Exploratory Research in Clinical and Social Pharmacy 11 (2023) 100303

Contents lists available at ScienceDirect

Exploratory Research in Clinical and Social Pharmacy

journal homepage: www.elsevier.com/locate/rcsop

Stakeholders' perspectives and use of web-based knowledge support for environmental information on pharmaceuticals

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ARTICLE INFO

Keywords:
Sweden
Environment
Pharmaceuticals
Qualitative study

ABSTRACT

Background: Pharmaceuticals treat and prevent diseases but can pose a risk to organisms, predominantly in aquatic environments. The use of pharmaceuticals is predicted to increase due to, among other factors, a growing and aging population and climate change. Therefore, it is important to develop mitigation strategies to prevent pharmaceutical residues from entering the environment. In Sweden, two public pharmaceutical web-based knowledge supports provide information on the environmental impact of pharmaceuticals.
Objective: To explore stakeholder perspectives, use and future opportunities related to two webbased knowledge supports publicizing environmental information on pharmaceuticals.
Methods: Stakeholders identified for their experience with the knowledge supports, pharmaceutical policy, and stakeholder collaboration were recruited using purposive and snowball sampling for semi-structured interviews. Interviews were conducted in person or via video calls. Respondents included twenty-one representatives from the pharmaceutical industry, regional and national authorities, academia, and an independent research institute. Interview transcripts were analyzed using content analysis.
Results: Respondents valued having environmental information on pharmaceuticals publicly accessible on two well-known pharmaceutical knowledge supports. The knowledge supports have been used in Sweden and internationally. Perceived differences were recognized between the impact and perspectives of the two knowledge supports with a general preference for the Janusinfo knowledge support. The preference was especially identified regarding transparency and the use of the information in clinical practice. Barriers to impact were a lack of resources and decision-making criteria. Respondents believed that the impact and value of the knowledge supports could be improved with more authority involvement.
Conclusion: Public knowledge support providing environmental information on pharmaceuticals has been valuable across sectors, especially, among Drug and Therapeutics Committees. We believe the results from this study could be useful for other countries interested in implementing a similar system.

1. Introduction

Pharmaceuticals play a crucial role in the treatment, prevention, and cure of diseases for humans and animals.[1] However, pharmaceuticals may also negatively impact the environment. Large numbers of Active Pharmaceutical Ingredients (APIs), metabolites, and transformation products are emitted into the environment at different stages of the product lifecycle. Approximately 4000 APIs are administered worldwide and approximately 100,000 tons are produced globally every year.[2] Increasing literature on the topic reports that pharmaceutical residues from >600 human and veterinary pharmaceuticals have been detected in the environment worldwide; in surface waters, sewage effluent, rivers, ground- and drinking water, manure, soils, and other environmental matrices. These findings have led scientists and regulatory agencies to increasingly recognize pharmaceutical residues as Contaminants of Emerging Concern (CECs), which pose an environmental and potential health risk globally.[3,4] This understanding has prompted stakeholders across the lifecycle of pharmaceuticals to discuss measures to reduce pharmaceutical residues entering the environment.

Since 2006, an environmental risk assessment (ERA) has been required to accompany the European Medicines Agency (EMA) market authorization application for most pharmaceutical products. This risk assessment is completed according to the EMA Guideline on The Environmental Risk Assessment of Medicinal Products for Human Use.[5] The ERA can be used to organize strategies to limit the environmental impact of pharmaceutical

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http://dx.doi.org/10.1016/j.rcsop.2023.100303
Received 28 October 2022; Received in revised form 22 June 2023; Accepted 7 July 2023
Available online xxxx

products, but not as a criterion to refuse market authorization.[5] The ERA for pharmaceuticals in Europe has been further described and critically evaluated in previous literature.[6–8]

In Sweden, two web-based knowledge supports that provide environmental information on pharmaceuticals are publicly available on Janusinfo.se (Janusinfo), Region Stockholm's web-based knowledge support, and Fass.se (Fass), Sweden's national formulary.[9,10,1] In addition to environmental information, these web-based knowledge supports provide other publicly available pharmaceutical information. Pharmaceutical information on Janusinfo includes but is not limited to, drug-drug interactions and pharmaceuticals during pregnancy and breastfeeding.[12] Pharmaceutical information on Fass includes but is not limited to, the product summary, pregnancy and lactation classification, and educational material for patients.[13] Both provide decision support for healthcare professionals.[9,12,13]

