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How to address medicines shortages: Findings from a cross-sectional study of 24 countries

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ABSTRACT

Shortages of medicines have become a major public health challenge. The aim of this study was to survey national measures to manage and combat these shortages. A questionnaire survey was conducted with public authorities involved in the Pharmaceutical Pricing and Reimbursement Information (PPRI) network. Responses relating to measures as of March / April 2020 were received from 24 countries (22 European countries, Canada and Israel). In 20 countries, manufacturers are requested to notify – usually on an obligatory basis – upcoming and existing shortages, which are recorded in a register. Further measures include a regular dialogue with relevant stakeholders (18 countries), financial sanctions for manufacturers in cases of non-supply and/or non-compliance with reporting or stocking requirements (15 countries) and simplified regulatory procedures (20 countries). For defined medicines, supply reserves have been established (14 countries), and legal provisions allow the issuing of export bans (10 countries). Some measures have been introduced since the end of 2019 and countries are planning and discussing further action. While governments reacted by taking national measures, the COVID-19 crisis might serve as an opportunity to join forces in cross-country collaboration and develop joint (e.g. European) solutions to address the shortage issue in a sustainable manner. A practical first step could be to work on a harmonisation of the national registers.

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1. Introduction

Medicines shortages have become a major issue globally [1], as they affect numerous countries, including Canada [2,3] and European countries [4] (e.g. Belgium [5,6], Finland [7–9], France [10,11], Germany [12], Italy [13,14], the Netherlands [15,16] and Poland [17]).

Shortages relate to temporary (and sometimes permanent) disruptions of the supply of medicines. The national definitions of a shortage of medicines differ, and some countries do not have an official definition at all ([18,19], for examples see Supplementary Materials 1). A common feature of a shortage is that the supply of a medicine – which has been brought onto the market – is discontinued. There are other circumstances when medicines are unavailable for patients but they are not called shortage: medicines are not launched if a pharmaceutical company does not perceive a country’s market to be sufficiently attractive (e.g. in the case of small markets or lower-income countries with limited ability to pay [20,21]). Medicines may be launched with a delay of some months and even years; this delayed availability is frequently caused by the widespread use of the external price referencing policy (for instance, apart from Sweden and the UK, all European countries with price regulation use external price referencing, at least as supplementary pricing policy [22,23]). External price referencing incentivises pharmaceutical companies to bring medicines to market later in lower-priced countries so as not to reduce the benchmark price across countries (strategic launch of pharmaceutical industry) [24–26].

Shortages limit patient access to medicines which likely results in increased negative health outcomes (e.g. no or delayed therapy, risks for patient safety due to switches and medication errors [12,27]), increased workload for health professionals (e.g. searching for therapeutic alternatives) [6,7,28] and economic consequences (e.g. need to procure higher-priced alternatives) [29,30].

To respond to the public health threat resulting from shortages, governments started taking action to improve the management of...
these disruptions and to reduce and ideally prevent them. Measures reported in the literature include the obligation for industry to report shortages to authorities (e.g. France [10]), the Netherlands [15]) and the creation of national reporting systems (several countries [18,31]), supply reserve stocks (e.g. Finland [9]), notification of parallel exports [17] and collaborative projects with stakeholders such as representatives of the pharmaceutical industry, wholesale and pharmacies (e.g. Italy [14]). Most scientific articles related to single countries and reported measures as background information while the research question had a different focus (e.g. workload for pharmacists to manage shortages, types of medicines subject to shortages). Acosta et al. 2019 [18] presented some national approaches to manage shortages in their scoping study but their narrative review was limited to published articles. To the knowledge of the authors, no up-to-date overview of government policies to address shortages of medicines is available.

Therefore, this study aimed to present up-to-date information about the actions taken in different countries to manage, reduce and prevent shortages of medicines.

2. Methods

To ensure the collection of the most current information and inclusion of a high number of countries, including those that tend to be less covered in scientific research (e.g. smaller and/or less resourced countries), a primary survey (using a questionnaire) with public authorities was carried out.

The authors benefited from an existing collaboration with the Pharmaceutical Pricing and Reimbursement Information (PPRI) network. This network comprises public authorities for pharmaceutical policy, with a focus on pricing and reimbursement, in 47 countries (at the time of the study). Most PPRI member countries are from the WHO European region [32]. Given an ongoing exchange of information to update each other, PPRI network members are used to receiving and responding to requests, and involving further colleagues and institutions in their country if needed [33].

