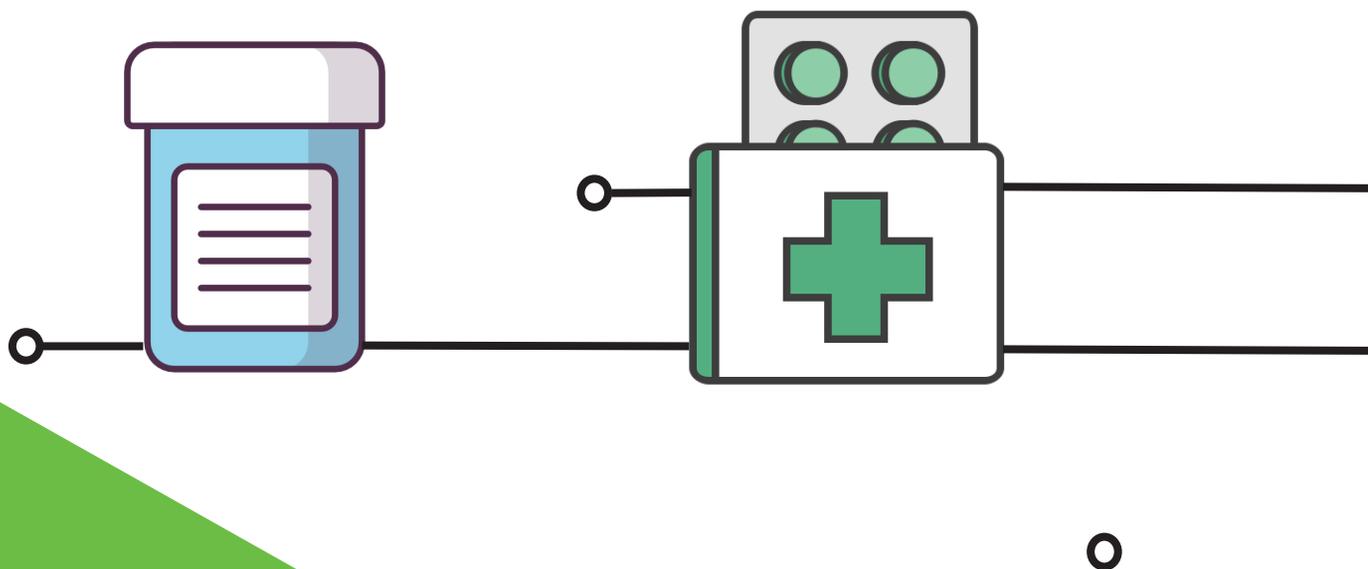


EAHP's 2018 Survey on Medicines Shortages to improve patient outcomes



MEDICINES SHORTAGES IN EUROPEAN HOSPITALS

Results of the largest pan-European survey on medicines shortages in the hospital sector, an overview of the situation and the key challenges that need to be tackled.

November 2018



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The European Association of Hospital Pharmacists (EAHP) is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education

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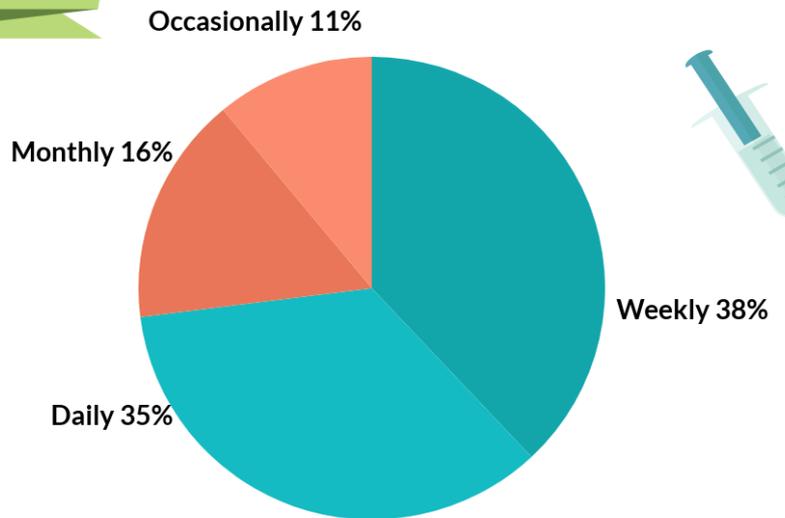
*The 2018 Medicines Shortages Report uses original quotes provided by survey respondents during the consultation period. These quotes have not been altered.

Medicines Shortages Survey results

Are medicines shortages a current problem?
91.8% (2018) vs 86.2% (2014)

1.666 responses from 38 countries

How often does your hospital pharmacy experience medicines shortages?



5 Hours per week spent dealing with medicines shortages



2.2 months is the duration of a typical medication shortages

Types of medicines most frequently reported



77%
Antimicrobial agents

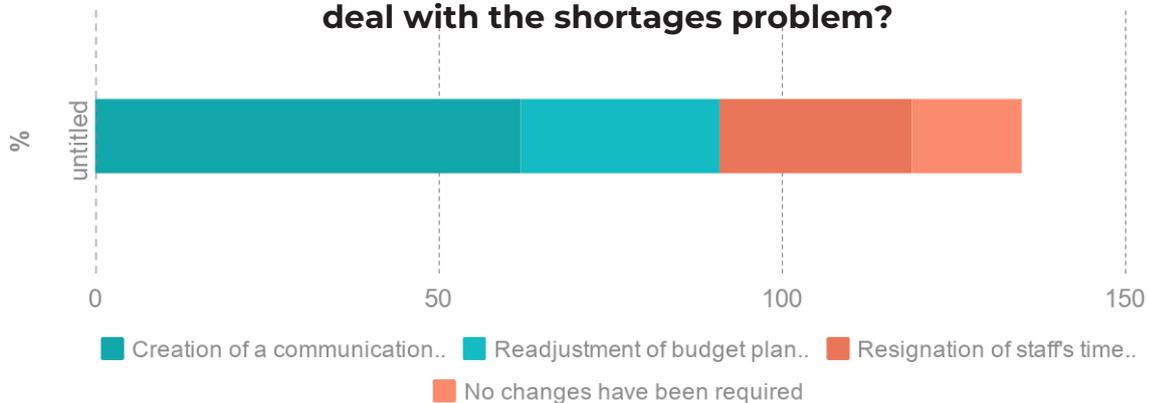


43%
Vaccinations



39%
Oncology medicines

What changes (if any) in practice has your hospital needed to make in order to deal with the shortages problem?



67% of respondents reported their country has a system for reporting shortages, but only 56% of those judge it to be effective



77% responded that generic medicines are most commonly in short supply

1. Foreword by the President

Problems caused by medicines shortages in Europe are a severe threat to patient care and should be addressed through adequate actions on the local, national and European level. The European Association of Hospital Pharmacists (EAHP) started investigating the issue in 2012 due to increased reports from its members expressing the difficulties in sourcing medicines.

In 2014, the first pan-European report on medicines supply shortages in the hospital sector shed more light on the issue. It highlighted that medicines shortages are a serious problem for hospital pharmacists resulting in the unavailability of certain antimicrobial agents, oncology and emergency medicines. To address the issues caused by shortages, such as the increase of staff time needed to solve them, hospital pharmacists urgently called for greater legal clarity regarding the responsibility of suppliers to report supply disruptions at an early stage.



Despite efforts by the supply chain actors, which resulted in the adoption of a joint statement containing recommendations on the provision of information designed to help tackle medicines shortages, the problem of medicines shortages continues to persist as highlighted by the results of the 2018 EAHP Medicines Shortages Survey. EAHP consequently calls on national governments and the European Commission to improve the communication on medicines shortages and to launch an inquiry at the European level into the primary factors causing medicines shortages.

Communication on medicines shortages

A reliable catalogue of medicines in shortage across Europe is needed listing the shortage reason, estimated duration and other advice to pharmacies, prescribers and patients. EAHP acknowledges the efforts by the task force on the availability of authorised medicines for human and veterinary use of the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA). However, in view of the limits of the current catalogue on European medicines shortages, EAHP urges the EMA and the HMA to consider the development of a comprehensive communication strategy on shortages which ensures that all supply chain actors, including hospital pharmacists, receive adequate information on the shortage of medicines.

An inquiry at European level into the primary factors causing medicines shortages

Similar to the findings of the 2014 survey, the result of the 2018 survey underlines again that medicines shortages are a pan-European problem that cannot be solved through national measures alone. Consequently, the EAHP is calling on the European Commission to start an investigation into the factors causing medicines shortages and as a first step to provide solutions that will help to solve preventable shortages.

The first half of 2019 will, in particular, be a crucial time for hospital pharmacists with new regulations coming into effect that aim at combating counterfeit drugs and Brexit. We hope that other stakeholders follow our call to action and help us in securing the necessary solutions to tackle the growing problem of medicines shortages.

EAHP thanks Amgen for supporting the realisation of this report and Keele University for the analysis of the survey results.

Petr Horák

President of the European Association of Hospital Pharmacists

2. Executive summary

Previous work done by the EAHP found that medicines shortages can have a significant impact on patient care. The aim of the 2018 EAHP Medicines Shortages Survey was to provide a clearer and up to date picture on the impact of medicines shortages.

There were 1,666 responses to the 2018 survey from 38 countries, a large increase from the 2014 survey which received 607 responses. Medicines shortages were reported to still be a major issue facing hospitals across Europe. For example, 75% of respondents to the 2018 survey reported that they experienced medicines shortages at least weekly. The reported mean duration of a typical shortage for countries was 2.2 months.

In a number of ways, these issues have become more problematic since the 2014 survey. The percentage of respondents in a country reporting shortages to be a problem in terms of delivering the best care to patients and/or operating the hospital pharmacy saw a statistically significant increase for the 2018 survey (M = 91.8%, SD = 9.5%) compared to the 2014 survey (M = 82.6%, SD = 17.6%), $t(27) = 2.721$, $p = 0.011$, $d = 0.514$. A paired samples t-test also showed a statistically significant increase in the mean percentage of respondents in a country reporting that more than 5 hours per week are spent dealing with medicines shortages for the 2018 survey (M = 42.0%, SD = 18.7%) compared to the 2014 survey (M = 33.1%, SD = 25.9%), $t(26) = 2.275$, $p = 0.031$, $d = 0.438$.

Antimicrobial agents were the type of medicine most frequently reported as having shortage problems, with 77%. Problems were also reported frequently with preventative medicines (vaccinations) (43%) and oncology medicines (39%). The medicine which was reported to be most frequently associated with supply issues was Piperacillin/tazobactam with 272 responses across 18 countries.

Financial issues caused by medication shortages can be due to having to pay more to procure a medicine from another supplier or paying more for an alternative (see Q21). Other issues were having to devote more staff time to the issue (see Q10) or having a direct impact on patient (such as potentially increased length of hospital stay, see Q22). When asked if medicines shortages are having a negative impact on overall budget, most chose either 'agree' (43% of responses) or 'strongly agree' (38% of responses).

When asked about the impact on patients, over half of the respondents have seen patient care delayed as a consequence of medication shortages (59% of respondents). The quality of care received by the patient is also directly affected with cancellations of care (31% of respondents), medication errors (25% of respondents) and suboptimal treatment for patients (25% of respondents) also being frequently reported. There were 12 reports of death as a result of medication shortages (1% of respondents).

When asked how often do you estimate your hospital is able to provide treatment to a patient by providing a therapeutic equivalent or near equivalent medicine, without major disruption to their treatment? 78% of responses were for either 'most of the time' or 'all of the time'. At this point it was questioned if this is sustainable (e.g. *"We have so far always managed to source a timely alternative - but unsure how long this will be sustained"*).

67% of respondents reported their country has a system for reporting shortages, but only 56% of those judged it to be effective. A frequently reported issue was the dependence on manufacturers/suppliers informing authorities of a shortage as this often does not happen or information is flawed (i.e., multiple push backs on restock dates).

Regarding existing policy solutions (Q30), the policy solution with the most support was the medicines shortages catalogue of the EMA, with 43% of respondents answering this question choosing this option. The second most frequent option was 'None of the above' from 42% of respondents, which may cover people who do not support any of the policies, but also people who are not aware of these policies and what they are (e.g. *"not sure what these and I don't have time to read up on each option"*).

When asked about proposed policy solutions (Q31) it is not surprising to see that 79% of respondents support greater legal clarity on the responsibility of manufacturers to report upcoming supply chain issues at an early stage; in question 10 many comments were observed regarding pharmacists not being aware of supply issues until a delivery did not show up and in question 14 it was observed that the reporting system for medication shortages were weakened by a lack of obligation for manufacturers to share information on supply issues. A comprehensive database run by EMA was also a popular choice with 65% of respondents supporting the proposal, followed by a high level investigation on the causes for shortages and annual reporting on the extent of the problem with 58% and 50% respectively. This is the same order the proposals were ranked in the 2014 survey.

Freetext recommendations from respondents (Q32) include mandatory reporting of shortages by manufacturers, as well as providing accurate information on return dates. Many respondents would like to see manufacturers to have a legal obligation to maintain stock levels and ensure supply of medicines. There are responses calling for a central lead/agency to work on the problem to reduce duplication of efforts in identifying alternatives (either at European, EU, or national level).

Identifying the root cause of shortages is also seen as important – *“A more holistic review needs to be undertaken to understand why shortages occur and try and prevent them. Currently most shortages are managed reactively instead of proactively.”*

3. Background

Work done by the EAHP has already provided evidence on the extent of the problem of medicines shortages, and the impact it has on patient care. EAHP's 2014 Medicines Shortages Survey was designed to provide policy and decision makers with a clearer picture, to adequately assess the nature and available solutions to the problem of medicines shortages ⁽¹⁾. When asked if the shortages of medicines were a problem in the hospital they work in, 86% of the 537 respondents responded 'yes'.

The issue of medicines shortages also appeared in another survey conducted by the EAHP. The primary focus of the 2017 EAHP European Statements of Hospital Pharmacy Survey was to identify the barriers to the implementation of the EAHP European Statements of Hospital Pharmacy (statement 2.5 reads 'Each hospital pharmacy should have contingency plans for shortages of medicines that it procures.'). The results of this survey saw 60% of respondents say they had reason to contact the medicines authority because of a shortage. The survey also showed that the number of fully qualified pharmacists working in a hospital was a significant factor on a hospital having contingency plans to deal with medication shortages ⁽²⁾.

The aim of the 2018 Survey on Medicines Shortages was to provide a clearer picture on the impact of medicines shortages on hospital pharmacists ⁽³⁾. This included:

- the current nature of medicines shortages problems in Europe, including their prevalence;
- the most common types of shortages;
- their impact on patient care and hospital pharmacy services;
- existing national mechanisms for dealing with or monitoring shortages;
- how hospital pharmacists typically manage the problems shortages cause; and,
- hospital pharmacist views on proposed policy solutions.

The 2018 Survey on Medicines Shortages was created using SurveyMonkey, and conducted by the EAHP. Keele University was commissioned to analyse the results. The survey ran from 19th March 2018 to 11th June 2018.

Significance testing was performed to compare the 2018 survey data with the 2014 survey data for questions asked in both surveys. Testing was carried out using IBM SPSS software, and firstly the Shapiro Wilk's test was performed to check for normality. If the differences between the distributions of data were approximately normal and no significant outliers detected, a paired sample t-test was used. If a parametric test was not appropriate, a Wilcoxon signed rank test was used where the distribution of differences between the 2 sets of data was symmetric, and a sign test was used if not ⁽⁴⁾.

Terminology

M	Mean
SD	Standard Deviation
p	p-value
t	t-value
d	Effect size
Z	Test statistic

4. Response rates

There were 1,666 responses to the 2018 survey, a large increase from the 2014 survey which received 607 responses. The table below shows the breakdown of responses by country, compared to the number of responses received in the 2014 survey. Note that the table only includes responses from countries which responded to the 2018 survey. The countries which saw the biggest increase in responses were the UK (+284) and France (+189).

Country	Responses (2018)	Responses (2014)	Country	Responses (2018)	Responses (2014)
Albania	1	0	Latvia	4	2
Austria	29	21	Lithuania	1	8
Belgium	90	94	Luxembourg	3	0
Bosnia & Herzegovina	19	9	Malta	6	11
Bulgaria	3	6	Montenegro	4	0
Croatia	26	25	Netherlands	20	11
Cyprus	2	1	Norway	21	11
Czech Republic	26	4	Poland	32	13
Denmark	10	25	Portugal	85	42
Estonia	17	15	Romania	24	2
Finland	33	1	Russia	1	0
France	192	3	Serbia	20	8
FYROM	14	4	Slovakia	23	16
Germany	78	10	Slovenia	18	5
Greece	84	14	Spain	190	105
Hungary	33	12	Sweden	5	0
Iceland	9	4	Switzerland	67	7
Ireland	51	47	Turkey	61	5
Italy	73	41	UK	291	7

6. Prevalence of shortages in your hospital (Q2-3)

Q2. Are shortages of medicines a current problem in the hospital you work in, in terms of delivering the best care to patients and/or operating the hospital pharmacy?