1.1. Previous literature

Previous literature has evaluated stakeholder motivations, expectations, and intentions in developing the Swedish environmental classification system for pharmaceuticals presented on Fass.se. The stakeholders encompassed the pharmaceutical industry, governmental agencies, and "other affiliations". They found that the industry believed the most influential factor in developing the Fass classification system was their company's responsibility. In contrast, governmental agencies found a government report to be the most influential.[14] Ramström et al.[9] studied the use of the knowledge support "Pharmaceuticals and Environment" on Janusinfo and described lessons learned from developing the knowledge support. From their perspective, lack of data, lack of transparency, and inconsistencies in available environmental information from EMA and Läkemedelsindustriföreningen (Lif, the trade association for the research-based pharmaceutical industry in Sweden), were challenges experienced in developing the knowledge support. They also perceived the environmental information in the knowledge support to be valuable as decision support for Drug and Therapeutics Committees (DTCs).[9] Academia has also noted discrepancies in Fass and has proposed improvements.[15]

Still, limited knowledge exists on different stakeholders' views and experiences of these web-based knowledge supports and how they may be developed to add further value as a tool for reducing the environmental impact of pharmaceuticals.

1.2. Aim

Consequently, this study aimed to explore stakeholders' perspectives on and use of the environmental information in the web-based knowledge supports as well as discuss future opportunities related to the environmental information in the knowledge supports. The objectives were to 1) collect the perspectives and experiences from different stakeholder groups including academia, industry, national and regional authorities, as well as a research institute and 2) present the stakeholders' perspectives and use of the environmental information in the knowledge supports.

2. Methods

2.1. The setting

In the early 2000s, an increased interest regarding pharmaceuticals in the environment manifested across sectors including healthcare, the public, and political.[9,14] However, the accessibility of data on a pharmaceutical's environmental impact can be a barrier for decision-makers (i.e., prescribers, authorities, or politicians) who may want to consider the environmental factors of pharmaceuticals in their work. As a result, different stakeholders in Sweden developed two separate environmental classification systems[9,14,16]. Today, the environmental classification systems are publicly available on two web-based pharmaceutical knowledge supports www.Janusinfo.se and www.fass.se. On Janusinfo, the page "Pharmaceuticals and Environment", owned by Region Stockholm, allows one to search for environmental information on an *API*.[9,17] The Swedish environmental classification of pharmaceuticals, owned by Lif, is presented on Fass.[10,15,18] The "Environmental Information" tab on a product page on Fass may provide environmental information on the specific *pharmaceutical product*.[10,15,18,2] European guidelines, namely, the European Commission Technical Guidance document on risk assessment, and the EMA Guideline for Environmental Risk assessment for Human Pharmaceuticals have influenced the availability of environmental information and the way environmental information is presented in the knowledge supports.[5,9,14,18,19]

The environmental risk classification for a pharmaceutical product presented on Fass is based on the ratio of the Predicted Environmental Concentration (PEC) and the concentration deemed to be safe for aquatic animals and plants (Predicted No Effect Concentration, PNEC).[5,15,19] The PEC value is generally the same for different pharmaceutical companies as it is based on the sales volume of all the specific products with the same API in Sweden. However, the PEC values may differ if they use sales data from different years. The PNEC is provided by individual companies, which can differ based on their supporting data. Thus, different pharmaceutical products with the same API can have different environmental classifications.[15] Assessments of environmental degradation and bioaccumulation (potential for accumulation in an aquatic organism), are also presented as part of the classification.[15,18] The environmental information on Fass is provided by the pharmaceutical industry voluntarily, which can be based on the companies' own studies as well as peer-reviewed literature.[10,14,18] The IVL Swedish Environmental Research Institute (IVL) reviews the environmental classification and supporting data before it is published on fass.se.[10,14,15,18] The environmental classification presented on Fass has been further described in previous literature.[10,14,15]

The environmental classification on Janusinfo is presented per API and is based on worst-case scenarios for environmental hazard (intrinsic properties of a substance and its potential to cause harm) and risk (calculated based on the ratio of the exposure to the hazard (PEC) and the concentration deemed safe for aquatic animals and plants (PNEC)).[5,9,20] The hazard summary describes data on an API's persistence (potential to avoid degradation), bioaccumulation, and ecotoxicity.[9] The risk summary is based on PEC/PNEC data. The environmental classification presented on Janusinfo is determined by a comparison of publicly available sources including Fass and European Public Assessment Reports (EPAR) available through EMA. Data from peer-reviewed literature may also be used when deemed reliable and relevant.[9] Since assessments can be based on Measured Environmental Concentrations (MEC) and risk of selection of antibiotic-resistant bacteria, they can differ from those from Fass and EMA.[5,9,17] The environmental classification presented on Janusinfo has been further described in previous literature.[9]

