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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

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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, wholesales 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	Managed by	Reports from	Medicines covered	Reporting time-lines
Austria	Yes	Obligatory (since April 2020; before: voluntary), no sanctions	Medicines Agency	MAH	POM	At least 2 months in advance if known; “immediately” for unforeseen shortages
Albania	No	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>
Bulgaria	No	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>
Canada	Yes	Obligatory, sanctions possible	Medicines Agency	MAH	POM and NPM administered under practitioner's supervision	6 months in advance, if known or within 5 days of becoming aware
Cyprus	Yes	Obligatory, no sanctions (but their introduction is being discussed)	MoH and Health Insurance Organisation	Local distributors	Reimbursed POM	“Immediately”
Czech Republic	Yes	Obligatory, sanctions possible	Medicines Agency	MAH	Any medicine	At least 3 months in advance
Denmark	Yes	Obligatory, sanctions possible	Medicines Agency	MAH	Any medicine if shortage is expected to influence the treatment of patients	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 circumstances ^a
Latvia	Yes	Obligatory, sanctions possible	Medicines Agency	MAH, wholesalers ^b	Any medicine	2 months in advance
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	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>
Netherlands	Yes	Obligatory ^c , 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	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>	<i>Not appl.</i>
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 ^c , no sanctions	Medicines Agency ^c	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.

^aLegal change in 2019: timeline of reporting was changed from 2 to 4 months in advance.^bAnyone can report to the register but MAH are obliged to do so; wholesalers have to report about their stock on a daily basis.^cIn 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.

Table 2
Measures to address and prevent medicine shortages as of March / April 2020.

Country	Measures relating to exports	Regulatory measures	Medicines supply reserves ^a	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	Yes, the Multi-Stakeholder Steering Committee on Drug Shortages with representatives of industry, federal, provincial and territorial governments, and health professional associations, assembled in 2012	2019 Minister of Health mandate letter to prioritise access to needed medicines
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	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) Discussion 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)	No, but a new law valid from April 2020 allows taking appropriate measures, including rationing	Yes, multi-stakeholder advisory board at 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

Table 2 (Continued)

Country	Measures relating to exports	Regulatory measures	Medicines supply reserves ^a	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	Yes, special permits for the import of defined medicines affected by a shortage	No	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). Yes, a working group of stakeholders (MAH, wholesalers, hospitals)	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, obligatory for a national reserve of defined medicines ("essential list") for emergency situations and recommended for hospitals		Regular revision of the list of emergency products Discussion of implementation of additional measures in the light of COVID-19 crisis None reported
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	No	None reported
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 Yes, special permits for the import of medicines (simplified process in shortage situations)	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, obligatory Wholesalers are asked to keep 2 extra months stock for outpatient sector, and hospitals / health enterprises are responsible for stocking for inpatient sector (agreements with wholesalers) Since March 2020: voluntary agreement (COVID-19 ad-hoc) between authorities and wholesalers to increase stock	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 reserves ^a	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 ban ^b	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 Reserves for 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	No	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 Organisation), INN = international non-proprietary name(s), MAH = marketing authorisation holder(s), MoH = Ministry of Health, PIL = patient information leaflet.

^a 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.

^b 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

Table 3
Financial sanctions related to medicine shortages as of March / April 2020.

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

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

^a Unless indicated (e.g. for Denmark), it is not known whether, or not, sanctions were actually enforced.

^b Since a legal change on 1 April 2020, which introduced the obligation to notify the register.

^c In addition, financial sanctions for the export of medicines which are prohibited to be exported.

^d Policy of supply reserves will be established in 2020, to be introduced with financial sanctions.

^e On the contrary, increased costs for wholesalers for additional stockpiling during the COVID-19 crisis are refunded by the state.

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

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>.