A questionnaire was developed based on a taxonomy of possible measures to manage, reduce and/or prevent shortages of medicines (implemented as well as under discussion), which were known from the literature [6,9,10,14,18,31] and policy debate [34,35]. The authors tested the questionnaire by pre-filling information for five pilot countries (Austria, Finland, Italy, the Netherlands and Sweden). The information for these countries was sought in an unsystematic literature review that considered peer-reviewed articles and grey literature (e.g. media reports, websites of the public authorities and private actors in the medicines supply chain) in national languages as well as in English. Additionally, the authors contacted national stakeholders (usually the medicines agency and the community pharmacy association) in the pilot countries (except Austria) and asked them in a telephone interview to identify further measures, including those already implemented or under discussion. The research for the pilot countries was conducted in January 2020.

The questionnaire asked for open-ended responses in seven sections: national register to report shortages, supply reserves, export ban / notification for medicines under risk of shortage, regulatory measures, financial measures, stakeholder involvement and further measures. Respondents were asked to report on government action in place as of the first quarter of 2020 and on planned measures and current discussions (see the questionnaire in Supplementary Materials 2). The information included for the five pilot countries aimed to guide the respondents in the other countries and to provide an indication of the kind of content (e.g. examples of measures) and level of detail expected. PPRI network members of the five pilot countries were asked to validate the pre-filled information.

The questionnaire was sent to the members of the PPRI network on 5 March 2020, with the request to respond within two weeks. The invitation to participate in the survey was accompanied by information on the authors’ intention to publish the findings. In March and April 2020 two rounds of reminders were sent to those network members that had not yet responded. In addition, during the compilation of answers in April 2020 some PPRI network members were contacted on an individual basis to clarify some ambiguous answers and ask for missing information. A summary table of the synthesised results was shared with all PPRI network members that participated in this study, thus allowing them to comment on possible errors.

In August 2020, as part of the revision of the paper, the authors analysed publicly accessible registers for notification of shortages with regard to the type of information provided (e.g. cause of shortage, information on alternative medicine for substitution).

3. Results

3.1. Response rate

Information was provided by 24 of the 47 PPRI network member countries at the time: 16 European Union (EU) Member States (Austria, Bulgaria, Cyprus, Czech Republic, Denmark, Finland, Germany, Italy, Latvia, Lithuania, Malta, the Netherlands, Portugal, Romania, Slovenia, Sweden) and eight further countries (Albania, Canada, Israel, Moldova, Norway, Russia, Switzerland and United Kingdom).

3.2. Compilation of measures to address shortages

A frequently used measure to manage shortages was a national register to which suppliers report current and upcoming shortages: In 20 of the 24 responding countries, regulatory authorities (usually the medicines agency or the ministry of health) ran a shortages register. In all countries with such a register, with the exception of Malta, suppliers were obliged to report to the register, while Austria and Germany had made their voluntary registers obligatory only on 1 April 2020 (Table 1). The majority of these registers were publicly accessible. The outlines of the registers and the kinds of information collected differed from country to country. While several registers provided for the possibility to include relevant dates (expected and/or actual start and end dates of the shortage), only few registers published information on causes and solutions (e.g., existence of alternative medicines) for managing the shortage situation (Supplementary Materials 3).

To cover shortages, 20 countries had simplified regulatory procedures, in particular related to the import, marketing authorisation and also dispensing of medicines procured on the world market. Usually, exceptions were granted with regard to labelling requirements of the packages and product information leaflets in other languages were permitted.

Banning exports of medicines that are critically needed for the supply in a national market was a less frequent measure, but it was increasingly being used at the time of the survey. Of the 24 responding countries, five countries provided for the possibility to impose export bans on defined medicines by the end of 2019, seven countries by the end of Q1/2020 and ten countries by mid-April 2020. Medicines eligible for an export ban were usually listed (e.g. the “ex-ante notification list” in Portugal). Three further EU Member States considered introducing export bans, and Israel discussed an extension to further medicines. In addition to export bans for some medicines, four countries asked for export notification of further selected medicines (Czech Republic, Norway, Portugal) or all medicines (Latvia), respectively. Romania, which requested distrib-
Table 1
National registers to notify shortages as of March / April 2020.