The novelty of having environmental information on pharmaceuticals publicly available on web-based pharmaceutical knowledge supports makes further examination relevant. Given the differences in content and functionality of the knowledge supports, it is important to study the Swedish stakeholder perspective. Studying the Swedish stakeholder perspective can also allow other countries interested in implementing similar knowledge support to learn from the experiences in Sweden.

A qualitative approach using semi-structured interviews was chosen to examine the stakeholders' perspectives. This approach gave an in-depth understanding and allowed the respondents to share their views and experiences in their own words. At the same time, the semi-structured interview approach allowed interviewers to probe their answers.[21–24] Qualitative inductive content analysis was used because research on different

[1] Governance in Sweden works at the national, regional, and local levels. Sweden is divided regionally into 21 counties, including Region Stockholm.[11]

[2] The environmental information on Janusinfo is presented in Swedish on the page "Läkemedel och miljö" and in English on the page "Pharmaceuticals and Environment".[12,16] The tab "miljöinfo" on Fass presents environmental information only in Swedish.[12,14]

stakeholders' perspectives is limited. This allowed themes to emerge from the data as opposed to defining preconceived themes.[25]

The following stakeholder groups were included:

- The pharmaceutical industry, as they can provide data and Lif owns the environmental classification system on Fass.
- The research institute, as they are reviewing the industry data.
- National authorities, as they are behind much of the national pharmaceutical policy.
- Regional authorities responsible for healthcare, as they provide knowledge support and implement it into practice.
- Academics, as they can provide knowledge, use the knowledge supports, and critically assess them.

2.2. Interview guide

An interview guide was developed before the interviews based on the research aim, previous literature on the knowledge supports [9,10,14–16], and discussions among the research team.[22] Major areas included in the interview guide were background information, use of the knowledge supports, and improvement of the knowledge supports (see further in Table 1). Interview questions were designed to explore respondents' perspectives and use of the environmental information in the knowledge supports. Questions were asked on both knowledge supports unless respondents thought that they could only answer the questions for one of the knowledge supports due to experience. At the beginning of each interview, it was described that the interviewers would refer to the knowledge support "Pharmaceuticals and Environment" available on Janusinfo.se as "Janusinfo" and the Swedish environmental classification of pharmaceuticals available on Fass.se as "Fass." This language is reflected in Table 1, which further illustrates the thematic guide. The same questions were prepared and asked for both knowledge supports, but Table 1 presents one or the other for simplicity.

2.3. Participants

Purposive and snowball sampling strategies were used.[24] The identified stakeholders included representatives from Swedish organizations encompassing regional and national authorities, universities, an independent research institute, and the pharmaceutical industry. The stakeholders were identified for their experience with the knowledge support(s), pharmaceutical policy, and stakeholder collaboration. Individuals representing the organizations were contacted through email, which included information about the researchers, the study, and an invitation to participate. Respondents were also asked to suggest other persons to include in the study (snowball sampling).

2.4. Data collection

The first (native English-speaking) and second (native Swedish-speaking) authors conducted interviews in November and December 2021. The first author had no prior relationship with the respondents, while the second author had met some of them in professional contexts. Interviews were conducted individually in the professional office of the respondent or via a videoconferencing platform (Zoom® or Microsoft Teams®) given pandemic restrictions, or travel distance.[26] Four interview sessions included two respondents each at their request. Interviews were conducted in English, but respondents were given the option to respond in Swedish if they felt they could not express themselves in English.

Respondents were asked for their willingness to participate, given information about the study before interviewing and offered no incentives for participation. Respondents were also asked for permission to record the interview and use the transcript in the data analysis.

Interviews were audio recorded and transcribed verbatim by the interviewers. Respondents were invited to read and comment on the transcripts, and six respondents from five interviews requested to do so after being given the offer. Field notes were taken during the interviews.

Table 1
Thematic Guide.