References

- [1] Gray A, Manasse Jr HR. Shortages of medicines: a complex global challenge. *Bulletin of the World Health Organization* 2012;90(3):158–A.
- [2] Videau M, Chemali L, Stucki C, Saavedra-Mitjans M, Largana S, Guerin A, et al. Drug shortages in Canada and selected European countries: a cross-sectional, institution-level comparison. *The Canadian Journal of Hospital Pharmacy* 2019;72(1):7.
- [3] Drug shortages in Canada: data for 2016–2017 and perspectives on the problem. Videau M, Lebel D, Bussi eres J-F, editors. *Annales Pharmaceutiques Francaises*. Elsevier; 2019.
- [4] Huys I, Simoens S. European drug shortages: a call for action! *International Journal of Pharmacy Practice* 2013;21(1):1–2.
- [5] Bauters T, Claus BO, Norga K, Huys I, Simoens S, Laureys G. Chemotherapy drug shortages in paediatric oncology: a 14-year single-centre experience in Belgium. *Journal of Oncology Pharmacy Practice* 2016;22(6):766–70.
- [6] De Weerd E, De Rijdt T, Simoens S, Casteels M, Huys I. Time spent by Belgian hospital pharmacists on supply disruptions and drug shortages: an exploratory study. *PLoS ONE [Electronic Resource]* 2017;12(3).
- [7] Heiskanen K, Ahonen R, Karttunen P, Kanerva R, Timonen J. Medicine shortages – a study of community pharmacies in Finland. *Health Policy* 2015;119(2):232–8.
- [8] Heiskanen K, Ahonen R, Kanerva R, Karttunen P, Timonen J. The reasons behind medicine shortages from the perspective of pharmaceutical companies and pharmaceutical wholesalers in Finland. *PLoS ONE [Electronic Resource]* 2017;12(6).
- [9] Sarnola K, Linnolahti J. A regulatory perspective on the availability of medicines and medicine shortages in outpatient care: case Finland. *International Journal of Clinical Pharmacy* 2019;41(4):825–30.
- [10] Bocquet F, Albane Degrossat-Th eas A, Peign e J, Paubel P. The new regulatory tools of the 2016 Health Law to fight drug shortages in France. *Health Policy* 2017;121(5):471–6.
- [11] Bogaert P, Bochenek T, Prokop A, Pilc A. A qualitative approach to a better understanding of the problems underlying drug shortages, as viewed from Belgian, French and the European Union's perspectives. *PLoS ONE [Electronic Resource]* 2015;10(5).
- [12] Said A, Goebel R, Ganso M, Zagermann-Muncke P, Schulz M. Drug shortages may compromise patient safety: Results of a survey of the reference pharmacies of the Drug Commission of German Pharmacists. *Health Policy* 2018;122(12):1302–9. Epub 2018/10/20.
- [13] Tirelli U, Berretta M, Spina M, Michieli M, Lazzarini R. Oncologic drug shortages also in Italy. *European Review for Medical and Pharmacological Sciences* 2012;16(1):138–9.
- [14] Di Giorgio D, Scrofina G, Scognamiglio B, Di Carluccio N, Tulimiero R, Pietrosanto A, et al. Tackling distribution-related shortages of medicines: an Italian case study evaluated in the European Union framework. *Medicine Access @ Point of Care* 2019:1–7.
- [15] Postma DJ, De Smet PAGM, Gispens-de Wied CC, Leufkens HGM, Mantel-Teeuwisse AK. Drug shortages from the perspectives of authorities and pharmacy practice in the Netherlands: an observational study. *Frontiers in Pharmacology* 2018;9(1243):1–8.