This question received 1,666 responses, and an overwhelming 90% of respondents answered 'Yes', providing strong evidence that shortages of medicines is an extremely common problem in hospitals today. 7% of respondents answered 'No', and 3% were unsure.

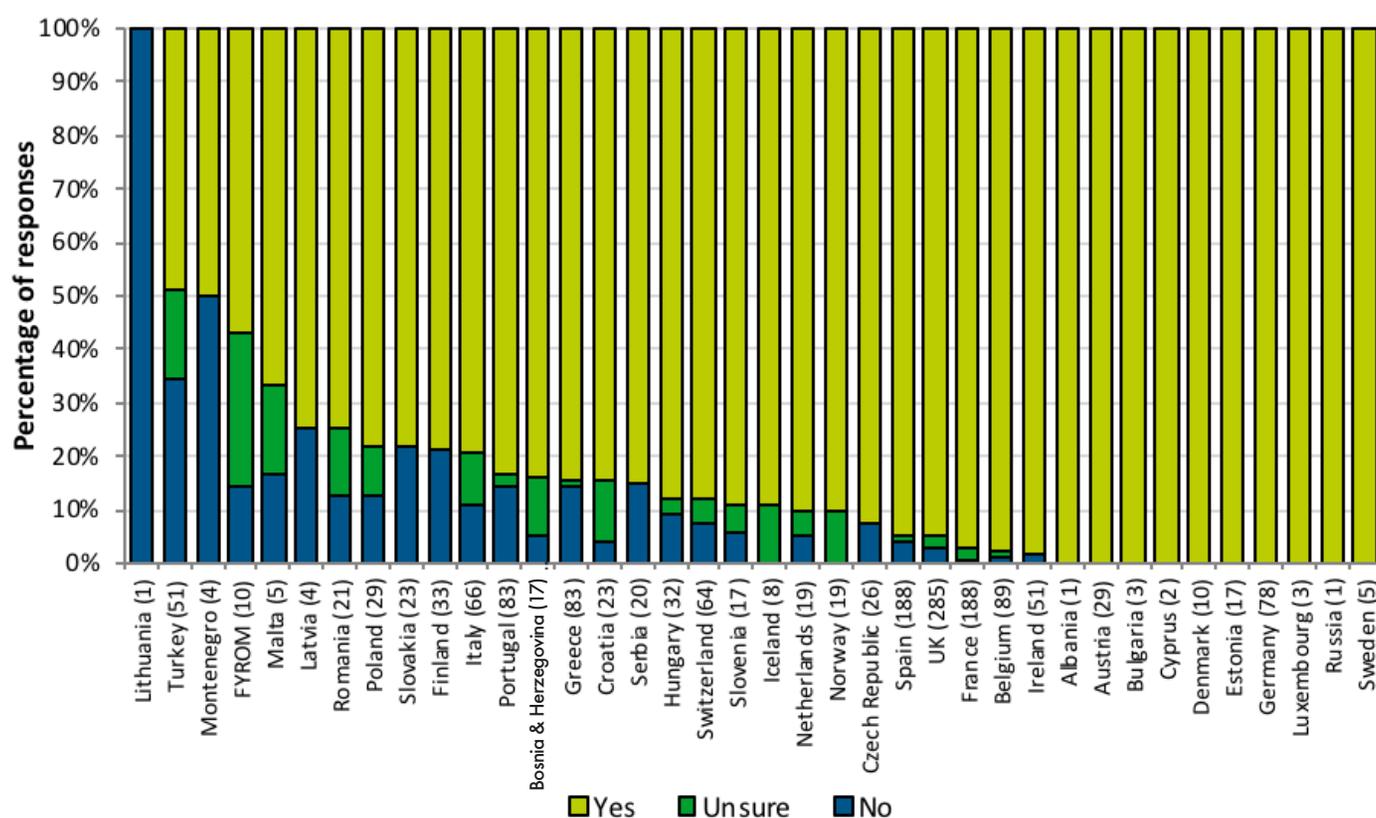


Figure 1 - Percentage of responses for question 2 'Are shortages of medicines a current problem in the hospital you work in, in terms of delivering the best care to patients and/or operating the hospital pharmacy?', grouped by country. Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 1**, where they are sorted by the proportion of respondents answering 'Yes'. In 10 countries, 100% of respondents answered 'Yes'. The only countries where more than 50% of respondents did not answer 'Yes' were Lithuania, Turkey and Montenegro.

The percentage of respondents in a country answering that medicines shortages are a problem in their hospital was compared to data from the 2014 survey where the same question was asked. A paired samples t-test showed a statistically significant increase in the mean percentage of 'Yes' responses for countries for the 2018 survey (M = 91.8%, SD = 9.5%) compared to the 2014 survey (M = 82.6%, SD = 17.6%), $t(27) = 2.721$, $p = 0.011$, $d = 0.514$. This indicates that more people consider this to be an issue today, in terms of delivering the best care to patients and operating the hospital pharmacy, than they did in 2014.

Q3. Approximately how often does your hospital pharmacy experience medicines shortages?

The most frequent response to this question, based on 1,666 responses, was 'weekly' with 39% of the responses, followed by 'daily' (36%), 'monthly' (16%) and 'occasionally' (11%), which shows most hospitals are experiencing shortages on a frequent basis.

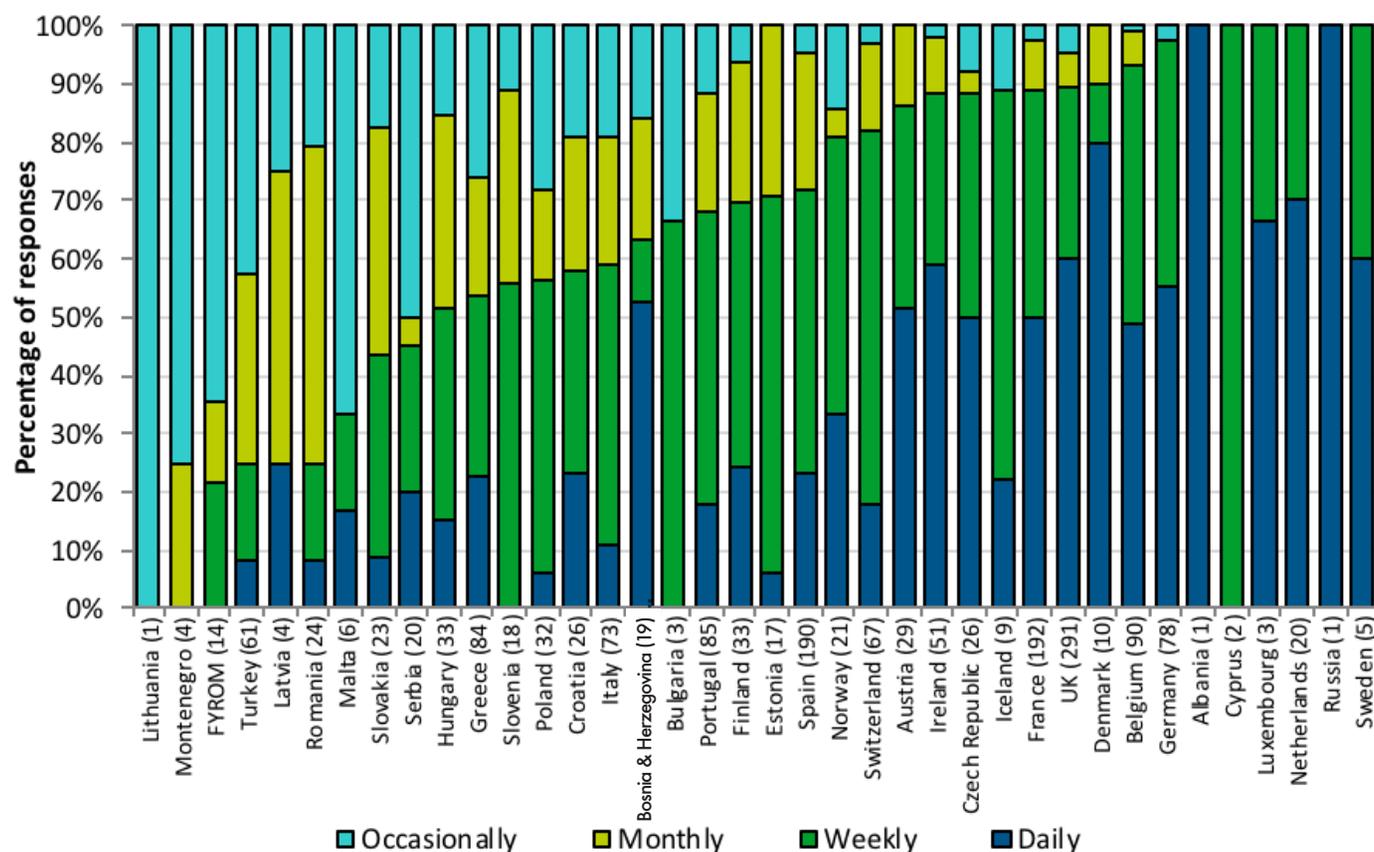


Figure 2 Percentage of responses for question 3 'Approximately how often does your hospital pharmacy experience medicines shortages?', grouped by country. Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 2**, where they are sorted by the percentage of respondents answering at least weekly (aka 'daily' responses + 'weekly' responses). Viewing the data this way helps to show that the frequency medicines shortages are experienced by hospitals varies greatly between countries.

A paired samples t-test indicated that the mean percentage of respondents in a country reporting that their hospital pharmacy experiences shortages at least weekly was not significantly different for the 2014 survey (M = 70.3%, SD = 21.0%) compared to the 2018 survey (M = 68.4%, SD = 22.2%), $t(27) = -0.414$, $p = 0.682$, $d = -0.0782$.

7. Nature of shortages (Q4-6)

Q4. Which type of medicine do you most commonly experience to be in short supply?

This question had 1347 people respond to it, with 77% of them reporting generic medicines to be the most common type in short supply, with originator medicines coming in second with 65% (although note that 46% of respondents selected both options to be most commonly in short supply.)

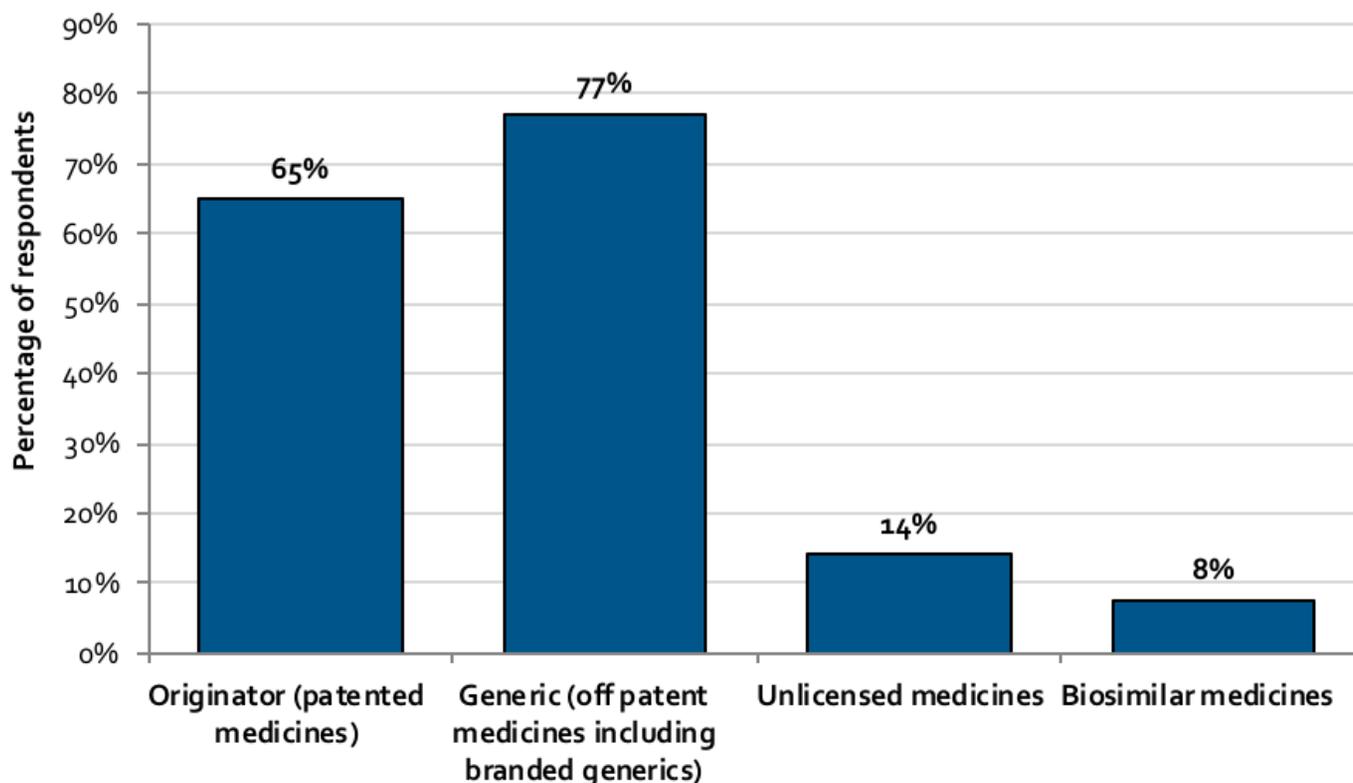


Figure 3 Percentage of participants in the survey who identified this type of medicine to be most commonly in short supply. (N=1,347) (Note that this was a tick all that apply question)

Only 14% of respondents experienced unlicensed medicines to be most commonly in short supply, followed by biosimilars with 8%, although these smaller numbers are likely since these medicines represent a smaller proportion of the total prescribing that occurs.

When this question was asked in the 2014 survey, originator medicines were the most commonly experienced type to be in short supply with 51% of the responses, compared to generic medicines which accounted for 37% of the responses. Note that when the question was asked in the 2014 survey, participants could only choose one of three options. In the 2018 survey the biosimilar medicines option was added, and also participants were able to select multiple options (tick all that apply), which needs to be taken into consideration when comparing the data.

Q5. In which area of medicine does your hospital experience shortage most commonly? Tick all that apply.

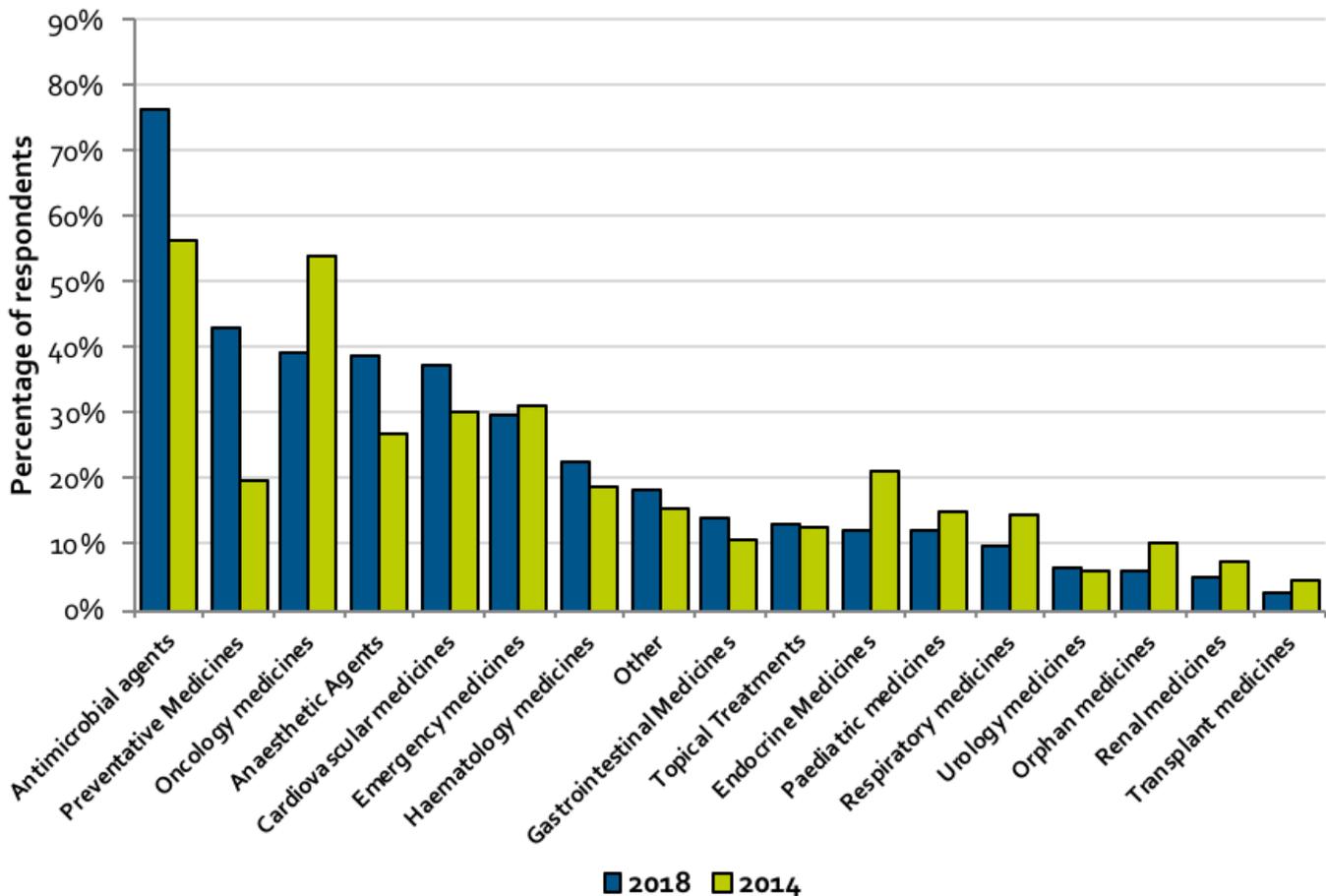


Figure 4 Percentage of participants in the survey who identified this area of medicine to be commonly in short supply. (N=1,348) (Note that this was a tick all that apply question)

Antimicrobial agents were reported to be commonly in short supply by 77% of the 1,348 respondents who answered this question in the 2018 survey.