Topic	Sample Question
Background	What is your experience working with the database "Pharmaceuticals and Environment" on Janusinfo?
	What do you know about the development of Fass?
Use	Who do you believe the audience is for Fass?
	How does [your organization] use the Fass classification system and/or Janusinfo?
	What challenges do medical professionals experience when considering this information in their work with the guidelines?
Improvement	What do you think the strengths of Janusinfo are?
	What do you think the limitations of Janusinfo are?

2.5. Data analysis

Data was analyzed using inductive content analysis.[25] The two interviewers independently conducted thematic analysis on the first three interviews to derive the themes. The interviewers began with many themes. However, at a consensus meeting, connections were created between existing themes, and they were merged into three major themes. The themes were validated by the last author. The first author completed most of the remaining analysis using NVivo Release 1.6.1 (1137) ® with the help of the second author. During this stage of the process, two consensus meetings were held with the second and last author where the analysis frame was further developed, including subthemes (see Fig. 1).

2.6. Preunderstandings

The first author has a PharmD from the United States, has been engaged in environmental issues – especially in connection to health care for some time, and had some previous experience from conducting qualitative research, but not qualitative interviews.

The second author has a pharmacist degree from Sweden, has also been engaged in environmental issues, especially related to pharmaceuticals, and had no previous qualitative research experience. Before and during the study, they were both supervised regarding qualitative research, with a focus on interviewing and analysis, by the last author.

The third author has an MSc in biology and marine ecology. She has worked with transdisciplinary environmental research since 2004 and with a focus on pharmaceuticals in the environment since 2019. She has previous experience in qualitative research and interview studies and has been professionally connected with most of the respondents.

The fourth author is a pharmacist by background. He was previously employed by Region Stockholm where he participated in the development of the Drug and Therapeutics Committee (DTC) guidelines, which involved environmental work to some extent. He had limited experience in qualitative research and has been professionally connected with most of the respondents.

The last author has a social science background and extensive experience in qualitative research, including teaching in pre- and postgraduate courses. She has a general interest in environmental issues.

2.7. Ethics

According to Swedish regulations, ethics approval was not needed for this study since only professional opinions were discussed and no personal or sensitive data was collected.[27] However, ethical considerations were taken into account with anonymity, informed consent, and data storage.

3. Results

In total, 21 respondents representing experiences from Swedish national authorities, regional authorities (including, but not limited to,

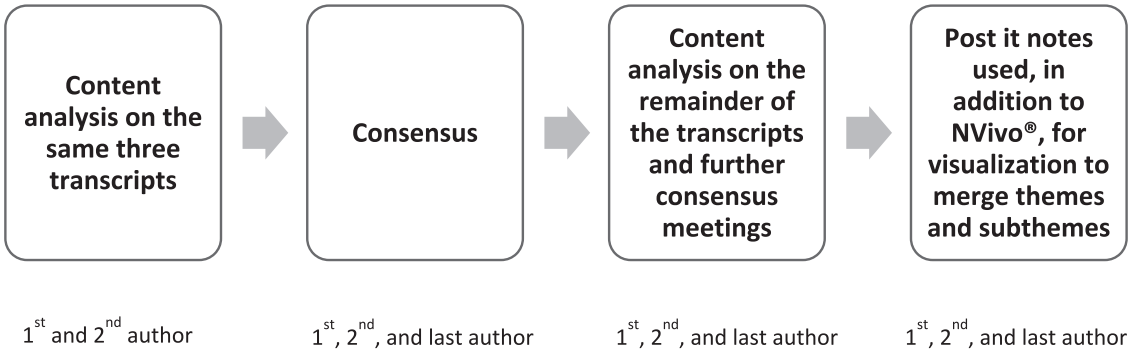

Fig. 1. Thematic analysis.

members of DTCs), a research institute, universities, and the pharmaceutical industry participated in 17 interviews; 13 interviews were individual and four interviews were conducted with two respondents at the same time. Respondents had expertise encompassing healthcare governance, consulting, policy, regulatory, and research related to the nexus of pharmaceuticals and the environment. Several respondents also had expertise in either medicine or pharmacy, see Table 2. Most respondents had experiences with developing, maintaining, researching, and/or using the information presented by the knowledge supports. The two respondents working at the national authority level did not have the experiences stated above but were included for their understanding of Swedish national pharmaceutical policy and perspectives on the value of the information. In addition, one respondent was included for their experience with interdisciplinary stakeholder collaboration addressing environmental issues pertaining to chemicals, including pharmaceuticals. The median interview time was one hour and three minutes (range 0:38–2:17). Further, 11 potential respondents were identified, but declined to be interviewed because they did not think that they could provide suitable information. Respondents are numbered throughout the text. R1–11 are from authorities, R12–14 are from a university, R15–17 are from the research institute, and R18–21 are from the pharmaceutical industry.