- [16] Postma D, de Wolf L. DSL-008 drug shortages in the Netherlands: monitored by farmanco. *European Journal of Hospital Pharmacy: Science and Practice* 2013;20(Suppl. 1):A90-A.
- [17] Zaprutko T, Kopciuch D, Bronisz M, Michalak M, Kus K, Nowakowska E. Drug shortages as a result of parallel export in Poland – Pharmacists' opinions. *Health Policy* 2020;24(5):563–7. <http://dx.doi.org/10.1016/j.healthpol.2020.03.003>.
- [18] Acosta A, Vanegas EA, Rovira J, Godman B, Bochenek T. Medicine shortages: gaps between countries and global perspectives. *Frontiers in Pharmacology* 2019;10(763):1–21.
- [19] De Weerd E, Simoens S, Casteels M, Huys I. Toward a European definition for a drug shortage: a qualitative study. *Frontiers in Pharmacology* 2015;6(253).
- [20] Iskrov G, Miteva-Katrandzhieva T, Stefanov R. Challenges to orphan drugs access in Eastern Europe: the case of Bulgaria. *Health Policy* 2012;108(1):10–8.
- [21] Vogler S, Paris V, Ferrario A, Wirtz VJ, de Joncheere K, Schneider P, et al. How can pricing and reimbursement policies improve affordable access to medicines? Lessons learned from European countries. *Applied Health Economics & Health Policy* 2017;15(3):307–21. Epub 2017/01/08.
- [22] Vogler S, Zimmermann N, Haasis MA. PPRI Report 2018: Pharmaceutical pricing and reimbursement policies in 47 PPRI network member countries Vienna: WHO Collaborating Centre for Pricing and Reimbursement Policies, Gesundheit Österreich GmbH (GÖG / Austrian National Public Health Institute); 2019. Available from: https://ppri.goeg.at/sites/ppri.goeg.at/files/inline-files/PPRI%20Report2018_2nd.edition.final.pdf (Accessed 23 August 2020).
- [23] Schneider P, Vogler S. Practice of external price referencing. In: Vogler S, editor. *Medicine price surveys, analyses and comparisons*. Elsevier; 2019. p. 345–68.
- [24] Danzon PM, Wang YR, Wang L. The impact of price regulation on the launch delay of new drugs—evidence from twenty-five major markets in the 1990s. *Health Economics* 2005;14(3):269–92.
- [25] Kyle MK. Pharmaceutical price controls and entry strategies. *The Review of Economics and Statistics* 2007;89(1):88–99.
- [26] Vogler S, Schneider P, Zimmermann N. Evolution of average European medicine prices: implications for the methodology of external price referencing. *Pharmacoeconomics - Open* 2019;3(3):303–9.
- [27] Phuong JM, Penn J, Chaar B, Oldfield LD, Moles R. The impacts of medication shortages on patient outcomes: a scoping review. *PLoS One [Electronic Resource]* 2019;14(5):e0215837.
- [28] Wickware C. Medicine shortages took an extra hour per week of pharmacist time in 2019, survey finds. *The Pharmaceutical Journal* 2020;(30 January). Available from: <https://www.pharmaceutical-journal.com/news-and-analysis/news/medicine-shortages-took-an-extra-hour-per-week-of-pharmacist-time-in-2019-survey-finds/20207631.article> (Accessed 13 April 2020).
- [29] De Weerd E, Simoens S, Casteels M, Huys I. Clinical, economic and policy implications of drug shortages in the European Union. *Applied Health Economics and Health Policy* 2017;15(4):441–5.
- [30] Miljković N, Gibbons N, Batista A, Fitzpatrick RW, Underhill J, Horák P. Results of EAHP's 2018 survey on medicines shortages. *European Journal of Hospital Pharmacy* 2019;26(2):60–5.
- [31] Bochenek T, Abilova V, Alkan A, Asanin B, de Miguel Beriain I, Besovic Z, et al. Systemic measures and legislative and organizational frameworks aimed at preventing or mitigating drug shortages in 28 European and Western Asian countries. *Frontiers in Pharmacology* 2018;8(942):1–24.
- [32] GÖG. PPRI network members. Vienna: Gesundheit Österreich (Austrian National Public Health Institute); 2020. Available from: https://ppri.goeg.at/PPRI_network_members (Accessed 13 April 2020).
- [33] Vogler S, Leopold C, Zimmermann N, Habl C, de Joncheere K. The Pharmaceutical Pricing and Reimbursement Information (PPRI) initiative—experiences from engaging with pharmaceutical policy makers. *Health Policy and Technology* 2014;3(2):139–48.