In 27 countries antimicrobial agents were the area of medicine which received the most reports. However, there was some variation in the most commonly reported area of shortage across countries, with 6 countries (Albania, Estonia, Montenegro, Poland, Romania and Sweden) reporting anaesthetic agents as the most common area of shortage. Bosnia reported oncology medicines, Cyprus reported haematology medicines, FYROM reported emergency medicines, and Slovakia reported cardiovascular medicines as the most common area of shortage within their country. Although preventative Medicines (e.g. vaccines) were the second highest reported area of medicines shortages with 43% of participants reporting them to be an issue, it was not the area of medicine which received the most reports in any country.

The biggest theme of responses from the 'Other' category was drugs related to mental health or antipsychotics (87 responses), followed by contrast/x-ray medicines (25 responses), analgesics (24 responses) and immunoglobulins (24 responses).

Compared to the 2014 survey, the areas with the biggest increase in reports of common shortages are antimicrobial agents (77% of respondents reporting this as an issue in 2018 compared to 57% in 2014), preventative medicines (43% in 2018 compared to 20% in 2014) and anaesthetic medicines (39% in 2018 compared to 27% in 2014), suggesting shortages in these areas have become more frequent. The area with the

biggest decrease in reports of common shortages was oncology medicines (39% of respondents reporting this as an issue in 2018 compared to 54% in 2014).

Q6. Please tell us the medicines in which the experience of shortages was most frequent during the past year. If possible please include their brand name, INN (International non-proprietary name) and common indications as appropriate or available.

There were 948 responses to this freetext question. As the responses were freetext, responses vary from referring to specific medicines to groups or classes of medicines. Some refer to the chemical name, particular brands or abbreviated names. After analysing and aggregating these data, the top 10 most frequently referred to items were:

1. **Piperacillin/tazobactam** (272 responses across 18 countries) – This drug elicited a huge number of responses and constitutes a big part of the antimicrobial results seen in Q6.
2. **Vaccinations** (144 responses across 18 countries) – Although referring to an area of medicines, many respondents reported experiencing shortages in all vaccinations without being specific, so these data have been aggregated together. Some of the most frequently specified vaccinations were Hepatitis B (65 responses), Pneumococcal (27 responses), Tuberculosis (25 responses), Tetanus (17 responses) and Hepatitis A (17 responses).
3. **Immunoglobulins** – (99 responses across 13 countries) – The majority of the responses for immunoglobulins did not specify a brand, so they have counted as a group (Privigen was the most frequent with 28 responses).
4. **Cephalosporins** (86 responses across 20 countries) – Another group of drugs that were grouped together due to the responses received. The most frequently specified Cephalosporins were Ceftazidime (29), Cefepime (19), Cefuroxime (16), Cefotaxime (15), and Ceftriaxone (7).
5. **Gentamycin** (80 responses across 7 countries).
6. **Co-amoxiclav** (Amoxicillin/clavulanic acid) (67 responses across 10 countries).
7. **Human Albumin** (68 responses across 12 countries).
8. **Xylocaine/adrenaline** (68 responses across 9 countries).
9. **Remifentanyl** (64 responses across 13 countries).
10. **Enoxaparin** (58 responses across 7 countries).

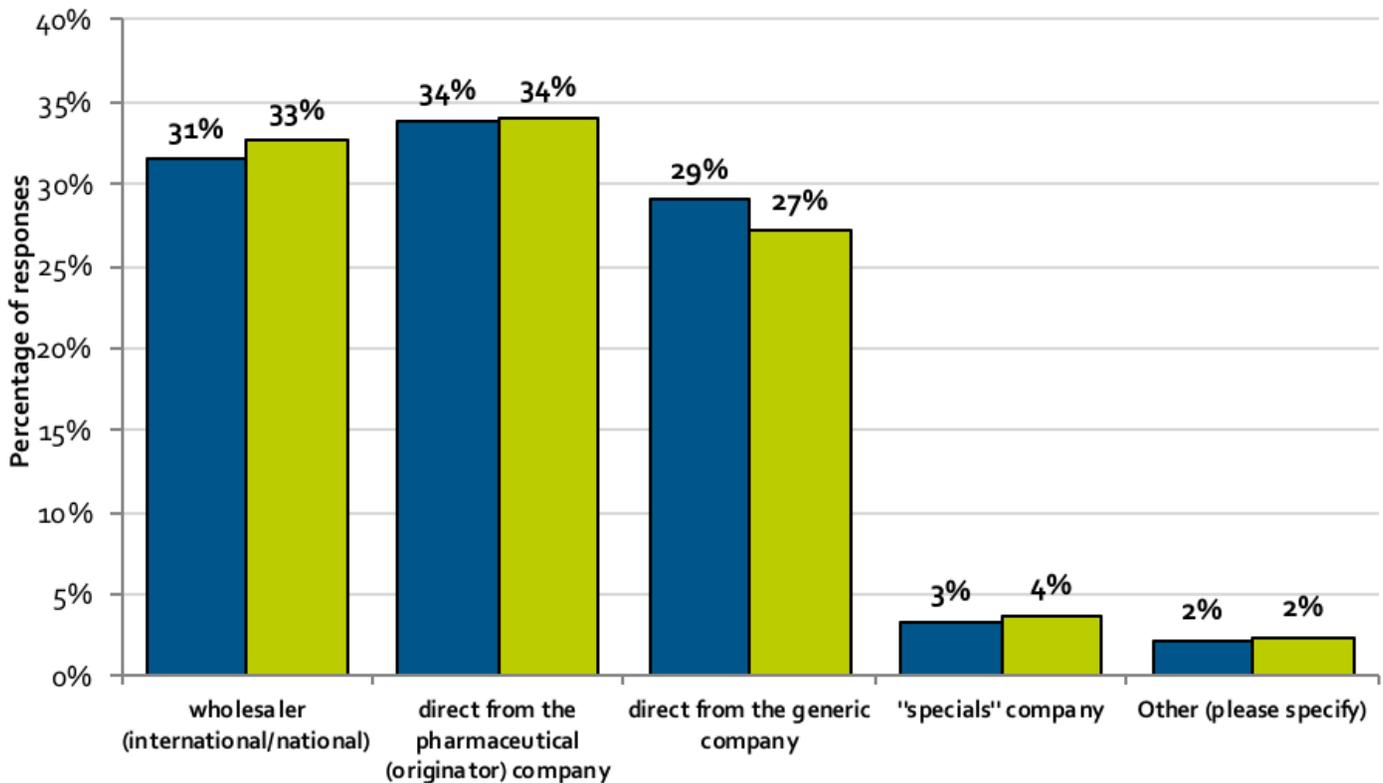
At the time of writing, there are seven medicines listed in the EMA Medicines Shortage Catalogue: Cerezyme (imiglucerase), DepoCyte (cytarabine), Maci (matrix applied characterised autologous cultured chondrocytes) implant, Nulojix (belatacept), Orgalutran (ganirelix), Trisenox (arsenic trioxide) and Tygacil (tigecycline). Only 3 of these appear in the responses, and only infrequently with 19 responses for DepoCyte (cytarabine), 5 for Trisenox (arsenic trioxide) and 1 for Nulojix (belatacept).

8. Sources of supply (Q7-8)

Q7. Which of the below categories best describes the main external source of supply of medicines to your hospital?

Q8. From which category of external supply does your hospital most frequently encounter problems with sourcing specific required medicines?

Data for questions 7 and 8 are shown together in **Figure 5**. From here it can be seen that the results of the two questions are extremely similar. In addition, after investigating the record level survey data it was observed that 63% of the 1,252 participants who answered both questions gave identical responses. This result implies that participants are saying that medication shortages are encountered among the various sources of supply to a similar degree.



■ 7. Which of the below categories best describes the main external source of supply of medicines to your hospital?

■ 8. From which category of external supply does your hospital most frequently encounter problems with sourcing specific required medicines?

Figure 5 Percentage of responses where this source of supply is identified in questions 7 and 8 of the survey. (Note that this was a tick all that apply question)

Comparing the sources of supply to the data from the 2014 survey is more difficult, as the 2014 survey only allowed participants to choose one option, whereas they could pick multiple options in 2018. For example, in 2014 only 12% of responses were for 'direct from the generic company', compared to 27% in 2018. We are unable to conclude that the source of supply from generic companies has greatly increased since 2014, since the more likely explanation is that respondents are choosing multiple options, and hence increasing the proportion of second/third line sources of supply compared to the 2014 data (53% of the 1,253 participants who answered this question in 2018 chose multiple options).

9. Duration of shortages (Q9-12)

Q9. In your experience, how long would you estimate the average or typical medicines shortage normally lasts for.

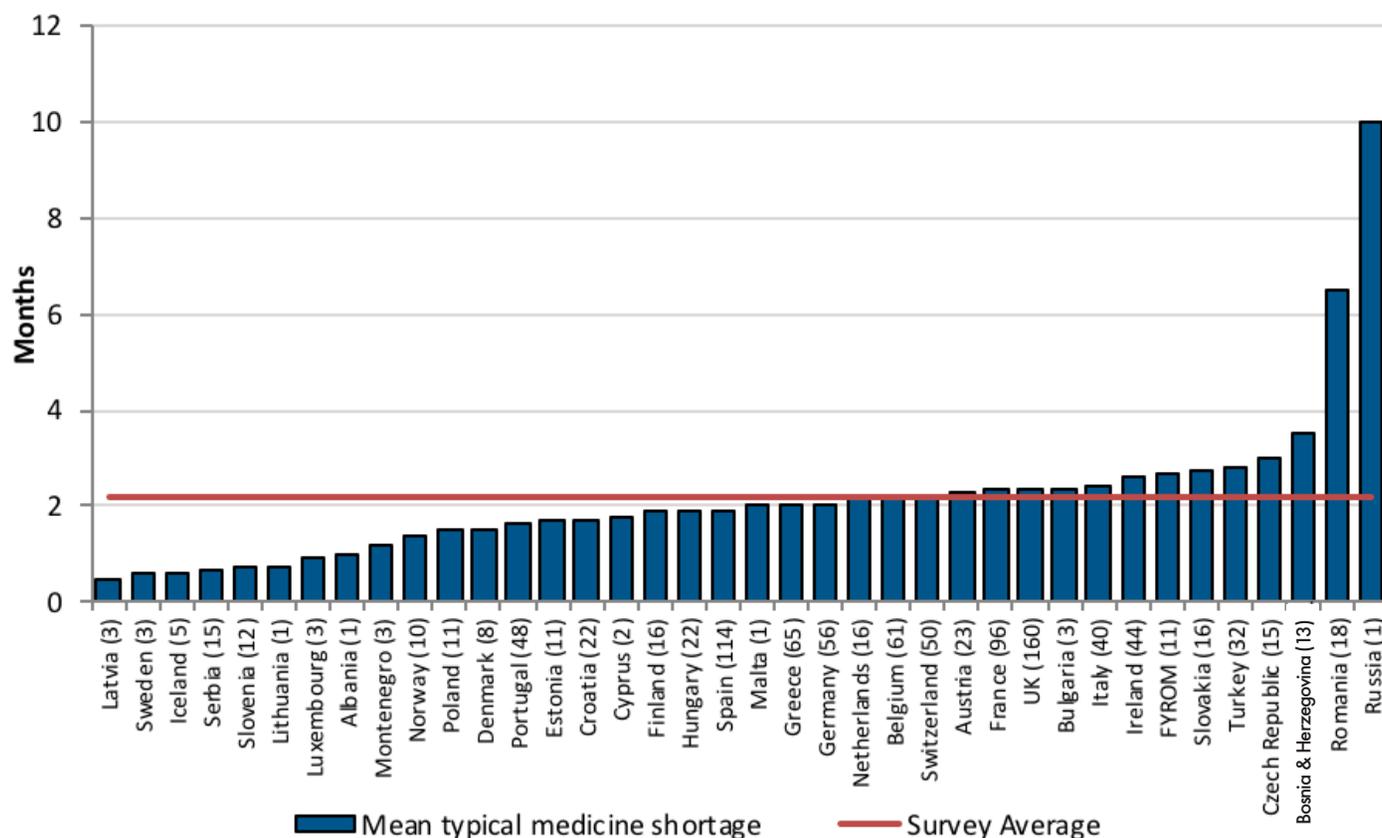


Figure 6 Mean duration (in months) of typical medicines shortage, grouped by country. Numbers in brackets represent number of responses from that country.

For this question, respondents gave a numeric value for the number of days/weeks/months that a typical shortage last for. Clearly erroneous data was removed, resulting in 1,031 useable responses which were all converted into number of months. The average duration of a typical medication shortage for the 2018 survey was 2.2 months, signifying the extent of the medication issue.

Figure 6 shows the data grouped by country, where it is observed that only 7 countries have an average typical shortage less than one month. Russia and Romania appear to be outliers with a mean shortage of 10 months and 6.5 months respectively but note that Romania's value is based on 18 responses which provides assurance that the result is valid.

Comparing data to the 2014 survey is difficult because the question was structured differently. Instead of requiring a numerical value for the number of days/weeks/months of a shortage duration the question was categorical with the choices for either a number of days/weeks/months. Of the 387 answering the question the most frequent response was a number of weeks (63%), followed by a number of months (30%) and a number of days (7%). Looking at **Figure 6**, most countries are measuring shortages in months rather than weeks, with over half of the countries (20 out of 38) displaying a mean shortage duration of over 2 months.

Q10. Please provide details about your personal experiences with typical shortage situations.

Response to this freetext question was quite varied, with some respondents focusing on the duration of typical shortages and others describing issues arising from shortages and the processes in handling them. One theme that emerged in the responses was the lack of reliable or timely information from manufacturers

and suppliers on the commencement or duration of shortages.

- *“Mostly there is no Information provided from the manufacturer. It should be as soon as possible, in detail and continuously.” – Austria*
- *“The worst is, that pharmaceutical companies do not communicate; the orders are not delivered and the information mostly is only achieved by asking the supplier.” – Germany*
- *“We are not informed about shortage, information from manufacturers is missing.” – Czech Republic*

There are some comments which suggest that the more advanced notice the hospital has on a shortage, they are able to manage the situation better, but sometimes notice of a shortage is not given and only found out about when products are not delivered.

- *“When there is sufficient or any notice they are easier to manage. Dealing with shortages when we get notice that the product is out of stock is much more challenging and reactive.” – Ireland*
- *“Not good. I found about shortage when wholesaler cannot deliver drugs when I order them.” – Croatia*
- *“Lack of information on availability from manufacturer and their wholesalers, lack of pre-warning of shortage resulting in panic buying, excess stock holding by some trusts. lots of time spent chasing orders, getting conflicting information, lots of time wasting trying to sort out what can be used as a replacement.” – UK*

Many respondents commented that information from companies about when stock will be back is very unreliable, and it has become normal to assume this date will be pushed back several times.