Content analysis of the interview transcripts resulted in themes describing the stakeholders' perspectives on and use of the environmental information in the knowledge supports. These themes included transparency, impact, and barriers to impact. Perceivable differences were noticed concerning views and use of Fass vs Janusinfo. With the analysis, further subthemes were identified within each theme.

3.1. Transparency

Respondents perceived transparency as a major factor influencing the value of the knowledge supports. Respondents connected transparency to accessibility/communication of the environmental information in and credibility of the knowledge supports.

Table 2
Respondent Characteristics, Sampling, and Participation.

Respondent characteristics	Interviewees (n = 21)	Declined participation (n = 11)
Stakeholder		
National authority	2	4
Regional authority	9	2
Pharmaceutical industry	4	1
Research institute	4	2
Academia / University	3	2
Recruitment strategy		
Networking	16	
Snowballing	5	
Gender		
Female	11	
Male	10	

3.1.1. Accessibility/communication

In general, respondents from regional authorities, academia, and the research institute saw value in having the information publicly available and recognized it as an opportunity to create awareness. A respondent from the industry thought that it was advantageous to have the information on a well-known platform, presented alongside other pharmaceutical information.

> *"/…/and we do have the perfect platform to present this kind of data. All others who would take an initiative like this would have to create a new platform to present this. We have Fass. Fass is the platform when it comes to information on pharmaceuticals in general for both professional users and the general public."* (R20)

3.1.2. Credibility

Respondents related credibility to the ownership and organization of the knowledge supports. Most respondents from academia and the regional authorities expressed that the pharmaceutical industry was not suited to own a knowledge support since they have economic interests. However, some respondents from academia stated that Region Stockholm also has economic interests as a healthcare payer and provider. Respondents from the research institute and the industry thought it was right for the industry to own a knowledge support since they are the ones providing the information.

To enhance credibility, respondents from academia and regions stressed the importance of having authority involvement in ownership and regulation of a knowledge support. Respondents suggested this involvement be at the authority level in Sweden (especially the Medical Products Agency); at the EMA level in Europe; at the WHO level internationally.

> *"The industry does not have an inherent interest in being completely honest. It is obvious, from the business model, that it is not good to say that our product is causing risk."* (R12)

> *"The system should be based on an authority level so it can be scrutinized and revised, and there is no stakeholder conflict of interest."* (R9)

In addition to ownership, most respondents from academia and the regions thought several other aspects of Fass limited its credibility, especially when compared to Janusinfo. This included its voluntary element, IVL's role, and the presentation of environmental information.

Respondents from regional authorities and academia were frustrated with the voluntary elements because data has been removed. In contrast, respondents from regions and academia felt that Janusinfo was up-to-date and preferred it for that reason.

> *"What we see then is instead of updating it, it is being removed. And this is, I think because there is no benefit of being part of the system."* (R14)

> *"The Janusinfo database is also up to date, so when new information is available, it is added, or if we have a question, they look deeper into it."* (R10)

Respondents from academia and the industry noted the importance of having an expert external reviewing body to enhance the credibility of information presented on the knowledge supports. However, most respondents from academia and regional authorities were skeptical of IVL's role in performing the external review for Fass. This is because pharmaceutical products with the same API can have more than one environmental classification, and IVL is paid by the industry. A respondent from the industry stated that having different classifications for the same API is a weakness as it makes it more difficult to use. However, they were keen on the idea that each company owns its product information on Fass.

> *"I think it is really important to discuss when you are independent. If you are being paid by Lif, how much can you say or criticize the system?"* (R14)

Respondents had varying opinions on how the use of peer-reviewed literature affected the credibility of a knowledge support. Although both knowledge supports allow for the use of peer-reviewed literature to support the environmental classification presented, the use of peer-reviewed literature was more often associated with Janusinfo. The use of peer-reviewed literature was criticized by respondents from the industry and a national authority because it could bring subjectivity into the environmental classification. In contrast, some respondents from academia and the regional authorities were positive about the use of peer-reviewed literature as they thought that the data used should not exclusively come from the industry. A respondent from academia noted that the use of peer-reviewed literature could provide data on environmental risk when sources on Fass state that "*Environmental risk cannot be excluded, since there is not sufficient ecotoxicity data available.*"

