pfleger†, and Karin Helwig*

Eco-directed pharmaceutical prescribing is a vital sustainable healthcare strategy. This CREW Policy Note discusses Scotland's pharmaceutical prescribing and environmental monitoring policy landscapes; its barriers; and policy options to support eco-directed pharmaceutical prescribing in the NHS.

Overview

- Pharmaceutical residues can enter the water environment, endanger aquatic life, and contribute to antimicrobial resistance.
- There is a push for environmentally informed pharmaceutical prescribing in NHS Scotland.
- Current health and environmental policies could support the adoption of environmentally informed pharmaceutical prescribing. Yet there is a need to integrate environmental criteria in pharmaceutical prescription and improve environmental monitoring of pharmaceutical substances.
- We propose a three-pronged policy framework that includes: 1) a coordinative mechanism between health and environmental expert groups; 2) systematic integration of environmental criteria in pharmaceutical prescription; and 3) improving knowledge and skills of prescribers and the public on sustainable healthcare.

BACKGROUND

Medicine use in Scotland

Scotland's pharmaceutical use and expenditure have increased steadily in primary and secondary care, accounting to £1.76 billion in 2019[1]. This is 16.1% of the total expenses of Scotland's National Health Service (NHS) or 13.1% of the country's health budget[2]. A large proportion of prescribed pharmaceuticals comes from primary care. For the past 10 years, the overall cost of primary care's dispensed medicines increased by 19%, with total (net) cost at £1.4 billion for 2020/21[3]. The number of medicines dispensed in primary care also increased by 7.7% from 2011-2021[1] due to the ageing population; increasing prevalence of chronic diseases; and increased use of evidence-based clinical and prescribing guidelines[4]. The top medicines prescribed in primary care are for treatment of cardiovascular, respiratory, mental health, pain, and other chronic disease conditions [3].

Pharmaceuticals in the water environment

The healthcare sector is one of the major emitters of greenhouse gases and pollutants. Pharmaceutical use contributes to 25% of NHS total carbon emissions[5,6]. Aside from carbon emissions, pharmaceuticals in the water environment is a main health and environmental concern.

Pharmaceutical substances, excreted from the patient's body or improperly disposed leftover medicines, find their way into the water environment via wastewater[7]. Whilst some medicines are degraded by wastewater treatment works, many are only fractionally removed[8]. Advanced treatment technologies are available, but these are cost and energy-intensive and not all technologies remove all substances efficiently[7]. Scotland has approximately 2000 wastewater treatment plants, serving populations from a few households to a large city; it is impracticable and unaffordable 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[7]. Once in the aquatic environment, predicting the fate and behaviour of pharmaceuticals is complex[7]. Some degrade into harmless constituents, some disintegrate to unknown metabolites, some transfer into the sediments on the riverbed, and some persist in water environments[7,9,10]. Even if pharmaceuticals are degraded or removed, their continual emission has led to some 'pseudo-persistent' pollutants[11]. Moreover, as new medicines are introduced to the market, the number of used pharmaceuticals continues to rise[12], which increases the complexity of the 'chemical cocktail' in water environments[7]. At the moment, there are more than 3000 pharmaceutical compounds in use that could reach and harm aquatic environments[13].

Effects of pharmaceuticals in water environments

Medicines are designed to be biologically and chemically resistant to metabolic degradation and, consequently, recalcitrant to disintegration when released in water environmenta[7,11,14]. Pharmaceutical substances can affect survival, reproductive ability, and behaviour of aquatic organisms, mammals, and other wildlife[7,15]. There are still many unknowns on the impacts of pharmaceutical pollution[7]. Ecotoxicity information is not available

*Glasgow Caledonian University, Cowcaddens Road, Glasgow, Scotland, G4 0BA
†National Health Service (NHS) Highland, 3099 Old Perth Road, Inverness, Scotland, IV2 3FF

for all medicines as this marketing authorisation requirement was only introduced in 2006[16]. Moreover, pharmaceuticals enter water environemtns as complex mixtures, and the interactions of different compounds with each other and with the receiving environment are poorly understood[7]. Nevertheless, negative impacts on the environment have been demonstrated for many pharmaceuticals, and they are likely to contribute to decline in biodiversity[15]. Pharmaceuticals in the environment, particularly antimicrobials, was also associated with antimicrobial resistance in bacteria, fungi, and other microorganisms[7,17]. Whilst there is limited understanding on the contribution of environmental antimicrobial resistance on population health, this is nevertheless an area of concern, since antimicrobial resistance is a global heath problem which accounted to 4.95 million deaths in 2019[18].