- *“Very often the companies announce a duration of the shortage which isn’t correct, so it goes longer and longer all the time. It would be better in this case to describe the duration as unknown.” – Switzerland*
- *“In most cases there is no data when the product will be delivered again (end of shortage). When a firm does have a delivery-date, you cannot always depend on it!” – Belgium*
- *“... Then there will be information on when the drug is expected to be delivered again - but this information is never to be trusted. That is in my opinion the biggest problem - because we never know how to advice the hospital.” – Norway*

Some responses highlighted the effect the shortages have. This can include possible shortages of alternative medicines, time spent dealing with shortages, additional expense or the effect on patients.

- *“Usually the shortages occur to classic medicines of first line treatments that are cheap and irreplaceable. Therefore we have to use second line treatments and the additional unexpected increase in the consumption of newer agents causes the domino effect of their shortage as well”. – Greece*
- *“A pharmacist of the team spend about 8 hours per week to solve the problems of drug shortage.” – France*
- *“The shortage of medicines in our hospital carries the following consequences: - an increase in extra work both at the care and administrative level - discomfort and nervousness on the part of all personnel, both health and non-health - Distrust towards the supplier laboratory - Increase in additional costs (loans between hospitals, importation of medicines) - Increase the chances of error in the dispensing of the substituted medication - Discontinuity in the treatment of the patient, so that the quality of care decreases.” – Spain*

Some hospitals have taken measures to deal with shortages, hiring staff dedicated to the issue or determining shortage durations based on previous data.

- *“We document every delivery shortage and can therefore determine the typical duration.” – Germany*

- *“... I have to create a ‘shortage memo’ for all relevant medical, nursing & pharmacy staff to inform them of the latest shortage (every time), proposed alternative, expected timeframe for shortage & any other important information (if alternative product is majorly different to original/needs manipulation etc).” – Ireland*
- *“For many issues we have sufficient stock to see us through to the end of the problem and we have to keep higher than desirable stock levels to mitigate against supply issues. Main problems are caused by single supplier products where there is no alternative often on critical lines. We have a full time post who spends all her time managing supply shortages and we are looking at needing to add addition resource to support this due to the growing issues.” – UK*

Q11. What is the longest duration that you can recall a medicine being in shortage for in the last 4 years?

This question was structured similarly to question 9, as respondents gave a numeric value for the number of days/months/years for the longest duration a medication has been in shortage. Again, clearly erroneous data was removed, resulting in 1031 useable responses which were then all converted into number of months.

Some of the answers raise the question of at what point should a product stop being considered in shortage and instead be considered to be discontinued. The average maximum medication shortage reported in the 2018 survey was 13.2 months.

When this question was asked in the 2014 survey, the response was entirely freetext. The data was investigated, and responses containing a specific duration were used to calculate an average maximum duration from the 2014 survey.

For example, a response specifying 3 months was used, but a response stating a few months was not. Based on the 250 responses which contained suitable data, the average maximum medication shortage duration reported in the 2014 survey was 9.3 months, providing more evidence that the magnitude of the medication shortages problem is increasing.

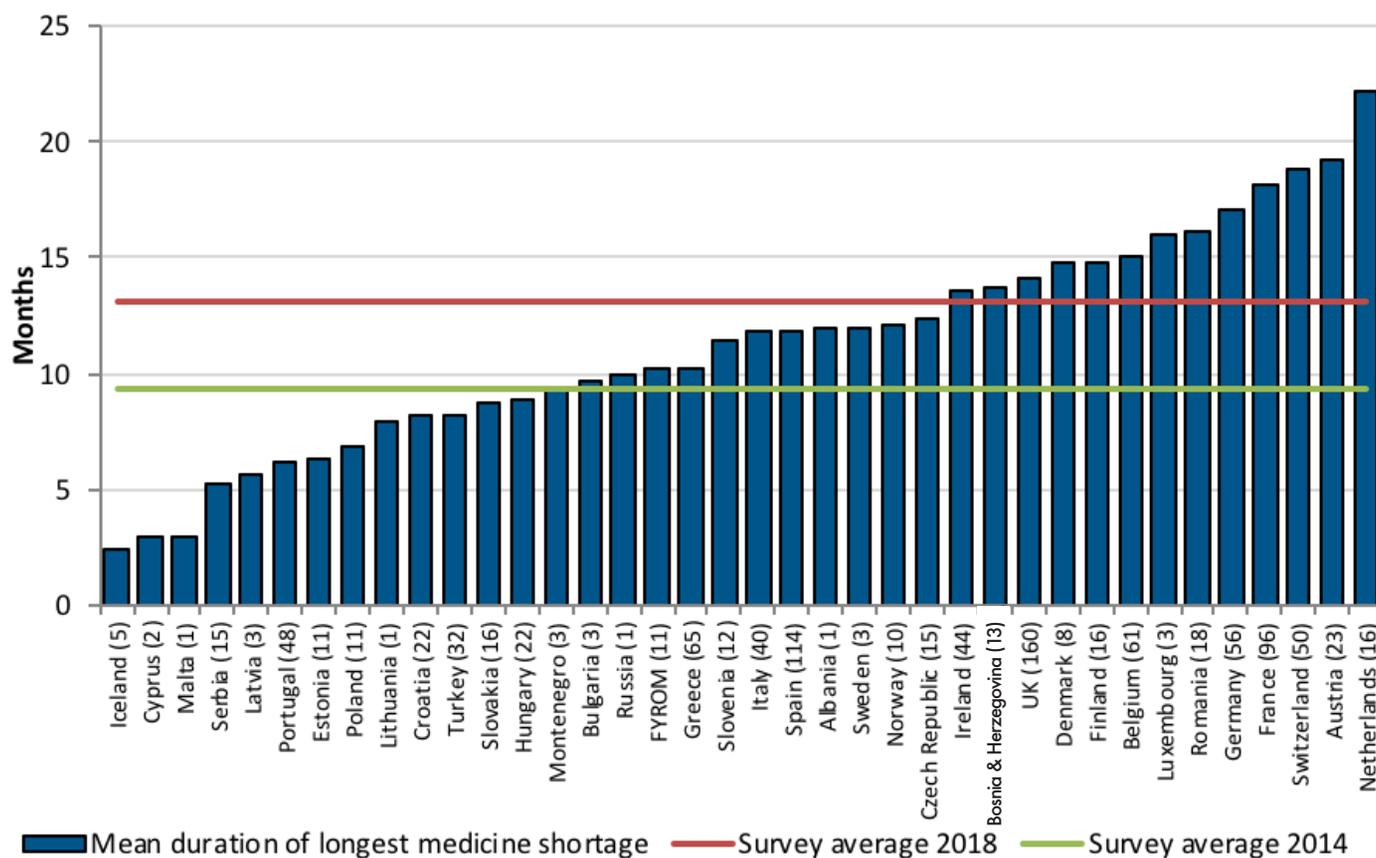


Figure 7 Mean duration (in months) of longest medicines shortage, grouped by country. Numbers in brackets represent number of responses from that country.

The 2018 survey data grouped by country is shown in **Figure 7**, alongside the average maximum medication shortage duration reported in both the 2014 and 2018 surveys for comparison.

Q12. Please provide details about the longest shortage you have personally experienced.

There were 503 freetext responses to this question. Freetext responses where both the product and shortage duration were specified were analysed and a list of examples was produced where the duration has been specified to be at least a year (duplicate mentions of a medicine were removed).

Approximately one year

- “Almost for one year we had a shortage of Lasix amp. which is unacceptable, since we are Institute for cardiovascular diseases and Lasix is one of our most used drugs. The shortage was in the whole country, and ministry of health did nothing to help.” – Serbia
- “That’s rather approximately 1 year. Piperacillin/Tazobactam - explosion in a factory.” – Norway
- “clonazepam (rivotril) injection - went short for approx one year. Consultant used midazolam instead during this period.” – Ireland

Up to two years

- “relistor (1,5 years and still on shortage)” – Austria
- “Guanethidin, novaban is still not available. Maniprex will not be available in the next 2 years.” – Belgium
- “alosplastine, colpotrophine (2 years shortage and then stop). The most difficult situation were shortage of enoxaparine.” – France

- “2 years waiting for Ativan” – Ireland
- “Deanxit shortage lasted for 2 years approx.” – Spain
- “The longest shortage was with Temesta (lorazepam im/iv) and it lasted approximately 2 years.” – Slovenia
- “Depocyte>1 year” – Ireland
- “Bleomycin has not been available on the market in Romania for almost 2 years now.” – Romania
- “For MAGNEZII SULFAS 207,4 mg/ml, vials, the longest shortage I experienced was approx. 2 years.” – Romania
- “There are no melfalan inj Product in Norway With a marketing authorisation and we depend on the “spotmarket” in Europe. For almost 2 years we had to ration the use of melfalan inj and there was a national consensus for which patients should receive treatment.” – Norway
- “Ultiva got delivered only occasionally for about 2 years” – Germany
- “Phenindione - over a year.” – United Kingdom
- “Fortum injection 500mg, 1g and 2g due to be out until January 2019 already short for over a year.” – Ireland
- “Tobramycin inj. (Brulamycin) shortage lasted a year there was another brand that was imported and cost almost twice as more.” – Hungary
- “Aztreonam has been on restricted supply for around 2 years now.” – United Kingdom
- “Heparin-Natrium (Liquemin 5000 E/0.5 ml) is out of stock for 2 years now.” – Switzerland
- “Tri-anal suppo’s : 2 years, Augmentin : 6 months cefotaxim sandoz: 7 months.” – Belgium
- “Gentamicin LEK inj sol 10x2ml/80mg - 8 months; eye drops Ophthlmo-septonex gtt oph - drops with antiseptic combination of drugs - 18 months.” – Czech Republic

Up to three years

- “cefamandol = 3 years, still not available amox/acide clav = several months, still in continency ropivacaine = several months, still in continency.” – France
- “Hyaluronidase (Hylase Riemsler), for our cytotoxic agents paravasation set and operating theatre of our clinic for ophthalmology, not available for over two years because of production problems.” – Germany
- “The shortage of IMMUCYST BCG INMUNOTERAP 27MG 3 INJECTABLES INTRAVESICAL 1ML even meant the impossibility of treating new patients with bladder cancer and the substitution by other alternative drugs, other presentations and even other doses. The supply was not restored until two or three years later.” – Spain
- “Co’trimoxazole IV has been in shortage for a few months at a time for last 3 years.” – United Kingdom
- “Penadur, out of stock since 2015.” – Belgium

More than three years

- “4 year (Antepsin - sucralfat oral) since 2014” – Finland
- “Shortage claventin (ticarcilline/ac clav) since 3-4 years” – France
- “more than 3 years (4-DMAP)” – Germany
- “Pentagastrin (used for the so called Pentagastrin test) has been out of stock since more than 5 years if I’m not mistaken.” – Germany
- “gentamicin, longest shortage in Switzerland since Minimum 5 years” – Switzerland

- *“Both UK Sucralfate (Antepsin) tablets and suspension have been unavailable for four years.”* – United Kingdom

Unspecified number of years

- *“Worldwide shortage of Adrenaline Minijets for emergency trolley for a number of years.”* – Ireland
- *“maxipime - cefepime. Was several years not available before was communicated, that it would not come again. Later it was brought by generic companies.”* – Switzerland
- *“Adrenaline 1:10,000 10ml Prefilled syringes. Critical resuscitation medicine. Intermittent supply problems for years but previously there was NO alternative on the market. Luckily now new supplier.”* – United Kingdom

10. Early reporting (Q13-15)

Q13. Does your country have a reporting system for shortages in place?

When asked if their country had a reporting system in place, 67% of respondents answered 'Yes' (N=1,029). However, when looking at the results broken down by country the response is much more varied, as seen in [Figure 8](#), where the results are ordered by the percentage of respondents in the country answering 'Yes'.

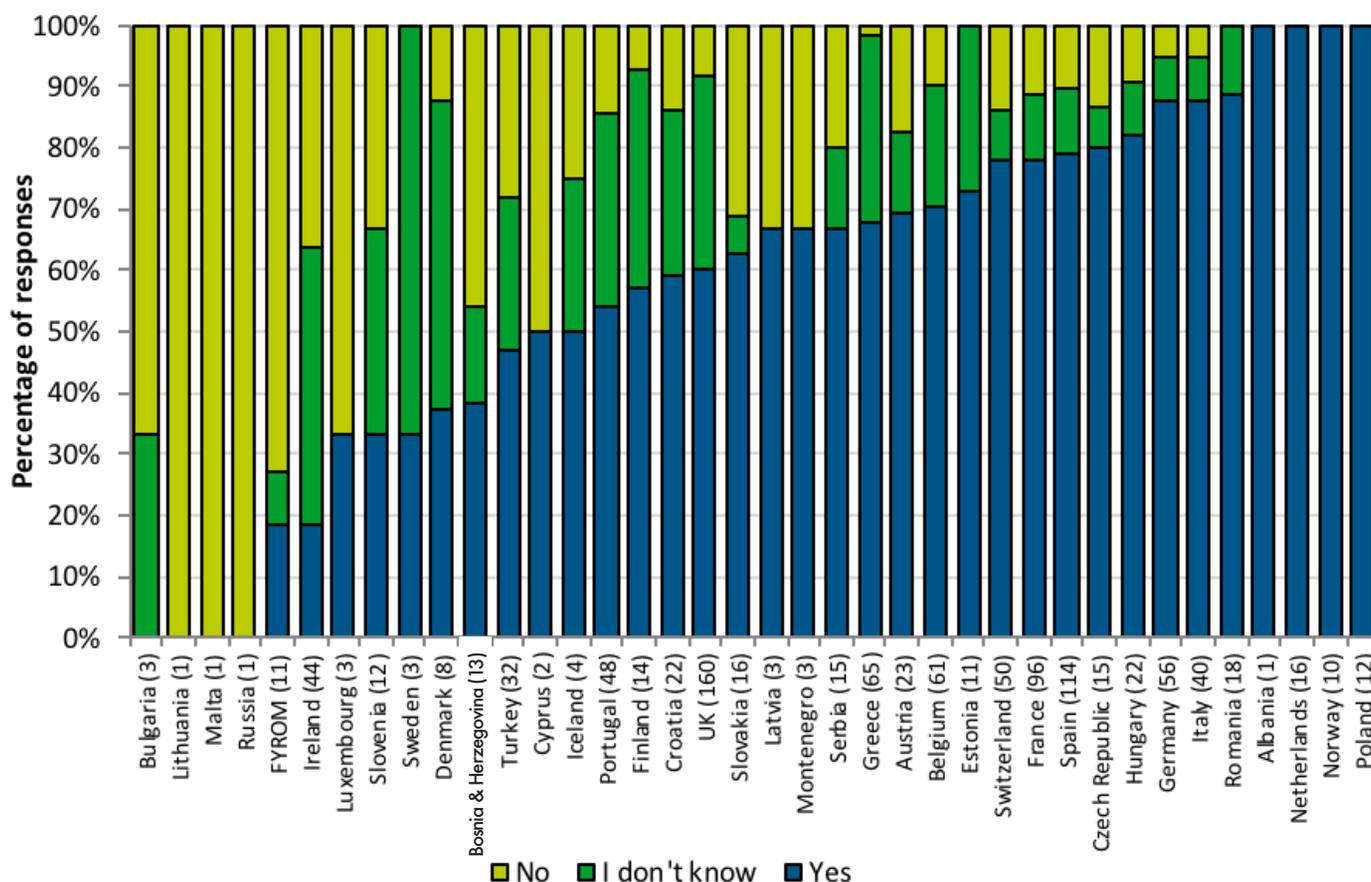


Figure 8 Percentage of responses for question 13 'Does your country have a reporting system for shortages in place?', grouped by country. (N=1,029). Numbers in brackets represent number of responses from that country.

Since this question is asking about a country level reporting system, it is surprising to see such a mixed response in individual countries. An explanation for this could be some of the respondents answering 'No' are not aware of the reporting system in place in their country, meaning work needs to be done in increasing awareness of such systems and the process in that country for reporting medicines shortages.

Q14. Please briefly explain how it works and include website if available.

In most countries the reporting system is part of a website, with data typically provided either by industry or hospitals. The completeness of the list of shortages and quality of other information provided varies by country. A list of website links and additional information based on the responses are provided in full in Appendix A. Some of the freetext responses have also been incorporated into the analysis of question 15.

Q15. Do you judge it as effective/working/functional?