> *"We have to recognize that there is a large uncertainty that we deal with, and a large challenge with the variability in the quality of data. But we cannot completely dismiss the scientific literature."* (R12)

3.1.3. Lack of data

To address the lack of ERA data for products approved before 2006, a respondent from the industry felt it would be difficult to point to who is responsible for the environmental risk assessment, especially if the pharmaceutical products have lost their patents. The respondent noted that they did not want pharmaceuticals to be part of a consortium where information would have to be shared between different manufacturers. The respondent from the industry expressed that sharing the information between manufacturers could be difficult to do without breaking anti-trust laws.

> *"It is extremely hard to point to who is responsible. Since all of those substances have lost their exclusivity, their patents are gone, the whole idea that when we lose exclusivity is that it is somehow a common [public] good. Anyone who wants to do these substances are allowed to do that. The recipe is out there, no one owns it."* (R20)

In addition to the lack of ERA data for products approved before 2006, respondents from academia, regional authorities, and the industry thought that the knowledge supports were limited by the absence of environmental information relating to manufacturing. Respondents said manufacturing data could be used in the procurement processes, which could increase the impact of the knowledge support.

> *"But if you could add on manufacturing releases there would be a potential difference between products a, b, c, d all of them containing omeprazole [for example]. And that information is more of interest to public procurement."* (R20)

3.2. Impact

Respondents appreciated the availability and accessibility of the knowledge supports and recognized the impact they have had in Sweden and internationally. They thought different stakeholders including academics, government agencies, nongovernmental organizations, policymakers, healthcare professionals (pharmacists and prescribers), and DTCs could take advantage of the data to make an impact on prescribing, procurement policy, as well as research.

3.2.1. General

Respondents from the regional authorities noted that Janusinfo has had inquiries from other countries wanting to know more. Respondents from the industry noted that Norway and Finland have provided environmental information on pharmaceuticals using PNECs from Fass. A respondent from the research institute explained that policymakers at the EU level use Fass to show that having public information on the environmental impact of pharmaceuticals is possible. Neither system has, according to respondents from the national authorities, to date, had an impact on the regulatory approval process for pharmaceuticals.

3.2.2. Sweden

Respondents from regional authorities valued having a knowledge support organized like Janusinfo (per API) so that the DTCs can include environmental considerations in their treatment recommendations. They generally preferred the API presentation on Janusinfo as opposed to the per product presentation on Fass as they thought it was more user-friendly.

> *"So for us, it is a very useful tool. We have used this a lot both in terms of - recommendations, but also for follow up on prescriptions, which we communicate to our prescribers and sometimes to media in this [geographical] area."* (R9)

> *"One of the strengths [of Janusinfo] is that it contains information on an active [pharmaceutical] ingredient rather than a specific product. So, it is easier to gather information about the ingredient itself rather than having to scroll through many, many pages of Fass texts."* (R11)

Respondents representing regional authorities stated that the DTC may consider environmental aspects of a pharmaceutical in their treatment recommendations after therapeutic efficacy and safety.

> *"When the recommendations are made you obviously first look at the effectiveness of the treatment and the safety further down the line you look at things like cost and environmental impact."* (R11)

Additionally, the environmental impact can support the DTC's decision to remove a pharmaceutical from the DTC recommendation list in addition to the potential for patient harm.

> *"We should prescribe it [oxazepam] a lot less than we do today. We still hang on to old knowledge. The problem here is not only the environment but also the dependency problem, which is a bigger problem in my opinion. But here they go hand in hand."* (R9)

According to respondents, Fass is used by Janusinfo to provide environmental information for their knowledge support, and by academics for research and teaching. The environmental information on Fass, however, according to a respondent from the industry, seems to be minimally used by healthcare providers.

3.3. Barriers to impact

While the knowledge supports have had an impact in different ways, several barriers to impact were expressed by respondents. These barriers specifically related to using the environmental information and encompassed the balance between considering environmental aspects versus other decision-making criteria, and lack of resources.

3.3.1. Decision-making criteria

The DTCs consider several criteria when deciding whether a pharmaceutical should be included in their treatment recommendations including

efficacy, safety, and cost-effectiveness. In recent years, in Sweden, environmental considerations have also been included as a criterion in some regions. However, respondents expressed that cost and patient ethics could be barriers to using the environmental information provided by the knowledge supports in their decision-making.