| Country          | In place | Obligation (since April 2020; before: voluntary), sanctions | Managed by                        | Reports from | Medicines covered                               | Reporting time-lines |
|------------------|----------|------------------------------------------------------------|-----------------------------------|--------------|------------------------------------------------|----------------------|
| Austria          | Yes      | Obligatory                                               | Medicines Agency                 | MAH          | POM                                            | At least 2 months in advance if known; “immediately” for unforeseen shortages |
| Albania          | No       | Not appl.                                                | Not appl.                         | Not appl.    | Not appl.                                      | Not appl.            |
| Bulgaria         | No       | Not appl.                                                | Not appl.                         | Not appl.    | Not appl.                                      | 6 months in advance, if known or within 5 days of becoming aware |
| Canada           | Yes      | Obligatory, sanctions possible                           | Medicines Agency                 | MAH          | POM                                            | “Immediately”        |
| Cyprus           | Yes      | Obligatory, no sanctions (but their introduction is being discussed) | MoH and Health Insurance Organisation | Local distributors | POM and NPM administered under practitioner’s supervision | At least 3 months in advance |
| Czech Republic   | Yes      | Obligatory, sanctions possible                           | Medicines Agency                 | MAH          | Any medicine                                  | At least 2 months in advance |
| Denmark          | Yes      | Obligatory, sanctions possible                           | Medicines Agency                 | MAH          | Any medicine of importance                      | At least 2 months in advance |
| Finland          | Yes      | Obligatory, no sanctions (but their introduction is being discussed) | Medicines Agency                 | MAH          | Any medicine                                  | 2 months in advance |
| Germany          | Yes      | Obligatory (since April 2020; earlier: voluntary), sanctions possible | Medicines Agency                 | MAH, wholesalers | POM that are relevant or critical for supply | Existing or upcoming shortage (no timeline defined) |
| Israel           | Yes      | Obligatory, sanctions possible                           | MoH                               | MAH          | Any medicine                                  | 3 or 6 months in advance (unless “immediately” in case of immediate shortage) |
| Italy            | Yes      | Obligatory, sanctions possible                           | Medicines Agency                 | MAH          | Any medicine                                  | At least 4 months in advance except for unpredictable circumstancesa | 2 months in advance |
| Latvia           | Yes      | Obligatory, sanctions possible                           | Medicines Agency                 | MAH, wholesalersb | Any medicine                                    |                      |
| Lithuania        | Yes      | Obligatory                                                | Medicines Agency                 | MAH          | Any medicine                                  | “Immediately”, in some cases at least 3 months in advance |
| Malta            | Yes      | Voluntary                                                 | Medicines Agency                 | MAH          | Any medicine                                  | As soon as possible, but at least 2 months in advance |
| Moldova          | No       | Not appl.                                                | Not appl.                         | Not appl.    | Not appl.                                      | Not appl.            |
| Netherlands      | Yes      | Obligatory, sanctions possible                           | Medicines Agency                 | MAH          | Any medicine                                  | 2 months in advance |
| Norway           | Yes      | Obligatory, no sanctions                                 | Medicines Agency                 | MAH          | Any medicine                                  | As soon as possible, but at least 2 months in advance |
| Portugal         | Yes      | Obligatory, sanctions possible in cases of non-reporting or delayed reporting without justification | Medicines Agency                 | MAH          | Any medicine                                  | 2 months in advance |
| Romania          | Yes      | Obligatory, sanctions possible                           | Medicines Agency                 | MAH          | Any medicine                                  | Apart from exceptional cases, at least 6 months (and 12 months for commercial reasons) |
| Russia           | No       | Not appl.                                                | Not appl.                         | Not appl.    | Not appl.                                      |                      |
| Slovenia         | Yes      | Obligatory, sanctions possible                           | Medicines Agency                 | MAH          | Any medicine                                  | At least 2 months in advance |
| Sweden           | Yes      | Obligatory, no sanctions                                 | Medicines Agency                 | MAH          | POM                                            | At least 3 months in advance |
| Switzerland      | Yes      | Obligatory, no sanctions                                 | Medicines Agency                 | MAH          | Defined essential medicines, including vaccines | 5 days in advance for a shortage of a defined medicine to last for more than 14 days |
| UK               | Yes      | Obligatory (since January 2010), sanctions possible       | Department of Health              | MAH          | Any health service (i.e. reimbursed) medicine | At least 6 months in advance (or at least, as soon as the MAH becomes aware) |

MAH = marketing authorisation holders, not appl. = not applicable, NPM = non-prescription medicines, POM = prescription-only medicines.

a Legal change in 2019: timeline of reporting was changed from 2 to 4 months in advance.
b Anyone can report to the register but MAH are obliged to do so; wholesalers have to report about their stock on a daily basis.
c In addition, voluntary registers are run by the Dutch Pharmacy Association (in the Netherlands) as well as a hospital pharmacy in Basel and a private consultancy firm (in Switzerland). Any medicine can be reported to the voluntary registers.

Further information on the accessibility of the shortages registers maintained by public authorities and their contents is provided in Supplementary Materials 3.
utors to notify the export of reimbursed medicines, had planned to introduce an export ban in 2019, however, it had withdrawn this measure due to changes in the political environment.

In 14 countries (including the Netherlands which planned to implement this measure in the course of 2020) marketing authorisation holders and/or wholesalers have the obligation to keep a stock of defined medicines for a certain period (usually at least three months). Such stocking requirements were also built into tender contracts (e.g. Albania, Denmark).

Most of the surveyed countries (18 countries) reported regular meetings with relevant stakeholders, in particular marketing authorisation holders, wholesalers and community pharmacists and, but less frequently, patients and the public (e.g. in Finland). This exchange usually took place in a rather formal setting of a working group or task force. In Germany, the stakeholder dialogue was officialised as an advisory board to the medicines agency (“Jour Fixe”) in a law that came into effect on 1 April 2020 (Table 2).