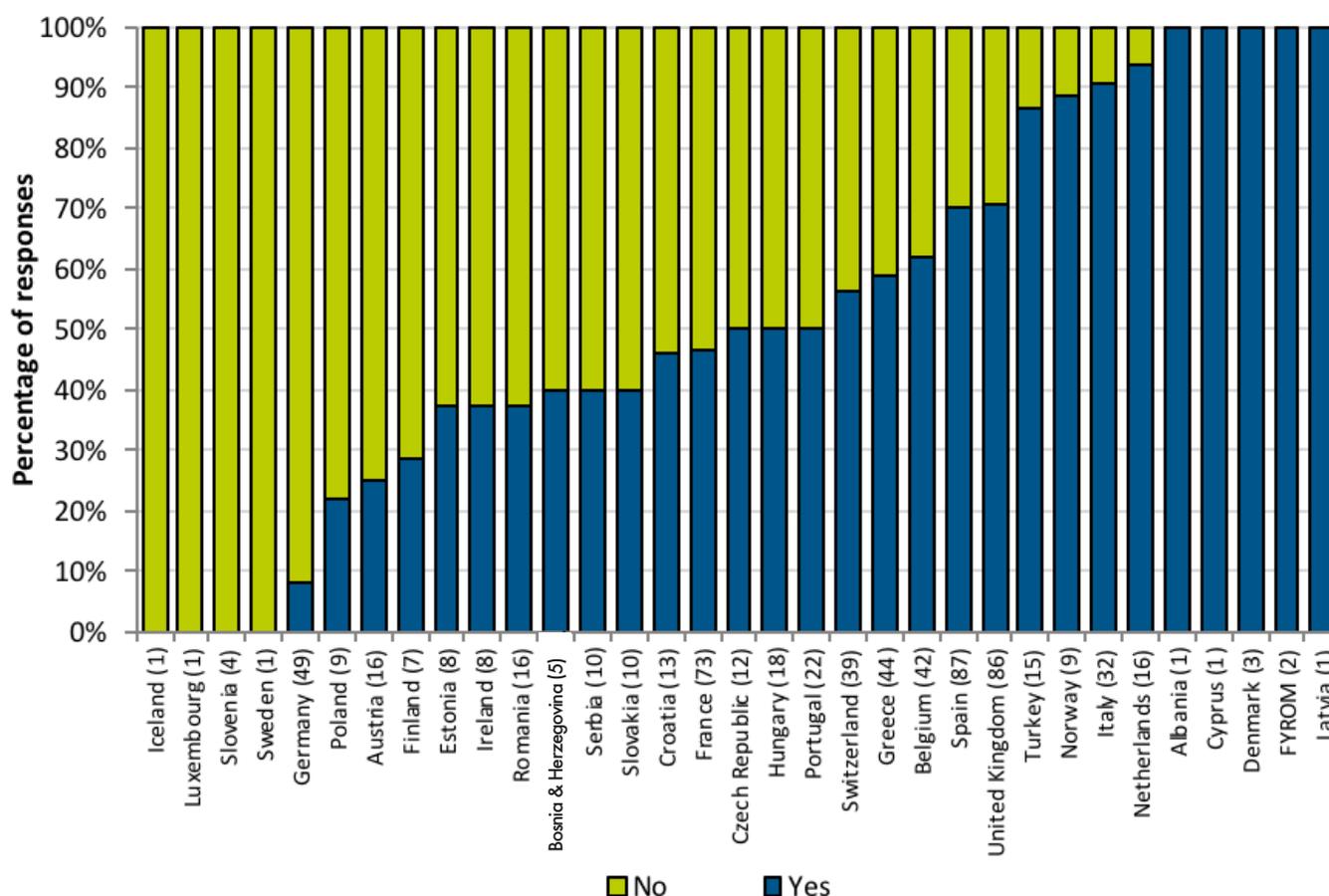


Figure 9 Percentage of responses for question 15 ‘Do you judge it as effective/working/functional?’, grouped by country. (N=663). Numbers in brackets represent number of responses from that country.

Only 56% of the 663 participants who answered this question judged their countries reporting system for shortages to be effective/working/functional. When grouping the results by country, there is a large range of responses, as seen in **Figure 9**. Participants were also asked to explain how their country’s reporting system works, which was used to further investigate the response from countries who gave very positive or negative opinions of their reporting systems.

In Poland, 22% of respondents (N=9) judged their system to be effective. A freetext response from Q14 provides some insight into this, as the self-reporting of shortages from pharmacies may be underreported, and the system is not user-friendly: “Chief Pharmaceutical Inspectorate collects data reported by pharmacies regarding drug shortages and produces a list of medicines at risk of being illegally exported. Pharmacists are obliged to report shortages online giving details of nature of shortage. Shortages are underreported due to pharmacy staff and time shortages. The reporting system is web based but considered by many not user friendly which may hinder the reporting system.” – Poland.

In Slovenia (0% positive, N=4) the main reported issue was that the output to pharmacists from the reporting system was not useful: “The main problem, as we see it is, that JAZMP (reporting system) does not inform pharmacies about received notifications, so we are usually notified about a drug shortage from a wholesaler when we’d like to purchase a drug and can’t get it. The information they put on their website is in form of a pdf file with over 600 pages and is certainly not user-friendly because it is hard to search for information.” – Slovenia.

From Germany (8% positive, N=49) there were several responses reporting that the main problem was that their system relies on companies to report shortages, but they are under no obligation to do so: *“The companies report shortages to different institutions which list them in the internet. The list is often not up to date, and not all shortages are listed here because it is not mandatory and there are different limitations (just shortages > 2 weeks etc.)”* – Germany.

In Cyprus 100% of respondents reported the system to be effective (N=1). The freetext response details a forum used by hospitals to share information on shortages which seems to be an effective and low cost solution, although it relies on people both knowing about it and utilising it: *“We have just created a forum in the common hospital purchasing database (SAP) where every hospital facing a drug shortage can notify other hospitals and seek for help.”* – Cyprus.

In Latvia (100% positive, N=1) a website is used where shortages can be reported by anyone, increasing the likelihood of a shortage being reported, addressing an issue observed in other systems. *“Anyone (hospital, pharmacy, patient) could use this website to make our medicines agency know about shortage.”* – Latvia.

In the Netherlands (94% positive, N=16) the shortage information is frequently updated, which based on some of the feedback seen in Q10, is important for helping pharmacists to manage shortages. *“The national society of pharmacist publicise the known shortages and alternatives on their website. It is updated on a daily basis.”* – Netherlands.

11. Impact of shortages (Q16-22)

Q16. Are causes for medicines shortages reported by suppliers/producers to health authorities/hospitals in your country?

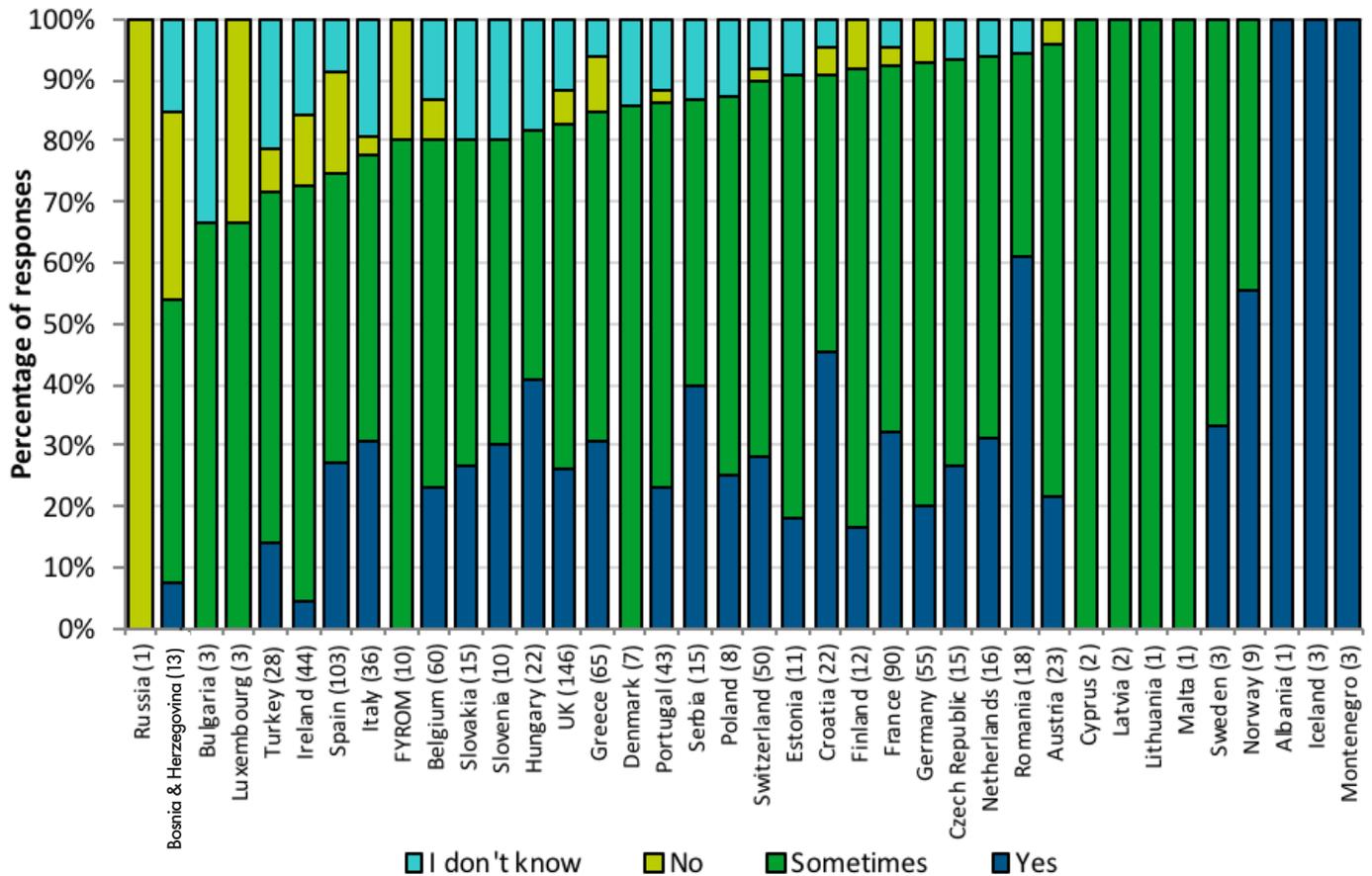


Figure 10 Percentage of responses for question 16 'Are causes for medicines shortages reported by suppliers/producers to health authorities/hospitals in your country?', grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

Of the 969 respondents who answered this question, the most common was 'Sometimes' with 57% of the responses, followed by 'Yes' with 27% of the responses. Responses for 'No' and 'I don't know' were much lower, at 7% and 9% respectively. The results broken down by country can be seen in **Figure 10** where it can be observed that in most countries the causes for medicines shortages are reported by suppliers/producers at least sometimes.

An intuitive assumption may be that countries where causes for shortages are frequently reported by suppliers may correlate with countries whose reporting system for shortages is deemed effective, as they may have up to date information from suppliers to share. However, several countries stand counter to that theory, for example, Iceland, Romania, Croatia, Sweden and Germany all have a comparatively high proportion of 'Yes' responses to causes for shortages being reported by suppliers, but all have less than 50% of respondents reporting the system to be effective.

Q17. In the case of a medicine in short supply, how often do you estimate your hospital is able to provide treatment to a patient by providing a therapeutic equivalent or near equivalent medicine, without major disruption to their treatment?

This question received 969 responses, with the most common response being 'most of the time' (69% of responses). 19% responded 'sometimes', and 9% responded 'all of the time'. There were few responses for 'rarely' and 'never', which received 2% and 0.3% of responses respectively.

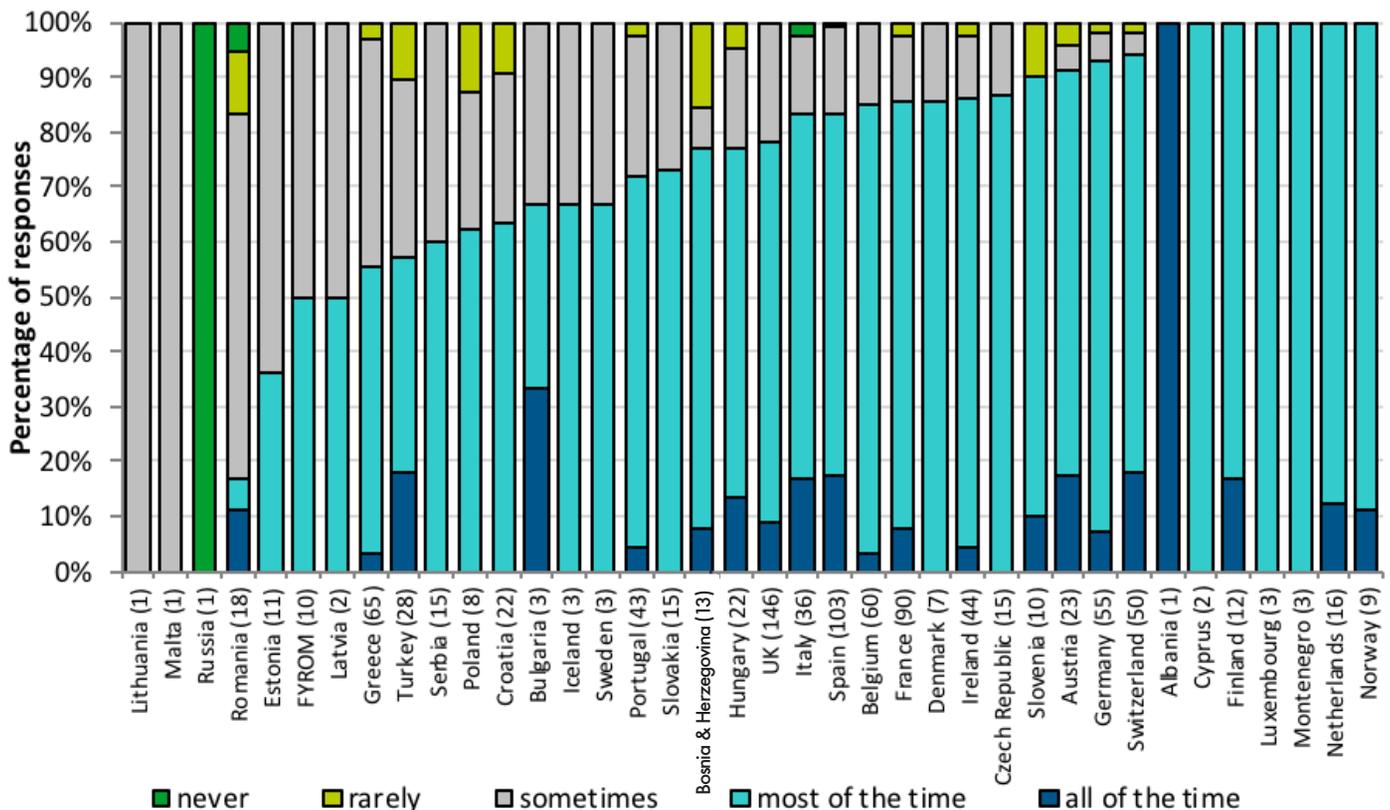


Figure 11 Percentage of responses for question 17 'In the case of a medicine in short supply, how often do you estimate your hospital is able to provide treatment to a patient by providing a therapeutic equivalent or near equivalent medicine, without major disruption to their treatment?', grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 11**, where they are sorted by the percentage of respondents reporting their hospital is able to treat a patient by providing alternative medication without major disruption at least most of the time (aka 'most of the time' responses + 'all of the time' responses). There are only 5 countries where less than half of respondents report not being able to provide alternate medication without disruption at least most of the time (Lithuania, Malta, Russia, Romania and Estonia).

These data were compared to results from the 2014 survey. The median percentage of respondents in a country reporting their hospital is able to provide treatment to a patient by providing alternative medication without major disruption at least most of the time decreased, from 80% in the 2014 survey to 78% in 2018 survey, although a sign test determined this decrease was not statistically significant ($Z = -1.540$, $p = 0.124$, $r = -0.296$).

Q18. In an average week in your hospital, how much time (staff working time) do you estimate is diverted because of medicines shortage problems?