Respondents from the regional authorities, national authorities, and industry expressed that it is unethical to withhold treatment due to environmental risk when no alternative treatment exists. Respondents from the regional authorities noted that this is the case, for example, with the female sex hormone ethinylestradiol, and serotonin reuptake inhibitors used for depression and anxiety.

> *"[There is a] list of 25 pharmaceuticals that are especially harmful for the environment. 16 of them are recommended on the Wise list [=recommendation list for Region Stockholm]. So, the medical aspect is very important. The patients need to get the pharmaceuticals."* (R1)

Regarding cost, a respondent from a regional authority cautioned that society should consider the cost of harming the environment in their decision-making.

> *"The medical effect is the first thing you care about and then it's the cost and then the environment. But the environment is climbing up a little bit to the second place, so the cost and the environment are quite similar now. If we release these harmful substances [APIs] into the environment, it might be more expensive."* (R3)

3.3.2. Lack of resources

Other barriers to using the environmental information were a lack of resources encompassing time and collaborations. Prescribers do not have the time to think about the environmental aspects of pharmaceuticals during patient interactions. Additionally, the environmental information may be difficult for them to understand. Therefore, it is important to have people collaborating with them on these questions. However, those working with the knowledge supports and treatment guidelines in the regions are not working full-time with these questions but expressed they wish they could dedicate more time.

> *"They [prescribers] don't have the time in the prescribing situation to make that choice between other pharmaceuticals/…/environmental information should be included in the pharmaceutical recommendations."* (R1)

> *"We need to have someone to guide us, some experts, both with environmental knowledge and also clinical knowledge."* (R9)

4. Discussion

Growing literature supports that pharmaceuticals in the environment can pose a risk to aquatic health[3,4,28]. Sweden has been at the forefront of this issue with, among other initiatives, developing and implementing two public web-based knowledge supports that provide environmental information on pharmaceuticals. To the best of our knowledge, this is the first qualitative study examining different stakeholders' perspectives and use of the knowledge supports. It is also the first study exploring the perspectives of both Fass and Janusinfo together. We identified important considerations related to the impact of, and barriers to using these knowledge supports, as well as perspectives regarding transparency. We believe that these insights may be useful for other countries interested in implementing a similar system.

This study indicates that the environmental information in the web-based knowledge supports is used in different manners by stakeholders across sectors. Academics seem to use the knowledge supports to retrieve environmental information on pharmaceuticals for teaching, or research. EU authorities may use the knowledge supports as examples to demonstrate that having this information publicly available is possible. Swedish regions may consider environmental aspects of pharmaceuticals when making their treatment recommendation guideline using the information provided by the knowledge supports. However, it is important to note that the regions generally preferred Janusinfo.

Respondents were generally positive about the knowledge supports but noted several limitations regarding their transparency. Their perception of transparency was dependent on the credibility of the organization owning the knowledge support as well as the structure of the knowledge support. Many thought that information coming from the public healthcare administration in a region as opposed to the pharmaceutical industry was more trustworthy as the industry could have an economic interest. It was noted, however, that Region Stockholm has economic interests as well. Additionally, respondents overwhelmingly preferred the presentation of environmental information per API on Janusinfo as opposed to per pharmaceutical product on Fass. They thought the per API presentation enhanced the credibility of Janusinfo as it eliminated the ambiguity of having different classifications for the same API. Despite transparency limitations, some respondents applauded the industry's willingness to assume responsibility for making environmental information publicly available, and it should be acknowledged.

Respondents generally felt that an independent reviewing body is important to facilitate critical evaluations of the industry's work. This is in line with the United Nations Environment Programme's report on Company Environmental Reporting, stating that the value of such decision-making is dependent on the ability of the external consultant to give professional opinions.[29] Ball et al.,[30] evaluated the role of third-party statements in adding value to corporate environmental reports. Their content analysis of verification statements, listed on the Association of Chartered Certified Accountants Environmental Reporting Awards, concluded that limited value is added to a corporation's external transparency and accountability, and the verifiers lacked flexibility.[30] Given previous experiences with third-party reviews of environmental information from the literature, and the experiences in Sweden, it is evident that there is a need for a system that gives the reviewers flexibility to make critical evaluations.