Norway was the sole country to offer financial support to economic operators. In a COVID-19 related voluntary agreement of March 2020 between the authorities and wholesalers, the latter were asked to extend their stock to a wider range of medicines (this request added to a previously defined supply reserve obligation). The additional costs for wholesalers would be covered by the state. In several countries, financial sanctions were in place to penalise non-compliance (in cases of non-supply – 6 countries, of non-compliance with reporting requirements – 12 countries and of non-compliance with stocking requirements – 4 countries plus the Netherlands in the planning phase). Nine countries did not report the use of financial sanctions (Table 3).

4. Discussion

The study showed an increasing level of measures to manage and prevent shortages of medicines. Frequent measures include registers to report shortages, facilitated regulatory procedures and stakeholder dialogue. To a lesser extent, legal provisions permit imposing export bans and establishing supply reserves. These findings allow some observations.

First, there is variation in the number of measures taken among the countries. Lower-income countries tend to implement fewer measures: for instance, Albania, Bulgaria, Moldova and Russia have not yet established a register. The hesitancy may result from a lack of capacity, as the implementation of such measures requires resources.

Second, several measures were introduced in the months preceding and during the survey, i.e. in the course of 2019 and 2020. For instance, in 2019 Italy allowed its medicines agency to issue export bans, extended the notification period for upcoming shortages from two to four months and introduced financial sanctions in case of non-reporting to the register. The number of countries whose national authorities may impose export bans has considerably grown since 2019. At the time of the survey, some countries were considering the introduction of additional measures (e.g., a register and export bans in Bulgaria, supply reserves and export bans in Sweden). This is likely attributable to the growing relevance of shortages. Available data confirm the increase in notified shortages, particularly in the last years (Finland: an 18-times increase from 2010 to 2018, with a doubling of notifications between 2016 and 2018 [9]; Netherlands: from 91 notified shortages in 2004 to 769 in 2018 and 1492 in 2019 [36]; Germany: from 42 shortages in 2013 to 268 in 2018 and 355 in 2019 [37]). In addition, the COVID-19 pandemic that hit European countries in the course of March 2020, prompted further measures (e.g., the “COVID-19 ad-hoc agreement” as of 6 March 2020 in Norway, which asked wholesalers to stock more, and export bans imposed in Israel and Russia in March 2020 and in Latvia in April 2020, respectively). However, the legal changes in Austria and Germany, which made reporting to registers mandatory in April 2020, had been decided at earlier times, and it was a coincidence that they entered in force in COVID-19 times.

Third, in addition to obligations and regulatory measures, supplemented by sanctions in some countries, public authorities tend to seek collaborative action with stakeholders. Canada started its stakeholder dialogue already in 2012. Italy opted for a large stakeholder platform that involved law enforcement institutions besides national and local authorities and associations (industry, wholesale, pharmacy). In a joint project (“inspection campaign”), first done as a pilot in one region and later repeated at national level, economic operators responsible for illegal transactions and breaches of the Good Distribution Practice were identified and penalised (over 20 withdrawals of licences, financial sanctions of nearly €800,000) [14]. It is interesting to note that in most countries marketing authorisation holders are the sole economic operators that have to report to the register (in 18 of 20 countries with a register). In this respect, the introduction of the notification obligation in Germany that is also targeted at wholesalers may serve as a good practice example. Despite obligatory notification to the register in all countries except Malta, not all countries impose financial sanctions in case of non-compliance (e.g. Norway: obligatory, but no sanctions). However, a few countries (e.g. Cyprus and Finland) were discussing the introduction of sanctions at the time of the survey.

Fourth, access to information related to the shortage situation plays a major role, not only for public authorities, but also for health professionals such as pharmacists who are involved in the management of shortages [29,30]. In several countries, public authorities responded to this need for information for health professionals by offering publicly accessible registers. For health professionals it is particularly important to learn about the expected duration of the shortages and possible approaches on how to ensure access to (similar) treatment. However, in only few countries do the regulatory authorities publish on alternative medicines or other solutions. In some countries (e.g. Italy, the Netherlands), pharmacists have established their own registers to cover for missing data of the authorities’ registers [38].

Fifth, differences exist with regard to the medicines that are subject to shortages-related measures. Most countries apply a rather broad approach for the registers (12 of the 20 countries with a register report shortages on any authorised medicine; 3 countries on prescription-only medicines or prescription-only and selected non-prescription medicines, respectively, and 2 countries on reimbursed medicines), while three countries (Denmark, Germany and Switzerland) limit the reporting requirements to medicines that are considered critical to ensure supply and treatment of patients. Medicines supply reserves and particularly export bans are usually more focused and often concern considerably fewer medicines compared to the medicines requiring notification.