The most frequently given responses to this question was 'up to five hours', with 46% of 969 respondents

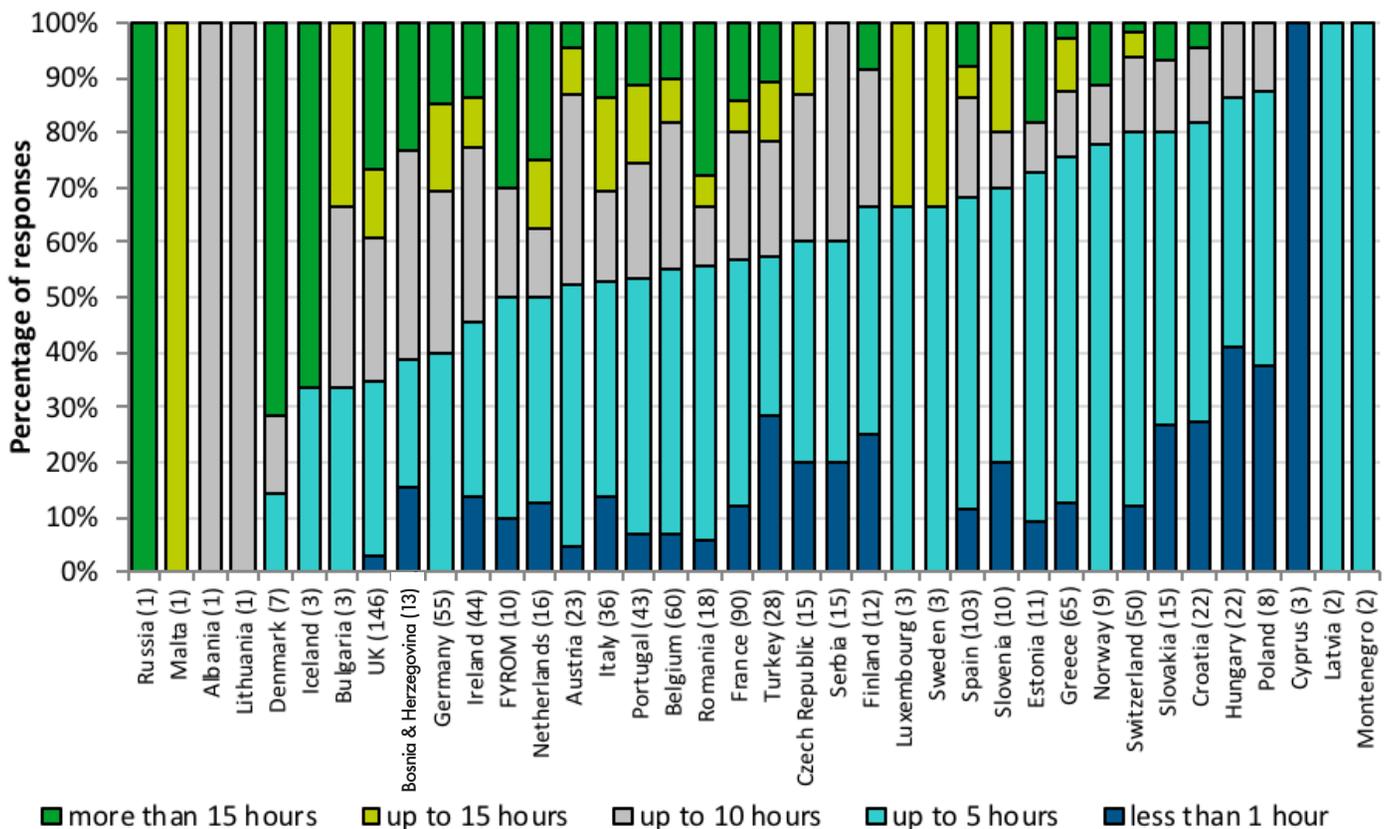


Figure 12 Percentage of responses for question 18 'In an average week in your hospital, how much time (staff working time) do you estimate is diverted because of medicines shortage problems?', grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

Figure 12 shows the responses grouped by country and sorted by percentage of respondents in a country reporting that more than 5 hours per week are spent dealing with medicines shortages (aka responses for 'up to 10 hours', 'up to 15 hours' and 'more than 15 hours'). Cyprus is the only country where the most frequent response was 'less than 1 hour', and Denmark, Iceland and Russia are the 3 countries where the most frequent response was 'more than 15 hours'.

This question was also asked in the 2014 survey, and the results were compared to see if the amount of time spent dealing with medicines shortages had changed. A paired samples t-test showed a statistically significant increase in the mean percentage of respondents in a country reporting that more than 5 hours per week are spent dealing with medicines shortages for the 2018 survey (M = 42.0%, SD = 18.7%) compared to the 2014 survey (M = 33.1%, SD = 25.9%), $t(26) = 2.275$, $p = 0.031$, $d = 0.438$.

Q19. Do you agree with the following statement? "Medicines shortages in my hospital are having a negative impact on patient care."

Of the 969 respondents who answered this question, there were very few who disagreed or strongly disagreed with the statement (8% of responses and 1% of responses respectively). The majority of respondents agreed or strongly agreed that medicines shortages in their hospital are having a negative impact on patient care (47% and 31% respectively), and 13% of respondents were unsure.

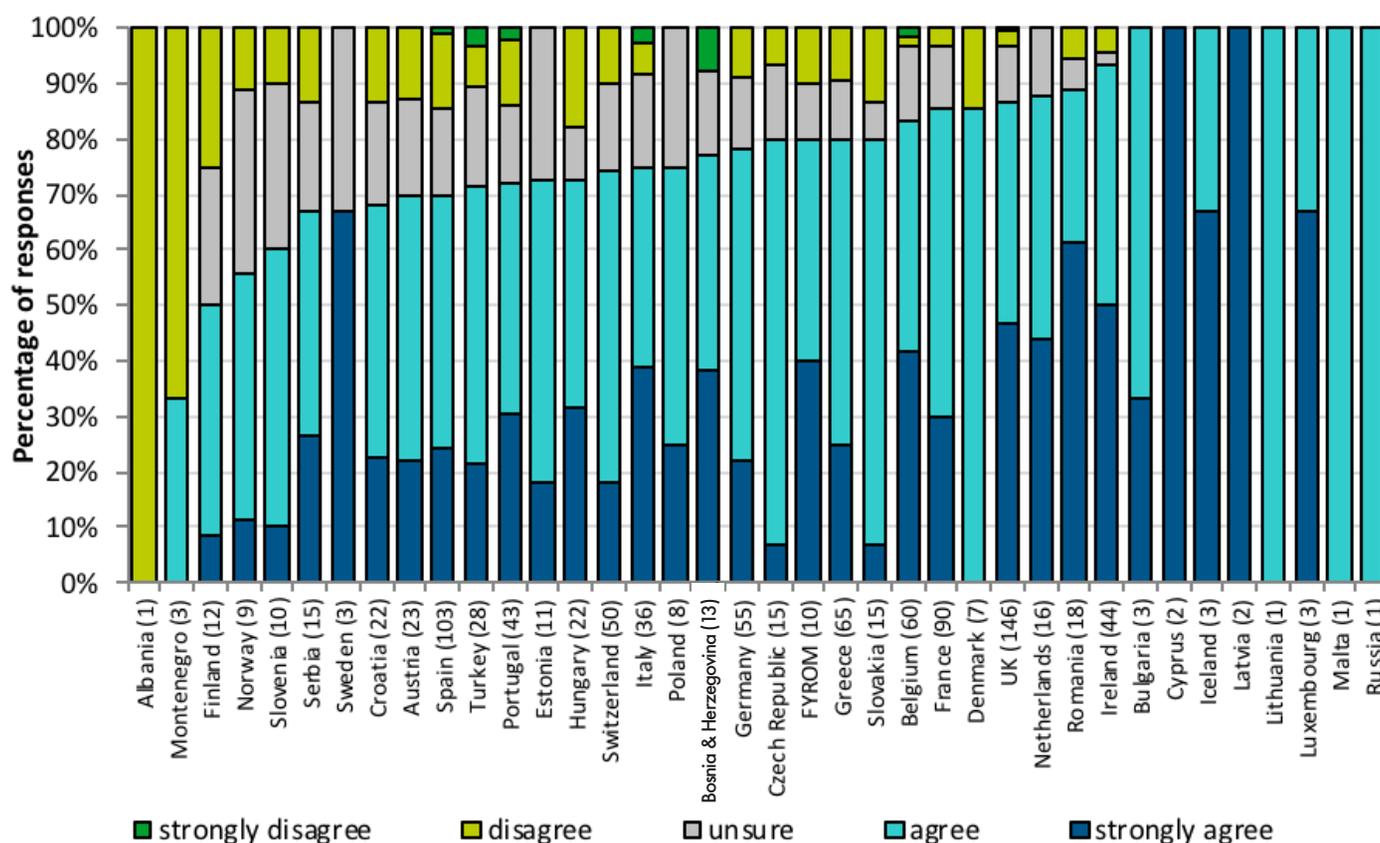


Figure 13 Percentage of responses for question 19 ‘Do you agree with the following statement? “Medicines shortages in my hospital are having a negative impact on patient care.”’, grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 13**, where they are sorted by the percentage of respondents who at least agree that medicines shortages are having a negative impact on patient care (aka ‘agree’ responses + ‘strongly agree’ responses).

Results from the 2018 survey were compared to results from the 2014 survey. The median percentage of respondents in a country reporting they agree or strongly agree that medicines shortages are having a negative impact on patient care decreased, from 79% in the 2014 survey to 77% in 2018 survey, although a Wilcoxon signed-rank test determined this decrease was not statistically significant ($Z = -.175$, $p = 0.861$, $r = -0.033$).

Q20. Do you agree with the following statement? “Medicines shortages in my hospital are having a negative impact on my overall budget.”

Budgetary issues caused by medication shortages can be due to having to pay more to procure a drug from another supplier or paying more for an alternative drug (see Q21), having to devote more staff time to the issue (see Q10) or due to the impact on patients (such as potentially increased length of hospital stay, see Q22).

There were 969 responses to this question, with most choosing either ‘agree’ (43% of responses) or ‘strongly agree’ (38% of responses). The remaining choices were ‘unsure’ (13%), ‘disagree’ (5%) and ‘strongly disagree’ (1%).

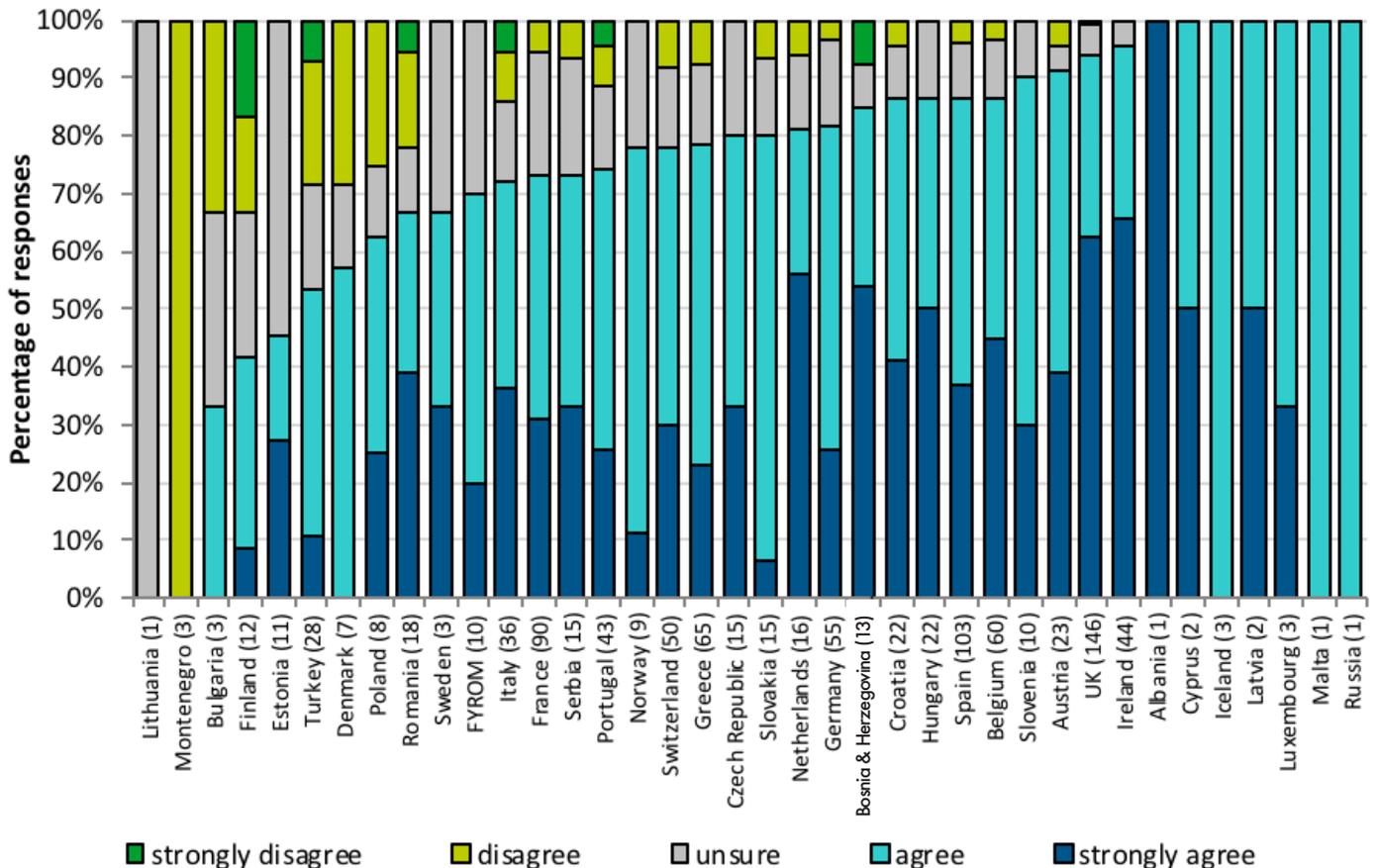


Figure 14 Percentage of responses for question 20 ‘Do you agree with the following statement?’ Medicines shortages in my hospital are having a negative impact on my overall budget.’, grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 14**, where they are sorted by the percentage of respondents who at least agree that medicines shortages are having a negative impact on their budget (aka ‘agree’ responses + ‘strongly agree’ responses).

Countries where over half of the respondents strongly agreed with the statement were Bosnia and Herzegovina, Netherlands, UK, Ireland and Albania. There were very few ‘strongly disagree’ responses overall, and countries which had more than 1 response of strongly disagree were Finland, Turkey, Italy and Portugal.

Q21. In case of shortage, how often do you have to pay a higher price to procure the drug from another supplier/hospital?

63% of responses for this question (N=969) report having to pay a higher price for drugs from alternate sources at least most of the time (46% most of the time, 17% all of the time), adding further evidence of the adverse effect on budgets due to medication shortages.

Only 6% of respondents rarely must pay a higher price for procurement from alternate sources, and 2% report never having to pay a higher price.

The results grouped by country can be seen in **Figure 15**, where the data has been sorted by the percentage of responses reporting at least most of the time. Interestingly, Cyprus, Lithuania and Montenegro only have responses for never or rarely.

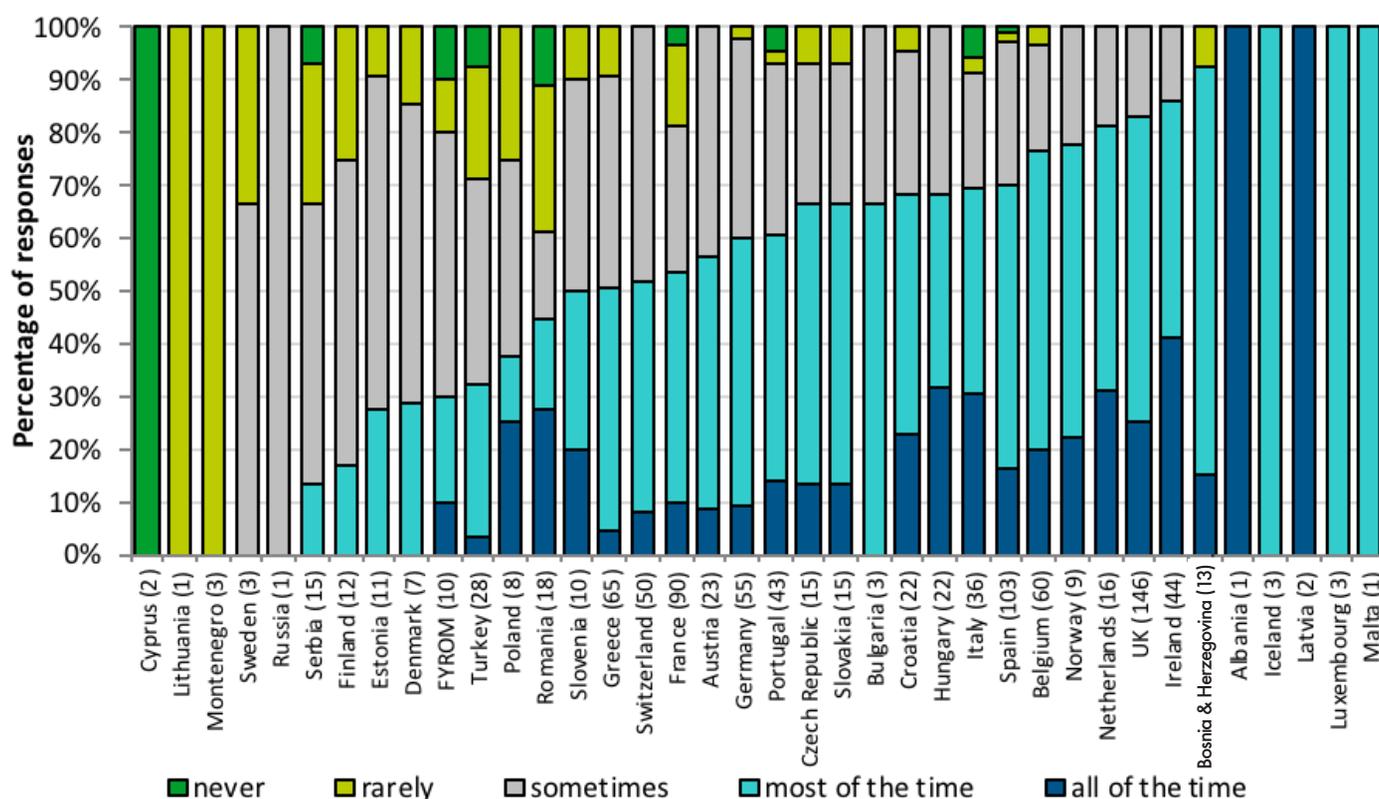


Figure 15 Percentage of responses for question 21 'In case of shortage, how often do you have to pay a higher price to procure the drug from another supplier/hospital?' grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

Q22. Please provide any relevant examples from your hospital over the past year of the impact medicines shortages have had on patient safety welfare. Tick all that apply.