We acknowledge the work done by both Lif and Region Stockholm in making this information publicly available. However, the existence of these knowledge supports would not be possible without interdisciplinary collaboration. Success in developing, maintaining, and using these knowledge supports is a result of the joint effort of those with expertise in areas including, but not limited to, research, politics, pharmaceutical regulations, environment, and healthcare. We would like to support the importance of collaborations between authorities and academia to bridge the knowledge gap and aid in regulatory decision-making.[31]

While this information has been of value in Sweden, pharmaceuticals in the environment is an international issue, and such information would be valuable for stakeholders globally. Therefore, in line with Ramström et al.,[9] we suggest that EMA take the responsibility of providing knowledge support on the impact of pharmaceuticals on the environment. Since EMA functions at the EU level, the information provided by them has the potential to reach more stakeholders than information provided by Sweden or other individual countries. Additionally, it is rational that they take accountability for providing this information as EMA is responsible for the guidelines and supervision of the environmental risk assessment for pharmaceuticals in the EU.[3,5] As mentioned before, having a trusted independent organization providing this information can increase its credibility and value. However, the responsibility for disseminating this information is multifaceted. Consequently, national and regional authorities need to be engaged in the dissemination and implementation of this information in different processes.[32,33]

It is also important to emphasize that a prerequisite for the dissemination is the availability of robust environmental data for pharmaceuticals. An environmental risk assessment was not required for approval of a pharmaceutical product before 2006.[5,9] Therefore, at this point, most older products and APIs have no data, which is a problem for both Fass and Janusinfo.[34] The PREMIER (Prioritisation and Risk Evaluation of Medicines in the EnviRonment) project consists of an international consortium working to identify and address environmental risks of pharmaceuticals with limited information.[35] This study supports the push for more robust

environmental risk assessment guidelines provided by the pertinent agencies for new and legacy pharmaceuticals.[6,9,36]

In addition to more ecotoxicology information, respondents wanted environmental information related to the manufacturing of pharmaceuticals. A transparency guide focusing on emissions from manufacturing has been initiated by the Swedish Pharmacy Association. The guide considers the company's overall sustainability work but focuses only on over-the-counter pharmaceuticals.[37]

4.1. Methodological considerations

This study had several strengths. The semi-structured interview methodology allowed the interviewers to develop a pre-determined questionnaire to address a framework of themes.[23,24] This methodology gave the interviewers flexibility to discuss other topics that may have spontaneously come up during the interviews, as well as ask follow-up questions.[23,24] The use of snowball sampling allowed the interviewers to connect with several respondents that would have been difficult to reach otherwise.[38] This study also included respondents from several different sectors with varying experiences giving rich information to the study.

Of the 6 respondents who wanted to review their transcripts, 4 respondents from 3 interviews added data at this stage, however, no data was deleted/withdrawn. Saturation was assumed to have been reached when no new respondents were recommended, and no new information emerged from the last few interviews.[39]

The results should be understood while considering the following limitations. Some of the respondents were outdated with their information (i.e., some participants were not aware that Janusinfo changed their presentation of environmental information). This could be because they were not working with this information anymore. Despite this, those respondents were still included for their experience and expertise. The interviewers tried to be neutral in the interviews, however prior involvement in the field surrounding the intersection of pharmaceuticals and the environment could have led to bias. Furthermore, social desirability bias could have risen as respondents may have given answers that they thought the interviewers wanted to hear. However, having prior contact with one of the interviewers (second author) could have allowed the respondents to be more open.

5. Conclusion

The public web-based knowledge supports in Sweden have been valuable across sectors for different purposes. Presenting knowledge support on the environmental impact of pharmaceuticals in a manner that is objective, transparent, and suitable for the intended audience could increase its impact. Future research is needed to evaluate other countries' interests and readiness to implement similar knowledge support.

The knowledge supports are only valuable if the information is included in them. On a global level, work needs to be done to provide more information on the environmental impact of pharmaceuticals in a transparent way. The results from this study could apply to other countries interested in implementing knowledge support for environmental information on pharmaceuticals, especially for use in healthcare.

Funding

The first author gratefully acknowledges the financial support from the Fulbright U.S Student Program sponsored by the U.S Department of State and the Swedish Fulbright Commission. The Fulbright Program had no role in the study design, data collection, data analysis and interpretation, writing of the report or decision to submit the article for publication. Its contents are solely the responsibility of the author and do not necessarily represent the views of the Fulbright Program, the Government of the United States, or the Swedish Fulbright Commission.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Thank you to Louise C. Druedahl for giving insightful feedback.

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