Sixth, the measures comprise different types of action, with different purposes. Registers and stakeholder dialogues are, in principle, measures to generate information before and during the shortages management. But they are not necessarily policies to prevent or combat shortages. Preventive measures and those to fight the shortages include export bans and reserve stocks, which aim to protect the supply of the national markets, as well as imports from other countries, with the intention to cover gaps in national supplies. Having a focus on the national markets, these preventive measures compete with similar initiatives of other countries that struggle with the same challenges. Anecdotal evidence on trucks and airplanes with COVID-related medical supply goods being stopped at borders or being redirected to other countries that were willing to pay higher prices as reported in the media [39,40] confirm conflicting national interests.
| Country     | Measures relating to exports | Regulatory measures | Medicines supply reserves¹ | Multi-stakeholder approach | Further measures |
|-------------|------------------------------|---------------------|----------------------------|---------------------------|------------------|
| Austria     | Yes, export ban for POM included in a special list (since 1 April 2020) | No                  | No                         | Yes, a working group led by the Medicines Agency with pharmaceutical industry | None reported    |
| Albania     | No                           | Yes, special permits for the import of medicines (simplified process in shortage situations) | Yes, obligatory MAH and wholesalers are asked to stock reimbursed medicines | Yes, a working group of stakeholders | None reported    |
| Bulgaria    | No, but export ban under discussion | No                  | No                         | Yes, a working group of stakeholders | None reported    |
| Canada      | No                           | Yes, special permits for import of medicines | Yes, the Public Health Agency of Canada maintains the National Emergency Strategic Stockpile which contains medicines (e.g. antibiotics and antivirals, analgesics, anaesthetics) for use in case of emergency event such as a pandemic | No, but under discussion | None reported    |
| Cyprus      | No                           | Yes, special permits for the import of medicines in non-registered packages (PIL must be in English and Greek) | No, but under discussion | No, but under discussion | None reported    |
| Czech Republic | Yes, export ban for critical medicines and export notification for medicines included in a list | Yes, special permits for the import of medicines with PIL not in national language | No | No | None reported    |
| Denmark     | No                           | Yes, exemptions by the Medicines Agency for sale and dispensing of medicines (e.g. related to labelling) in cases of shortage | Yes, as part of tender obligations MAH are asked to stock certain critical inpatient medicines on a shortlist (e.g. antibiotics and anaesthetics); for vaccines (e.g. for the Danish Childhood Vaccination Programme) by the Statens Serum Institut under MoH | Yes, regular bilateral meetings of Medicines Agency and MoH with stakeholders, 2019 multi-stakeholder meeting National task force to secure the supply of critical products in the inpatient sector | Implementation of suggestions of stakeholder meeting (e.g. notifying doctors of shortage of a medicine s/he aims to prescribe) are being explored |
| Finland     | Yes, export ban for medicines in the medicines supply reserve | Yes, special permits for the import of medicines with PIL not in national language | Yes, obligatory MAH, importers, health care units (e.g. hospitals) and National Institute for Health and Welfare are asked to stock 1457 medicines (list is updated once a year) for 3–10 months No, but a new law valid from April 2020 allows taking appropriate measures, including rationing | Yes, cooperation of all stakeholders, including public | Changes related to sanctions and obligatory stocks are planned. Discussion on facilitating substitution in community pharmacies (wider range of substitutable medicines) Discuss on possibility of standardised PIL for Nordic countries |
| Germany     | No                           | Yes, waiving the obligation to label in national language in cases of shortage (for defined medicines) | Yes, a working group of stakeholders led by the Medicines Agency working on shortages, officially noted in a new legislation in act since 1 April 2020 Since 1 April 2020: If case of non-availability of a medicine under a discount agreement (Rabattvertrag) in community pharmacy, immediate substitution to a higher-priced medicine in the reference group is possible, with the price difference being paid by the sickness funds | None reported    |
| Country     | Measures relating to exports                                                                 | Regulatory measures                                                                 | Medicines supply reserves*                                                                 | Multi-stakeholder approach                                                                 | Further measures                                                                 |
|-------------|--------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Israel      | Yes, export ban for some medical products that contain alcohol (since 26 March 2020; linked to COVID-19 crisis) and under discussion for further medicines | Yes, special permits for the import of medicines from certain countries               | Yes, obligatory MAH and wholesalers are asked to keep at least 30 days stockpile of all medicines | Yes, cooperation of all stakeholders, including public                                | None reported                                                                   |
| Italy       | Yes, special permits for the import of defined medicines affected by a shortage              | Yes, language exemptions for MAH and wholesalers and special permits for MAH and wholesalers to import medicines | Yes, obligatory for a national reserve of defined medicines ("essential list") for emergency situations and recommended for hospitals | Yes, the Medicines Agency set up a specific task force with the aim of ensuring a multidisciplinary approach in the assessment of critical issues and emergencies related to shortages. Since 2015 stakeholder project with ad-hoc working group of supply chain actors, health professionals and authorities (e.g. carabinieri). | Possibility to use national federal production sites (e.g. military) to produce medicines |
| Latvia      | Yes, export ban for listed emergency medicines and export notification for all medicines since 2 April 2020 | Yes, language exemptions for MAH and wholesalers and special permits for MAH and wholesalers to import medicines | Yes, voluntary MAH and wholesalers are asked to keep a 6-months stockpile of all authorised medicines | Yes, a working group of stakeholders (MAH, wholesalers, hospitals)                      | Regular revision of the list of emergency products Discussion of implementation of additional measures in the light of COVID-19 crisis |
| Lithuania   | No                                                                                         | Yes, special permits for the import of medicines with PIL not in national language to be dispensed by community pharmacy. No special permit for medicines without PIL in national language required for supply to hospitals | Yes, national reserve for emergency situations | None reported                                                                            | No                                                                                |
| Malta       | No                                                                                         | Yes, regulatory measures to mitigate shortages on a case-by-case basis               | Yes, voluntary MAH and wholesalers are asked to keep a 6-months stockpile of all authorised medicines | Yes, bilateral dialogue with wholesalers                                                | None reported                                                                   |
| Moldova     | No                                                                                         | Yes, a special commission for unregistered medicines to grant authorisation for import of needed medicines | No                                                                                       | No                                                                                     | None reported                                                                   |
| Netherlands | No, but export ban under discussion                                                        | Yes, special permits for the import of medicines (simplified process in shortage situations) | No, but in implementation in 2020 Obligation to cover supply of 5 months (3 months – MAH end 2 months – wholesalers) | Yes, a working group of stakeholders                                                  | In the past: Rationing of medicines under shortage (e.g. contraceptives)         |
| Norway      | Yes, export ban for pneumococcal vaccines since 6 March 2020 (COVID-19 related legislation) export notification for wholesalers have in case they want to parallel export a medicine out of a list of around 60 ATC codes, since 6 March 2020 (COVID-19 related legislation) | Yes, applications are prioritised according to urgency / medical need                   | Yes, voluntary MAH and wholesalers are asked to keep a 6-months stockpile of medicines for inpatient sector | Yes, since 2019, active dialogue of stakeholders ([industry association, pharmacies association, wholesalers); Since March 2020: weekly meetings / updates with stakeholders. | Rationing of scarce medicines (e.g. dispensing of only 1 month supply)            |
Table 2 (Continued)