The issues resulting from medication shortages in the last year are shown in **Figure 16**, which starkly shows the magnitude of this problem.

Over half of the 946 respondents to this question have seen care delayed as a consequence of medication shortages (59% of respondents), whilst the quality of care received by the patient is directly affected with cancellations of care (31% of respondents), medication errors (25% of respondents) and suboptimal treatment for patients (25% of respondents) also being frequently communicated. There were 12 reports of death being caused as a consequence of medication shortages (1% of respondents).

Reported events such as increased length of hospital stay (20% of respondents) and readmissions due to treatment failure (5% of respondents) add further strains to hospitals already struggling with capacity and budgetary issues.

Although not listed as specific option to the question, 19% of respondents chose none of the responses, presumably because they had not experienced any impact on patient care due to shortages or do not know. Responses to the 'Other' category were varied, with 5 responses saying there was no impact on patient care, and 4 responses restating the time burden of dealing with shortages and having less time to focus on patient care.

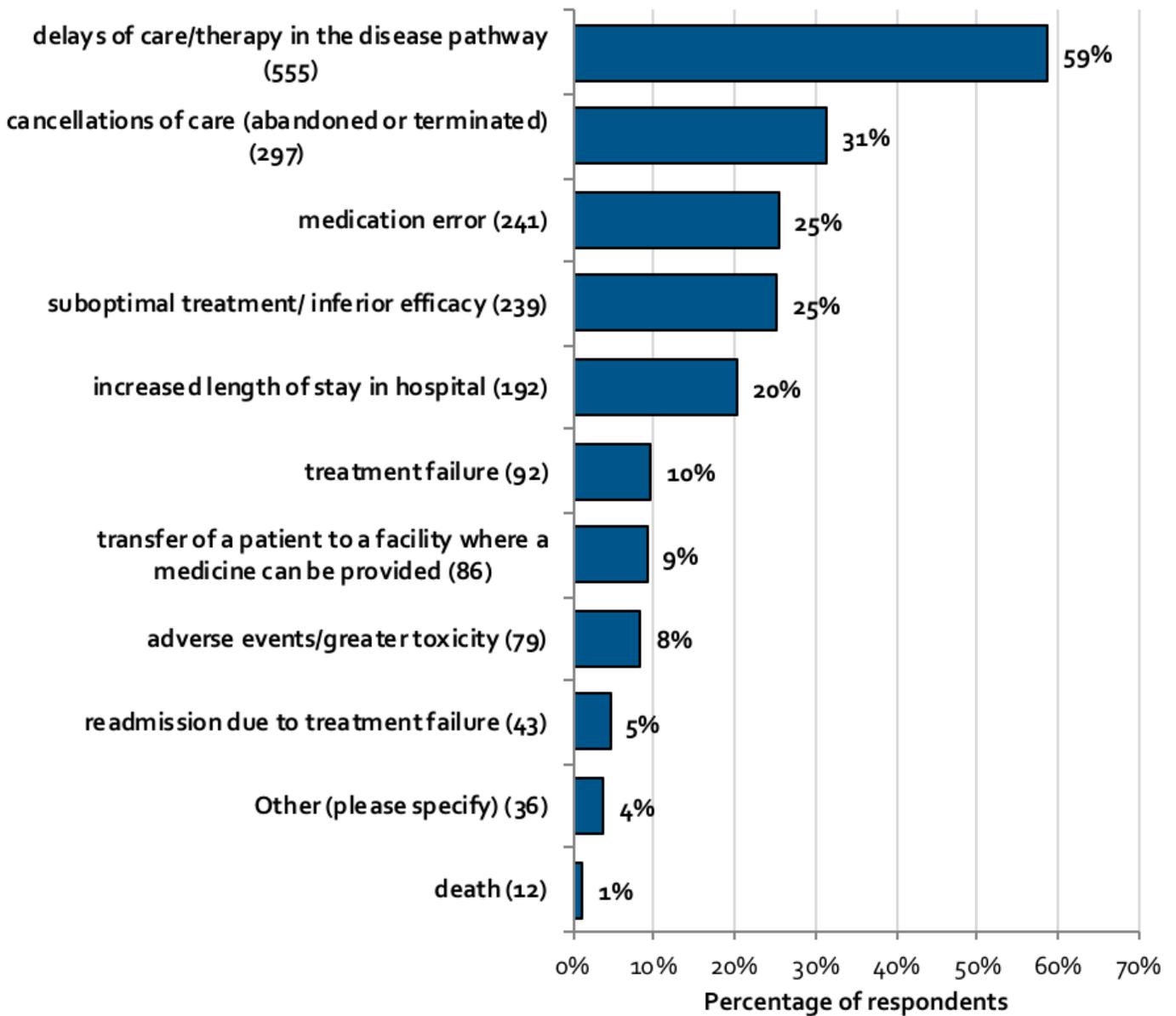


Figure 16 Percentage of participants in the survey who identified this category of impact on patient care due to medicines shortage. (N=946) (Note that this was a tick all that apply question)

12. Managing problems caused by shortages (Q23-26)

Q23. Please describe practically how a medicine in short supply is usually dealt with to minimise the impact on patient care. (Please tick all that apply)

The most frequently reported action in response to medicines shortages was to inform the prescriber and recommend an alternative (83% of 946 respondents). Over half of the respondents also reported attempting to source medicine from alternate sources, investigate when supply will be restored and to inform the prescriber with no recommendations (60%, 60% and 52% of respondents respectively).

45% of respondents selected both ‘inform prescriber and recommend an alternative’ and ‘inform prescriber of the shortage’. This is explained by the most frequent theme from the freetext comments from the ‘Other’ category, which was how the course of action depends on the shortage. For example, “*prescribers are informed based on the nature of the drug. if it is a straight swap of generic manufacturer for the same drug it may not be necessary to contact the prescriber. prescribers are contacted in circumstances where there may be an effect on the patient, for example appearance is significantly different, bioavailability is different, change of formulation, different excipients, significant cost pressure, etc. this is not an exhaustive list, each drug is assessed on an individual basis and the best course of action decided.*” – Germany.

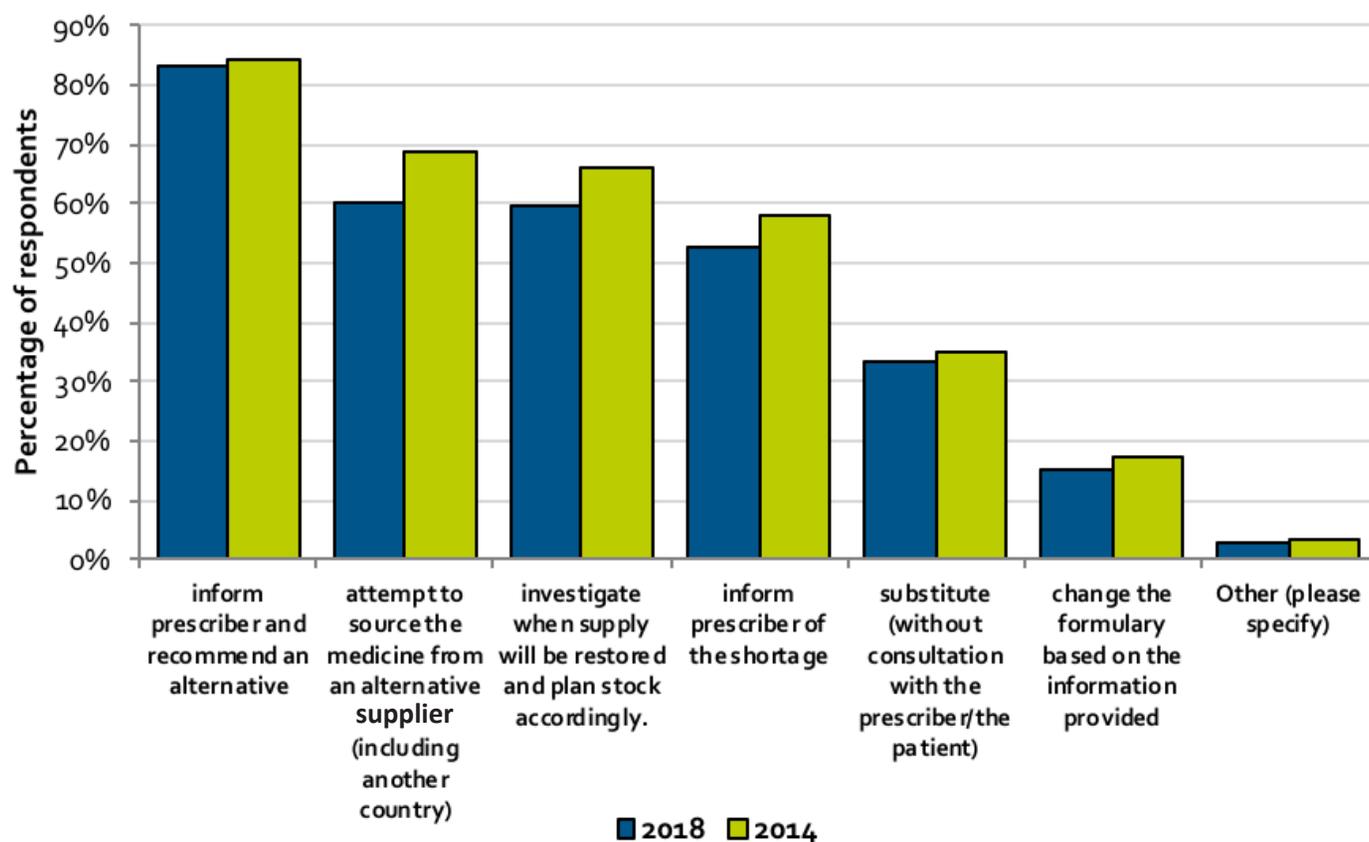


Figure 17 Percentage of participants in the 2018 and 2014 surveys who identified this action due to medicines shortage. (N2018=946, N2014=336) (Note that this was a tick all that apply question in both surveys)

Compared to the 2014 survey data, the percentage of respondents for each category is slightly lower, although the ranking of the options remains consistent, as seen in [Figure 17](#).

Q24. What changes (if any) in practice has your hospital needed to make in order to deal with the shortages problem? (Please tick all that apply)

Of the 946 respondents who answered this question, 62% report their hospital has created communication systems or tools to alert staff about shortages. Other common changes made include readjusting budget plans due to increased expenditure caused by shortages (29%) and reassigning staff's time to deal specifically with shortages (28%). 16% of respondents report that no changes have been required, up from 13% in 2014.

A common theme from the 'Other' freetext comments was that no changes had occurred but due to lack of resources and awareness of the problem ("*it is still a hidden problem but immense*" – Germany, "*No changes done but highly required. Burnout of the pharmacist*" – Spain).

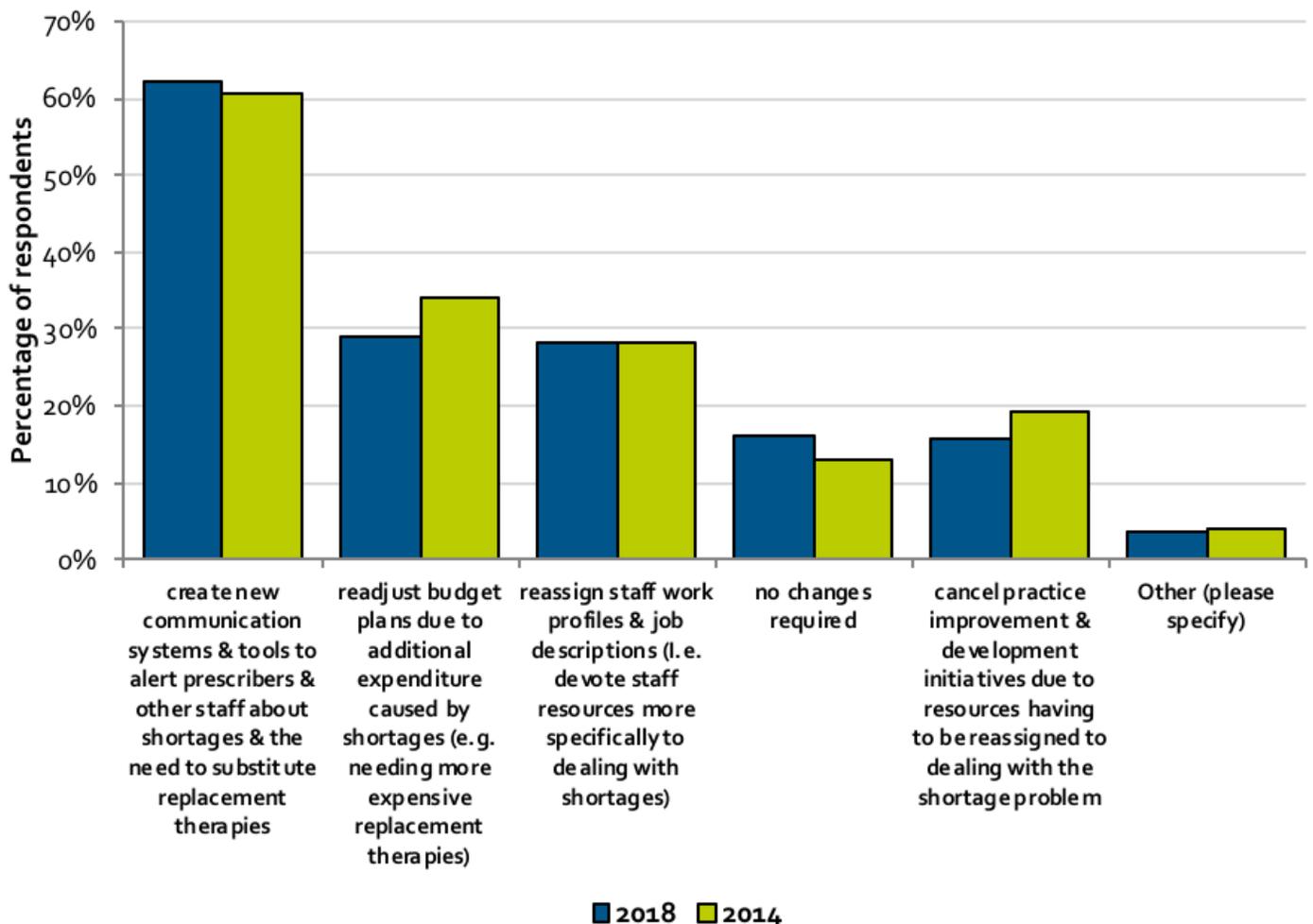


Figure 18 Percentage of participants in the 2018 and 2014 surveys who identified this change in practice due to medicines shortage. (N2018=946, N2014=331) (Note that this was a tick all that apply question in both surveys)

As with the previous question, the responses to this question are similar to the results from the 2014 survey.

Q25. Please provide any relevant anecdotal evidence from your hospital over the past year of the impact medicines shortages have had on patient safety and welfare.

Freetext responses to this question have been linked to the patient safety and welfare categories defined in question 22 to provide more insight into these issues.