In addition, even though pharmaceutical contaminants are found in the water environment[7], they are rarely detected in drinking waters[9,19,20].

Scale of pharmaceutical pollution in Scotland

Data on 60 substances in 11 distinct environmental matrices (including raw sewage, treated effluent, rivers, lakes and coastal waters), gathered from the Scottish Environment Protection Agency (SEPA), Scotish Water (SW), and academic sources were collated and entered into a database of over 3000 data points, providing a comprehensive baseline for Scotland[21]. Eight medicines – ibuprofen, clarithromycin, erythromycin, diclofenac, EE2, metformin, ranitidine, and propranolol – pose a higher ecotoxicological risk in inland surface waters. Three pharmaceuticals – clarithromycin, erythromycin, and ciprofloxacin – pose higher risk in terms of antimicrobial resistance. There were data gaps on spatial monitoring coverage and medicines investigated[21].

Eco-directed pharmaceutical prescribing

Environmentally informed or eco-directed pharmaceutical prescribing is a combination of: 1) reducing pharmaceutical consumption as appropriate through improved rational prescribing; and 2) prescribing medicines which have less environmental impact based on environmental information reflected by biodegradability (or persistence), bioaccumulation potential, toxicity, and excretion profile of pharmaceutical substances[22–24]. It can contribute to reducing the environmental footprint of medicine (e.g. pharmaceutical pollution and, possibly, carbon emissions due to reduced demand and use of medicines); and reducing medical costs due to reduced pharmaceutical dose and consumption patterns[22,23,24]. Eco-directed prescribing requires behavioural and systemic changes in health and environmental sectors[25] such as the development of and adherence to a strategy for the reduction of the environmental risks of pharmaceuticals through an environmental classification system of medicines[26] and modifications on pharmaceutical selection criteria and prescribing practices[22]. Examples of eco-directed prescribing were piloted elsewhere (e.g. Wise List in Sweden, ecopharmacovigilance in China)[27,28]. Prescribers have had high adherence to the changes[28] but knowledge and awareness of patients were low[29]. In some cases, reduction of pharmaceutical concentration in water environments has been achieved[27], but questions remain about the optimal design of an environmentally informed formulary (a list of prescribing choices of medicines)[30].

SCOTLAND'S POLICY LANDSCAPE ON PHARMACEUTICAL PRESCRIBING AND PHARMACEUTICAL POLLUTION

Ideally, prescribing policies need to support eco-directed prescribing, whilst environmental monitoring policies need to guide the development and impact evaluation of environmentally informed formularies. There is a clear difference on the 'policy readiness' of Scotland's health and environmental sectors to support eco-directed prescribing.

Analysed policies (**Box 1**) showed that the healthcare policy landscape has the necessary policy frameworks to consider environmental sustainability in pharmaceutical selection, prescription, usage, and disposal. These policies promote a patient-centred approach to public health promotion; optimising pharmaceutical use; reducing variations in clinical practice, and reducing pharmaceutical wastes, which are cognisant of the need to reduce pharmaceutical pollution. However, there are gaps in the integration of environmental criteria in medicine selection and prescribing. Environmental monitoring policies also offer limited opportunities for a full and regular impact evaluation of a changed prescribing strategy. Regular monitoring of pharmaceutical pollution is restricted to a small number of pharmaceuticals, selected by a risk-based approach driven by the European Water Framework Directive and its translation into Scottish policies.

FUTURE PERSPECTIVES FOR SCOTLAND'S ECO-DIRECTED PHARMACEUTICAL PRESCRIBING STRATEGY

The future success of eco-directed pharmaceutical prescribing in Scotland is dependent on closing policy gaps and implementation barriers. Identified gaps and barriers focus on: 1) limited strategies in integrating environmental information in pharmaceutical prescribing; 2) lack of a diverse national body coordinating high-level policy advocacy; 3) low stakeholders' knowledge on pharmaceuticals' environmental impacts; and 4) limitations on monitoring practices for pharmaceutical substances. These gaps and barriers could also direct future research that will contribute to the knowledge base for eco-directed pharmaceutical prescribing in the Scottish context.