| Country       | Measures relating to exports                                                                 | Regulatory measures                                                                                     | Medicines supply reservesa | Multi-stakeholder approach                                                                 | Further measures                                                                 |
|---------------|---------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|----------------------------|-------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Portugal      | Yes, export ban for defined medicines included in the “ex-ante notification list” (those with a high number of shortages) and export notification for all medicines included in the “ex-ante notification list” | Yes, special permits for MAH and pharmacies to import and dispense medicines with PIL not in national language | Yes, obligatory MAH and wholesalers are requested to keep sufficient stock for all medicines | Yes, meetings with representatives of national associations of MAH, wholesalers, pharmacies. | Unit in Medicines Agency to ensure communication on shortages. Daily pharmacy and wholesale reports on shortages. |
| Romania       | Yes, export notification for reimbursed medicines but no export banb                          | Yes, special permits for the import of medicines (simplified process in shortage situations)           | No                         | Yes, a working group of stakeholders                                                        | Plans to optimise the electronic reporting system in order to be informed even if some economic operators do not notify accordingly |
| Russia        | Yes, export ban since 2 March 2020                                                          | Yes, fast-track authorisation for medicines under shortage                                              | Yes, obligatory MAH should ensure supply of more than 200 INN across several ATC groups (except cancer medicines) under the responsibility of the MoH | No                                                                                       | None reported                                                                    |
| Slovenia      | No                                                                                          | Yes, special permits for the import of medicines under shortage (list of essential medicines)          | No, but national reserves for emergency situations                                                    | No                                                                                       | None reported                                                                    |
| Sweden        | No                                                                                          | Yes, special permits for MAH and pharmacies to import and dispense medicines with PIL not in national language | No, but medicines supply stocks are under discussion, a national reserve for emergency situations exist | Yes, a working group of stakeholders                                                        | None reported                                                                    |
| Switzerland   | No                                                                                          | No                                                                                                      | Yes, obligatory MAH are requested to stock a 3-month supply of defined medicines (e.g. antibiotics, neuraminidase inhibitors, opiates, haemostatics, insulin) | Yes, a working group of stakeholders                                                        | Discussion on expansion of stocks, increase in availability for supply-critical medicines, decentralised production of medicines and domestic production capacities for specific medicines |
| United Kingdom| Yes, export ban for defined medicines                                                        | Yes, as part of their contractual obligation suppliers who were commissioned have to store the Essential Medicines Buffer Stock (i.e. essential medicines to treat (1) conditions that are exacerbated by flu and (2) conditions that would lead to hospitalisations and deaths in case of major supply disruptions) for 4 years | Yes, as part of their contractual obligation suppliers who were commissioned have to store the Essential Medicines Buffer Stock (i.e. essential medicines to treat (1) conditions that are exacerbated by flu and (2) conditions that would lead to hospitalisations and deaths in case of major supply disruptions) for 4 years | Yes, a working group of stakeholders                                                        | None reported                                                                    |