- [34] HMA/EMA. HMA/EMA workshop on availability of authorised medicines. In: Report from a multi-stakeholder meeting held at EMA on 9th November 2018. London: Head of Medicines Agencies (HMA) / European Medicines Agency (EMA); 2018.
- [35] AESGP, EAEP, EFPIA, GPIE / EIPG, GIRP, Medicines for Europe, et al. *Addressing the root causes of medicines shortages. Supply chain Stakeholders' views on root causes and solutions*; 2019.
- [36] KNMP. Tekorten in cijfers [Shortages in numbers]. The Hague: Koninklijke Nederlandse Maatschappij ter bevordering der Pharmacie; 2020. Available from: <https://farmanco.knmp.nl/tekorten-in-cijfers> (Accessed 13 April 2020).
- [37] BfArM. Lieferengpässe [Shortages]. Berlin: Bundesinstitut für Arzneimittel und Medizinprodukte; 2020. Available from: https://www.bfarm.de/DE/Service/Presse/Themendossiers/Lieferengpaeasse/_node.html (Accessed 13 April 2020).
- [38] Vogler S, Fischer S. Lieferengpässe bei Arzneimitteln: Internationale Evidenz und Empfehlungen für Deutschland [Medicines shortages: international evidence and recommendations for Germany]. Vienna: Gesundheit Österreich Forschungs- und Planungs GmbH; 2020.
- [39] Benini F. Coronavirus: Die Schweiz liegt mit Deutschland im offenen Streit. NZZ am Sonntag 2020;(7 March). Available from: <https://nzzas.nzz.ch/schweiz/offener-streit-mit-deutschland-um-masken-ld.1545115?reduced=true> (Accessed 13 April 2020).
- [40] Willsher K, Borger J, Holmes O. US accused of 'modern piracy' after diversion of masks meant for Europe. In: *The Guardian*; 2020, 4 April. Available from: <https://www.theguardian.com/world/2020/apr/03/mask-wars-coronavirus-outbidding-demand> (Accessed 13 April 2020).
- [41] European Commission. Pharmaceutical strategy for Europe - timely patient access to affordable medicines. In: Draft for consultation; 2020. Available from: https://ec.europa.eu/health/human-use/strategy_en (Accessed 13 July 2020).
- [42] Bundesministerium für Gesundheit (Ministry of Health). Deutsche EU-Ratspräsidentschaft. Berlin: German Presidency of European Council 2020; 2020. Available from: <https://www.bundesgesundheitsministerium.de/eu2020/deutsche-eu-ratspraesidentschaft.html> (Accessed 20 August 2020).
- [43] EMA. Guidance on detection and notification of shortages of medicinal products for Marketing Authorisation Holders (MAHs) in the Union (EEA). EMA/674304/2018. Amsterdam: European Medicines Agency and Heads of Medicines Agencies; 2019. Available from: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-detection-notification-shortages-medicinal-products-marketing-authorisation-holders-mahs_en.pdf (Accessed 14 April 2020).
- [44] European Commission. Joint Procurement of medical countermeasures; 2020. Available from: https://ec.europa.eu/health/preparedness_response/joint_procurement_en (Accessed 14 April 2020).
- [45] European Commission. Medical Countermeasures that could be procured in common under the joint procurement agreement. Luxembourg; 2014.
- [46] Beneluxa Initiative on Pharmaceutical Policy. Beneluxa initiative - vision; 2020. Available from: <http://beneluxa.org/> (Accessed 18 April 2020).
- [47] Vogler S, Haasis MA, van den Ham R, Suleman F, Humbert T, Garner S. Cross-Country Collaborations to improve access to medicines and vaccines in the WHO European Region. World Health Organization Regional Office for Europe; 2020. Available from: <https://apps.who.int/iris/bitstream/handle/10665/332933/9789289055031-eng.pdf> (Accessed 16 July 2020).
- [48] De Weerd E, Simoens S, Hombroecx L, Casteels M, Huys I. Causes of drug shortages in the legal pharmaceutical framework. *Regulatory Toxicology and Pharmacology* 2015;71(2):251–8.
- [49] Food and Drug Administration. Drug shortages: root causes and potential solutions; 2019. Available from: <https://www.fda.gov/media/131130/download> (Accessed 13 April 2020).
- [50] Pauwels K, Huys I, Casteels M, Simoens S. Drug shortages in European countries: a trade-off between market attractiveness and cost containment? *BMC Health Services Research* 2014;14(1):1–9.