Limited strategies in integrating environmental information in pharmaceutical prescribing

Operational guidelines and specific interventions are limited

Box 1. Health and environmental policies analysed

Health policies

- *National Clinical Strategy for Scotland*
- *Realistic Medicine*
- *Health and Social Care Delivery Plan*
- *Effective Prescribing and Therapeutics*
- *Achieving Excellence in Pharmaceutical Care – A Strategy for Scotland*
- *Prescription for Excellence – A Vision and Action Plan*
- *Polypharmacy Guidance Realistic Medicine*
- *UK's 20-year Vision for Antimicrobial Resistance*
- *Introduction and Availability of Newly Licensed Medicines in the NHS Scotland*
- *Guidance to Further Strengthen the Safe and Effective use of New Medicines*
- *Scottish Medicine Consortium on Licensing Medicines*
- *RPS Competency Framework for All Prescribers*
- *RPS Sustainability Policies*

Environmental policies

- *A fairer and greener Scotland*
- *SEPA Regulatory Strategy on One Planet Prosperity*
- *SEPA Water and Wastewater Sector Plan*
- *The Water Environment (Controlled Activities) (Scotland) Regulations*
- *EU Water Framework Directive*
- *EU Environmental Quality Standards Directive*
- *EU Priority Substances Directive*
- *Strategic Approach to Pharmaceuticals in the Environment*
- *Control of Priority and Dangerous Substances and Specific Pollutants in the Water Environment*
- *The Scotland River Basin District (Standards) Directions*
- *Assessment of Numeric Discharge Quality Conditions*

RPS – Royal Pharmaceutical Society;
SEPA – Scottish Environment Protection Agency; EU – European Union

for environmental sustainability in pharmaceutical prescribing. Decision-making tools for prescribers are not available if they want to swap two medicines with similar clinical effects but different ecotoxicity values. Available environmental risk assessment reports for medicines' marketing authorisation are not transparent and some actors highlighted that these are not considered when the Medicines Healthcare Products Regulatory Agency (MHRA) and Scottish Medicines Consortium (SMC) license new pharmaceuticals in the UK.

These bodies only consider safety, effectiveness, and cost of pharmaceuticals when awarding licenses.

Lack of a diverse national body coordinating high-level advocacy for eco-directed pharmaceutical prescribing

The SMC, Scottish Antimicrobial Prescribing Group (SAPG), One Health Breakthrough Partnership (OHBP), and Scottish Environmental Anaesthesia Group (SEA-G) advocate for sustainable healthcare transition at national and regional levels. However, consulted stakeholders highlighted that their initiatives on reducing pharmaceutical pollution 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.

Trained ecotoxicity specialists have the technical expertise to evaluate environmental risk assessment reports of pharmaceuticals for market authorisation but they are not part of the SMC and Area Drug Therapeutic Committees. This aligns with other health technology appraisal bodies in the UK (e.g., MHRA, National Institute for Health and Care Excellence, and the All Wales Medicines Strategy Group) which also use the current criteria for authorisation. Moreover, SMC's composition (medical specialists, pharmacists, NHS board representatives, health economists, pharmaceutical industry, representatives from the public, and members providing administrative support) may not be aligned with requirements of the NHS's sustainability goals.

Low stakeholder's knowledge on pharmaceuticals' environmental impacts

There is low level of knowledge and awareness amongst healthcare professionals and the public about the impacts of pharmaceuticals on the environment. There is low public awareness on the environmental impact of pharmaceuticals beyond a limited awareness of good disposal practices (e.g. take-back schemes)[8]. There is an appetite to reduce pharmaceutical use and pollution; however, educational interventions are limited[8].

Limitations on monitoring practices for pharmaceutical substances

Environmental policies in Scotland are generally robust. However, due to the risk-based approach, key policies do not provide comprehensive monitoring requirements for pharmaceutical substances (e.g. Pollution Prevention and Control Regulations 2012). Moreover, policy provisions on pharmaceutical monitoring (e.g. Regulatory Method on the Assessment of Numeric Discharge Quality Conditions) only focus on compliance monitoring that do not support the need of eco-directed prescribing. Monitoring beyond compliance would help evaluate the impact of eco-directed prescribing; however, there is a need to identify who should bear the cost of sampling and analysis; and appropriate feedback mechanisms in sharing and utilising results for pharmaceutical prescribing decisions. Moroever, the selection of substances for monitoring based on current risk assessments could be hampered by knowledge gaps on ecotoxicity, chronic toxicity, long-term biological effects, and complex mixture interactions of pharmaceuticals.

POLICY RECOMMENDATIONS

Eco-directed pharmaceutical prescribing requires multi- and intersectoral policy change[7]. 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 programme within Scotland's health and environmental 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 Scotland, Public Health Scotland, SEPA) whilst addressing identified barriers. A three-pronged policy framework

is recommended based on related evidence on eco-directed prescribing from international studies (**Box 2**).