ATC = anatomic, therapeutic, chemical (classification of the World Health Organization), INN = international non-proprietary name(s), MAH = marketing authorisation holder(s), MoH = Ministry of Health, PIL = patient information leaflet.

b Information was sought as to whether, or not, MAH and wholesalers were requested to stock defined medicines for a certain period of time. Some countries responded by referring to national buffer stocks for emergency situations. Further countries may also have established such national buffer stock, e.g. for vaccines.

c In October 2019, a list of oncology medicines, for which an export ban was intended to be introduced, was notified to the European Commission. A new government withdrew the planned legislation.

More than five years ago, researchers called for collaboration among countries to tackle the shortages challenge: “Currently, the Member States of the European Union are striving to resolve the problem very much on their own, although a far more focused and dedicated collaboration may well prove instrumental in coping with drug shortages throughout Europe more effectively” [11].

The situation appears not to have changed considerably though some initiatives were launched and the topic has meanwhile become high on the political agenda [41,42]. In December 2016, the European Medicines Agency (EMA) created the “Task Force on the Availability of Authorised Medicines for Human and Veterinary Use” of EMA and the Heads of Medicines Agencies (HMA) to provide strategic support and advice to tackle disruptions in supply of medicines and ensure their continued availability. EMA and HMA also published guidance [43] for marketing authorisation holders on detecting and reporting medicines shortages which is based on an agreed harmonised definition of shortages. Furthermore, the 2014 Joint Procurement Agreement (JPA) on Medical Countermeasures in the EU provides a framework for jointly purchasing vaccines and medical countermeasures for serious cross-border
threats to health. As of March 2020, it has been signed by all 27 EU Member States and four additional European countries [44]. But the JPA framework was not intended to be extended to medicines in general [45].

In recent years, cross-country collaborations (such as the Benelux Initiative or the “Valletta Declaration”) were established between European countries. Their key aim is to ensure sustainable patient access to new innovative medicines [46]. Shortage management appears to be of lower importance for these collaborations, except for the Baltic Procurement Initiative of Estonia, Latvia and Lithuania. For the latter, managing shortages based on a “lending agreement” is a major collaborative action. In case of a shortage in one of the countries, another country lends the needed medicines or medical devices and does not charge any fees for this service. Once the beneficiary country receives its supply, it will return the products it borrowed to the lending country [47].

Major causes of shortages are production and quality problems [11,48–50]. In our research, two responding countries mentioned national production to overcome medicine shortages (Switzerland reported a discussion on strengthening the domestic production base, and Italy mitigates some shortages by using military sites for production). Bringing the pharmaceutical production back to Europe has been proposed and discussed in the political debate, including discussions initiated by the German Presidency of European Council in the second half of 2020 [42]. This longer-term endeavour would require joint efforts of several European countries, based on strong political will. It is beyond the scope of this paper to assess the feasibility and effectiveness of this measure. However, the COVID-19 crisis could offer an opportunity to use the momentum for change.

In the meantime, European countries could start collaborating in the more technical area of information sharing. Despite the above-mentioned agreement on a definition of a shortage between EMA and national regulatory agencies, the national legal specifications continue to differ among European countries ([14,18], see also Supplementary Materials 1). These differences are also reflected in the variation in the deadlines for the shortage notification. As shown in this study (Table 1), deadlines range from “immediately” to “at least six months in advance”. In addition, the structure and the contents of the national registers (e.g. frequency of updates, information on start and end of the shortages, causes) also vary among the countries ([18,31,38,50], Supplementary Materials 3). These challenges