Organise a nationwide multi-stakeholder expert group on eco-directed pharmaceutical prescribing

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, and under the remit of Scottish Government's Realistic Medicine strategy would be helpful in implementing high-level advocacy for the adoption of an eco-directed prescribing strategy within health and environmental sectors. These groups have unique expertise and remits on medicine appraisal (SMC), antimicrobial resistance (SAPG), reducing carbon footprint, specifically of inhalational anaesthetic gases (SEA-G), and reducing pharmaceutical pollution in the environment (OHBP), which should be brought together for a more coordinated approach. A nationally coordinated approach may save resources, concentrate expertise, and provide consistent guidance, however, but a national advisory group to inform regional teams is also feasible.

Including ecotoxicity specialist in the group is also important for advocating, assessing, and providing evidence-based environmentally informed recommendations on pharmaceutical use. Representation from Area Drug Therapeutic Committees should be ensured to safeguard potential concerns on the local usability of changed formulary. Ad-hoc committees for specific health conditions could also inform proper integration of environmental criteria on pharmaceutical prescription for specific therapeutic pathways.

Integrate environmental criteria in medicine appraisal and formulary development

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[19]. A new prescribing guideline and the inclusion of environmental criteria could result in changes to the therapeutic regime for some patients. A patient-centred approach through education and shared-decision making should be followed to appropriately prescribe medicines aligned with patients health choices and goals[34].

A pragmatic, stepwise, and regional development of a joint formulary has already started for some therapeutic areas (e.g. skin, gastrointestinal, or infections) in Lothian[35] and this is an opportunity for the integration of ecotoxicity data in medicine selection[19]. By doing so, an environmentally informed Lothian Joint Formulary (East)[35] could be the template for the North and West regions' formulary; eventually leading to a consistent and environmentally informed formulary development across Scotland.

Environmental monitoring beyond compliance is ideal to supporting the development of an environmentally informed formulary; however, this would require sustained investment for sampling and analysis. International collaborations for the creation of a definitive, enhanced, and transparent ecotoxicity database should be explored. Leveraging existing public-private partnership with pharmaceutical companies in the SMC's Users Group Forum is possible for sharing ecotoxicity data of pharmaceuticals; and possibly, funding environmental monitoring activities for more pharmaceuticals. Modelling based on local prescription data could also be a complementary way to measure the strategy's success.

Box 2. Three-pronged policy framework for eco-directed pharmaceutical prescribing in Scotland

- ***Organise a national level multi-stakeholder expert group.*** *Multi-sectoral collaboration was associated with reduced prescription of diclofenac in an eco-directed pharmaceutical prescribing study in The Netherlands[31].*
- ***Integrate environmental criteria in formulary development supported by regular environmental monitoring of pharmaceuticals.*** *Stockholm Region's Drug Therapeutic Committee in Sweden considers environmental criteria in formulary development[32]. Reduced antibiotic prescription in China was associated with eco-directed prescribing supported by monthly monitoring of antibiotic residues in a water environment[27].*
- ***Improve stakeholders' knowledge on sustainable healthcare.*** *Capability-building activities on sustainable pharmaceutical consumption delivered by pharmacists and doctors in German schools and sports clubs resulted in increased environmental awareness, proper disposal, and reduced painkiller use[8].Distribution of informative guide booklets on how to interpret environmental classification of pharmaceuticals was associated with increased prescribers' adherence to an environmentally informed formulary[33].*

Improve stakeholders' knowledge and skills on sustainable healthcare

An integrated and comprehensive communications and advocacy strategy to improve knowledge and skills of prescribers and the public on pharmaceutical pollution and ways to prevent it should be implemented with other NHS's health campaigns. Integrating key messages on pharmaceutical pollution and its prevention could be embedded in existing health education and campaigns (e.g. antimicrobial stewardship programme, pharmacy take-back scheme) for cost efficiency. Community pharmacies could help in consistent and widespread public messaging. Pharmacists are key implementers of clinical advice provision, prescribing guideline development, and capacity-building, which are essential components of the antimicrobial stewardship programme[34]. However, additional resources and careful messaging is needed to avoid blaming the patients.

In conclusion, there are opportunities through policy change to support eco-directed pharmaceutical prescribing in Scotland. These could be meaningfully utilised through robust, comprehensive, and coordinated strategies fostered by multi- and intersectoral collaboration between the health and environmental sectors. There is also a need to invest in a research agenda to evidence the need for policy changes as the Scottish Government adopts eco-directed prescribing[6]. Evaluation of environmental impact should be coupled with research on adherence to prescribing changes, health outcomes, and patient satisfaction. Full scale implementation of eco-directed prescribing is a long process and requires long-term investment, although eminently suitable for step-wise introduction.

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