### Table 3

| Country        | Financial sanctions in general | Financial sanctions* for non-supply | for non-compliance to reporting requirements | for non-compliance with stocking requirements |
|----------------|--------------------------------|-------------------------------------|---------------------------------------------|---------------------------------------------|
| Austria        | No                             | No                                  | No                                          | Not appl. (no reserve)                      |
| Albania        | Yes                            | No                                  | Not appl. (no register)                     | Yes (in contract)                           |
| Bulgaria       | No                             | No                                  | Not appl. (no register)                     | No                                          |
| Canada         | Yes                            | No                                  | Yes                                         | No                                          |
| Cyprus         | No                             | No                                  | (sanctions were being discussed)            | Not appl. (no reserve)                      |
| Czech Republic | Yes                            | Yes                                 | Yes (but not imposed)                       | Yes, under the contractual tender obligation (inpatient medicines) to stock listed medicines for 3–6 months |
| Denmark        | Yes                            | Yes                                 | Yes                                         | Yes                                         |
| Finland        | Yes                            | No                                  | No (sanctions were being discussed)         | No                                          |
| Germany        | Yes                            | No                                  | Yes*                                        | Not appl. (no reserve in principle)         |
| Israel         | No                             | No                                  | Yes                                         | No                                          |
| Italy          | Yes                            | No                                  | Yes (since 2019)                            | Not appl. (no reserve)                      |
| Latvia         | Yes                            | No                                  | Yes                                         | No                                          |
| Lithuania      | No                             | No                                  | No                                          | Not appl. (no reserve requirements for MAH) |
| Malta          | No                             | No                                  | No                                          | No                                          |
| Moldova        | No                             | No                                  | No                                          | No                                          |
| Netherlands    | Yes                            | Yes                                 | Yes (for winners of the tenders)            | Not appl. (no register)                     |
| Norway         | No                             | No                                  | Yes                                         | Not appl. (no reserve)                      |
| Portugal       | Yes                            | Yes (but not imposed)               | Yes (but not imposed)                       | Not appl. (no reserve)                      |
| Romania        | Yes                            | No                                  | Yes                                         | Not appl. (no reserve)                      |
| Russia         | No                             | No                                  | No                                          | Not appl. (no register)                     |
| Slovenia       | Yes                            | Yes, for wholesalers in case of non-supply with 24 h (weekdays) or 72 h (weekend) | Yes (for winners of the tenders) | Not appl. (no register) |
| Sweden         | Yes                            | Yes                                 | No                                          | Not appl. (no reserve)                      |
| Switzerland    | No                             | No                                  | No                                          | No                                          |
| United Kingdom | Yes                            | No                                  | Yes                                         | No                                          |

MAH = marketing authorisation holders, not appl. = not applicable.

* Unless indicated (e.g. for Denmark), it is not known whether, or not, sanctions were actually enforced.
* Since a legal change on 1 April 2020, which introduced the obligation to notify the register.
* In addition, financial sanctions for the export of medicines which are prohibited to be exported.
* Policy of supply reserves will be established in 2020, to be introduced with financial sanctions.
* On the contrary, increased costs for wholesalers for additional stockpilings during the COVID-19 crisis are refunded by the state.
would have to be addressed if a European register of shortages were created. Such a joint register would constitute a major step forward to better manage shortages and develop European solutions to prevent them.

This study has some limitations. Despite thorough data collection supplemented by validation done by national experts, the authors cannot exclude gaps and wrong reporting on behalf of the respondents due to misunderstandings. The study was prepared in February 2020, and respondents answered between 5 March 2020 and 8 April 2020. In this period, many European countries experienced the outbreak of the COVID-19 pandemic. A few countries reported immediate measures to address possible COVID-19 related shortages, whereas other countries might take similar action at a later stage. The survey was not planned as a COVID-19 related shortages survey, and we were overwhelmed by the developments. Furthermore, it is acknowledged that this study provides a descriptive comparison of measures; an analysis of the effectiveness of the measures was outside of the scope of the research. The authors are also not aware of the status of implementation and enforcement of some measures (e.g., whether, or not, sanctions are actually imposed). Finally, the analysis of published shortage registers done during the revision of the paper is based on a different methodology (authors’ screening of registers), and the findings relate to a later stage (August 2020) compared to the survey of measures. As it was not part of the originally designed study, only a preliminary analysis could be performed. An in-depth investigation of the structure and contents of the shortages registers would be an essential prerequisite for the establishment of a joint register.

5. Conclusions

Governments have increasingly been using a mix of measures to address and combat medicines shortages. In the months and even weeks preceding and even during this survey, some countries implemented additional measures. Regarding the design of policies, voluntary tools tend to have been substituted by obligatory mechanisms linked to sanctions. High-income countries were found to apply a higher number of measures, but the introduction of new policies in this field was also observed in some lower-income countries in Europe. The measures appear to be rather reactive with a focus on managing existing or upcoming shortages and not addressing the causes of shortages.

For the time being, measures to manage and combat shortages of medicines were predominantly taken at national level, though the need for a multi-country approach to identify global or at least European answers has been repeatedly voiced. The COVID-19 crisis that will likely aggravate the shortage situation could give new momentum to jointly search for solutions that go beyond national measures and could also address the causes of shortages.

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Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.healthpol.2020.09.001.

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