Delays of care/therapy in the disease pathway

- *“Delay in care or being prescribed 2nd line antibiotics for an infection. Being forced to prescribe broader spectrum antibiotics because narrower spectrum was not available and increase risk for antimicrobial resistance.” – Ireland*
- *“Delay on the beginning of an antibiotic therapy because of an unknown shortage.” – Spain*

Readmission due to treatment failure

- *“Psychiatric patients stopped their therapy and it caused readmissions.” – Croatia*

Medication error

- *“We had alternative generic parallel of antibiotic which had a confusing name so nurse almost gave the wrong antibiotic to the patient (I have found out by accident -cases like this for sure can be found out more in practice at the ward).” – Croatia*
- *“Drug error due to the look alike sound alike drug 2. shortage of noradrenaline HCl - need to use tartrate and reconstitution with glucose solution.” – Estonia*

Adverse events/greater toxicity

- *“The shortage of amoxicillin IV has lead to treatment of patient with gentamicine/vancomycine with more toxicity!” – Netherlands*
- *“Suspicion of adverse events using some medicines without or insufficiently studies for children.” – Romania*

Increased length of stay in hospital

- *“Longer wake up times after OP, because of Remifentanyl shortage -> Impact on Duration of the stay in intensive care unit -> less beds to offer -> less surgery possible.” – Switzerland*
- *“Multiple antibiotic shortages have led to delayed doses, suboptimal alternative therapy, increased length of stay.” – UK*

Cancellations of care (abandoned or terminated)

- *“Patients on treatment with amiodarone couldn’t get the drug for about 3 months. Some stopped treatment, some where changed to new and more expensive drugs.” – Spain*
- *“Cancellation of cure for shortage of polyvalent immunoglobulins.” – France*

Suboptimal treatment/ inferior efficacy

- *“A patient with NARDELZINE treatment had to stop the treatment during a month and had to change her treatment but it was less adapted.” – France*
- *“Shortage of fractioned heparine caused us to use a therapeutic alternative that has a worse risk/benefit ratio.” – Bulgaria*

Transfer of a patient to a facility where a medicine can be provided

- *“Lack of IgG immunoglobulin and transfer of patient to another hospital where the drug was available.” – Greece*
- *“Shortages of same antibiotics and cytostatics causes sending patients to other facilities.” – Serbia*

There were also some responses where the respondents did not know of any impact because they do not interact with patients (e.g. *No access to this data as hospital pharmacists in Croatia are not included in clinical circle and have no access to hospital wards, no insight in patient files or contact with patients at all.* – Croatia). The role of the hospital pharmacist varies between countries. The EAHP European Statements of Hospital Pharmacy Survey revealed in some countries the role is entirely focused on procurement, whereas in others the role has more clinical focus and more patient facing ⁽⁵⁾.

Q26. In the country you work in, are there national level approaches in place to address the medicines shortage problem e.g. websites with information about current shortages and linked proposed solutions for therapy substitution? If so, please give a short description of these, including reference to both your country of practice, and the extent to which you consider the approach is working.

The responses to this question heavily overlapped with question 14, where respondents described the reporting system for shortages. In many cases, the website used for reporting shortages was the only national level approach to address the medication shortage problem. The amount of information provided (expected return date, reason for shortage, alternative suggestions) varies by country, as does the completeness of the list of shortages.

The list of website links and additional information are provided in full in Appendix A.

13. Regulation (Q27-29)

Q27. Are there any legal regulations in your country to ensure supply over a certain period of time?

Almost half (46%) of the 945 respondents who answered this question were not sure if there are legal regulations in their country ensuring supply over a certain time. The percentage of respondents answering 'Yes' and 'No' were similar (26% and 28% respectively). The high proportion of 'I don't know' responses suggests there is room for improvement on the knowledge of this topic, potentially incorporated into or redirected from a country's reporting system/website.

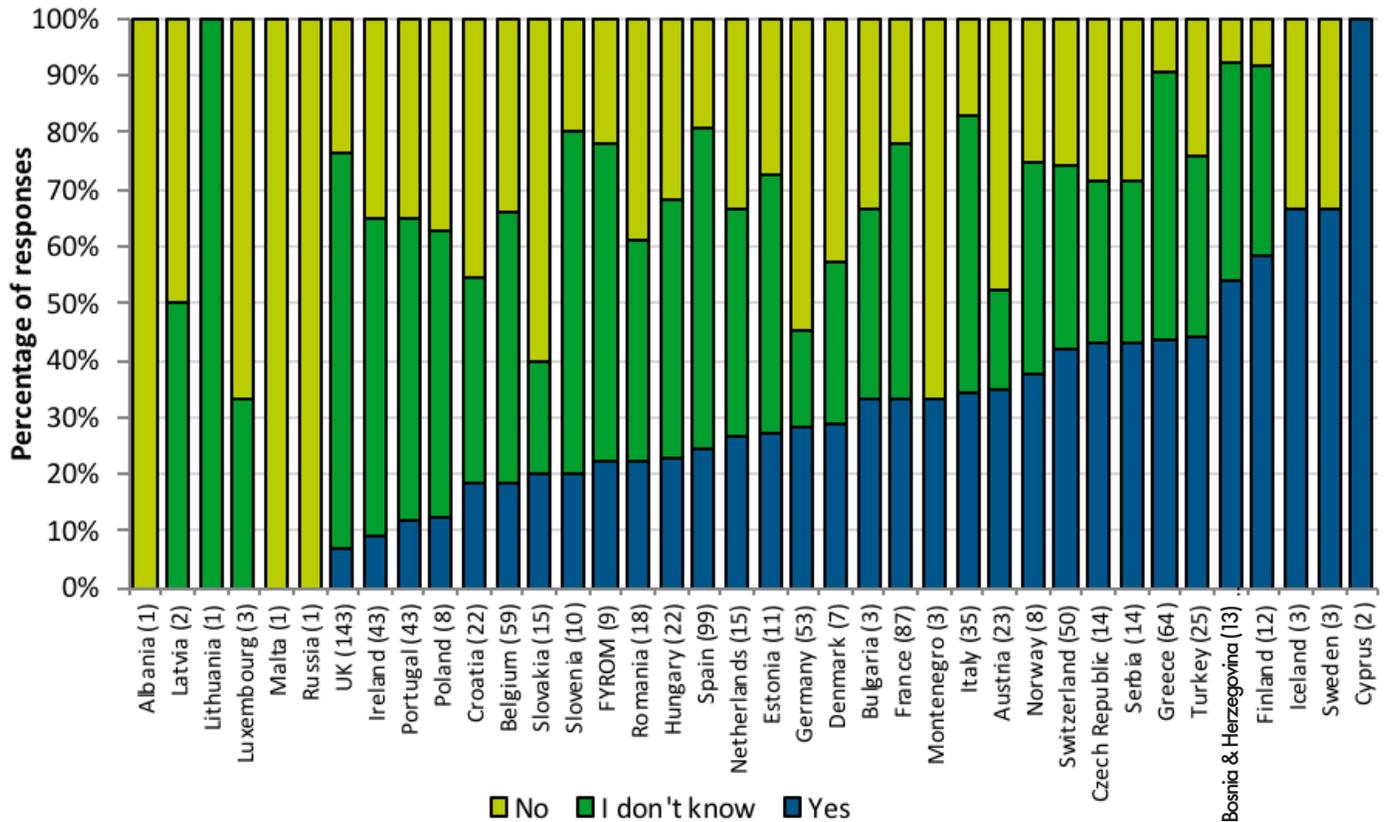


Figure 19 Percentage of responses for question 27 'Are there any legal regulations in your country to ensure supply over a certain period of time?', grouped by country. (N=945). Numbers in brackets represent number of responses from that country.

From looking at the data broken down by country in **Figure 19** it can be seen that there are only five countries where over 50% of the respondents answered 'Yes'.

Q28. For whom? (Are there any legal regulations in your country to ensure supply over a certain period of time?) (tick all that apply)

Following on from the previous question, respondents were asked for whom are there legal regulations (note that people responding 'No' to the previous question were not directed to this question). The most frequent response was the pharmaceutical industry (52% of 360 respondents reported this) closely followed by the hospital pharmacy (50% of respondents). Only 35% of respondents reported that wholesalers are subject to legal regulations to ensure supply.

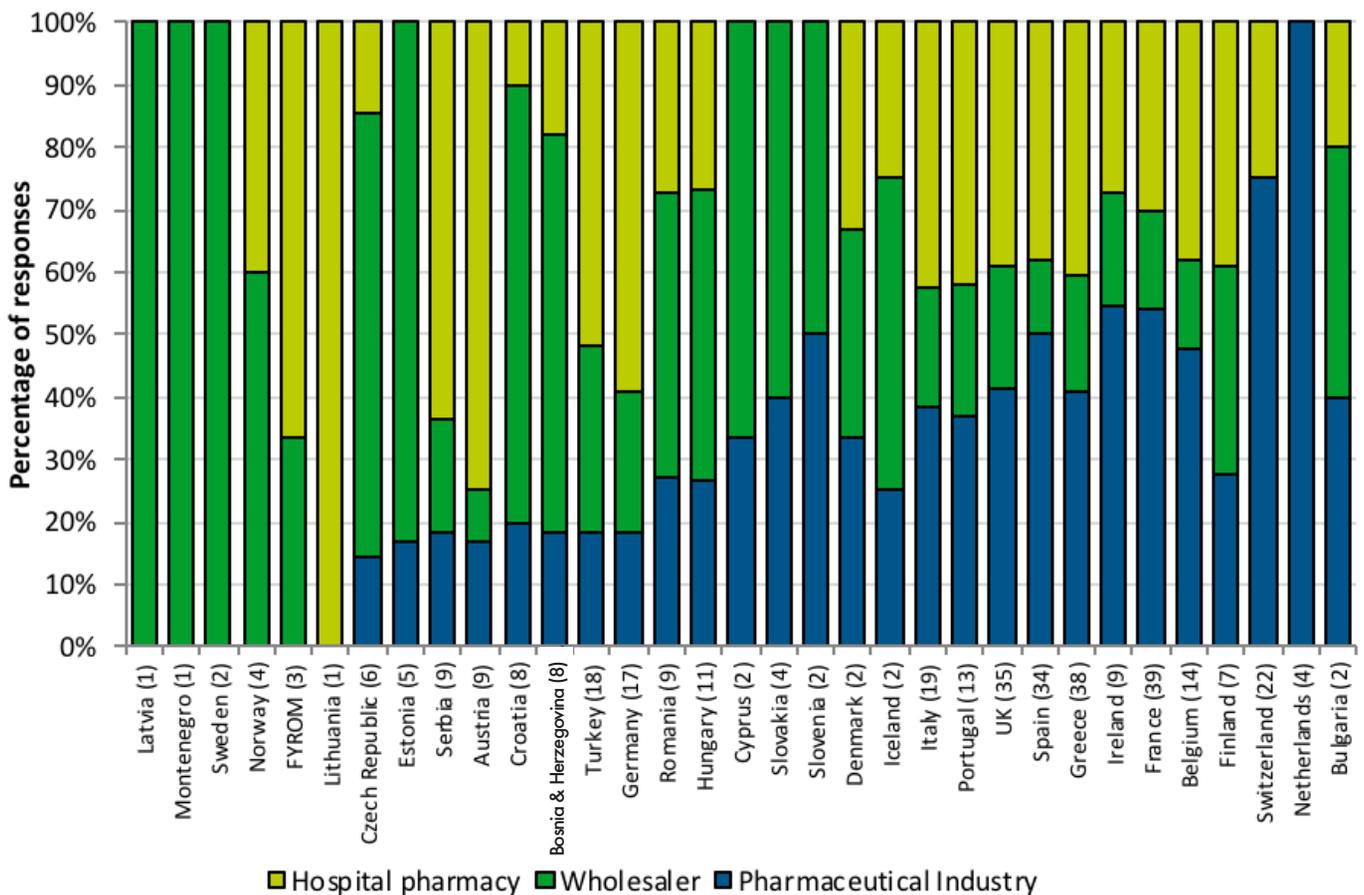


Figure 20 Percentage of responses for question 28 'For whom are there any legal regulations in your country to ensure supply over a certain period of time?', grouped by country. (N=360). Numbers in brackets represent number of responses from that country.

The results grouped by country are shown in **Figure 20**, where the reported subject of legal regulation varies greatly. 21 of 33 countries report all three options as being subject to legal regulations to ensure supply.

Q29. For how long? (Are there any legal regulations in your country to ensure supply over a certain period of time?)

This is the second follow up question regarding legal regulations for ensuring supply in a country. Of the 327 responses to this question 12% are for one week, 25% for two weeks and 23% for three weeks. The most frequent response was ‘longer (please specify)’ with 129 responses (39%).

Analysis of the associated freetext show 37 responses reporting they do not know, 30 responses reporting a duration of months, 14 responses reporting a duration of years and 17 responses saying as long as required. Data grouped by country is shown in **Figure 21**.

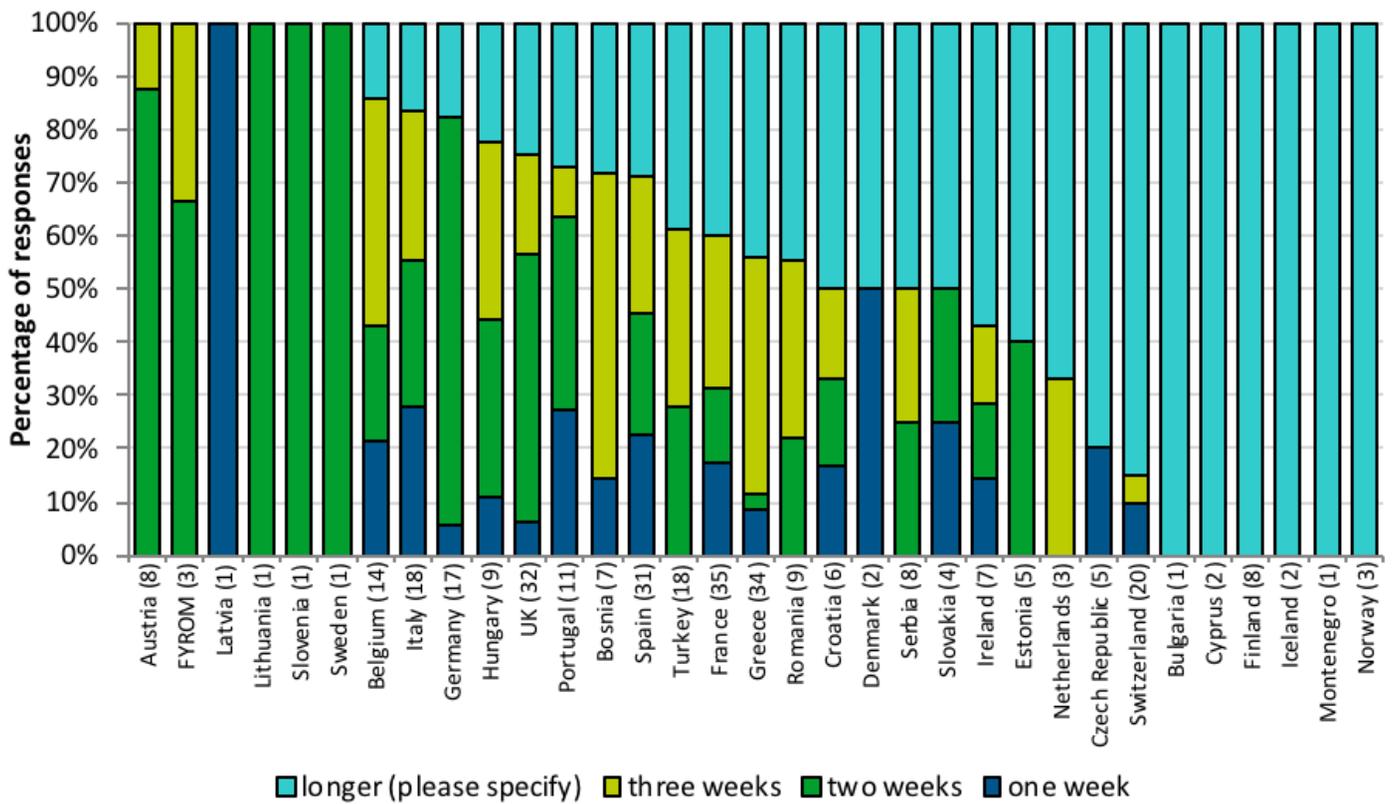


Figure 21 Percentage of responses for question 29 ‘For how long are there any legal regulations in your country to ensure supply over a certain period of time?’, grouped by country. (N=327). Numbers in brackets represent number of responses from that country.

14. Policy solutions (Q30-31)

Q30. Which of the following proposed policy solutions on medicines shortages do you personally support? (tick all that apply)

The proposed policy solution with the most support was the medicines shortages catalogue of the EMA, with 43% of the 918 respondents answering this question choosing this option.

The second most frequent option was 'None of the above' from 42% of respondents, which may cover people who do not support any of the policies, but also people who are not aware of these policies and what they are. Although there was no freetext option in this question, there are freetext responses from subsequent questions saying people are not aware of what these policies are (e.g. "not sure what these and I don't have time to read up on each option").

The third and fourth most frequent choices were the Heads of Medicines Agency/EMA taskforce on availability of authorised medicines and the activities of COST Action 15105 - European Medicines Shortages Research Network with 35% and 28% of respondents supporting these policies respectively.

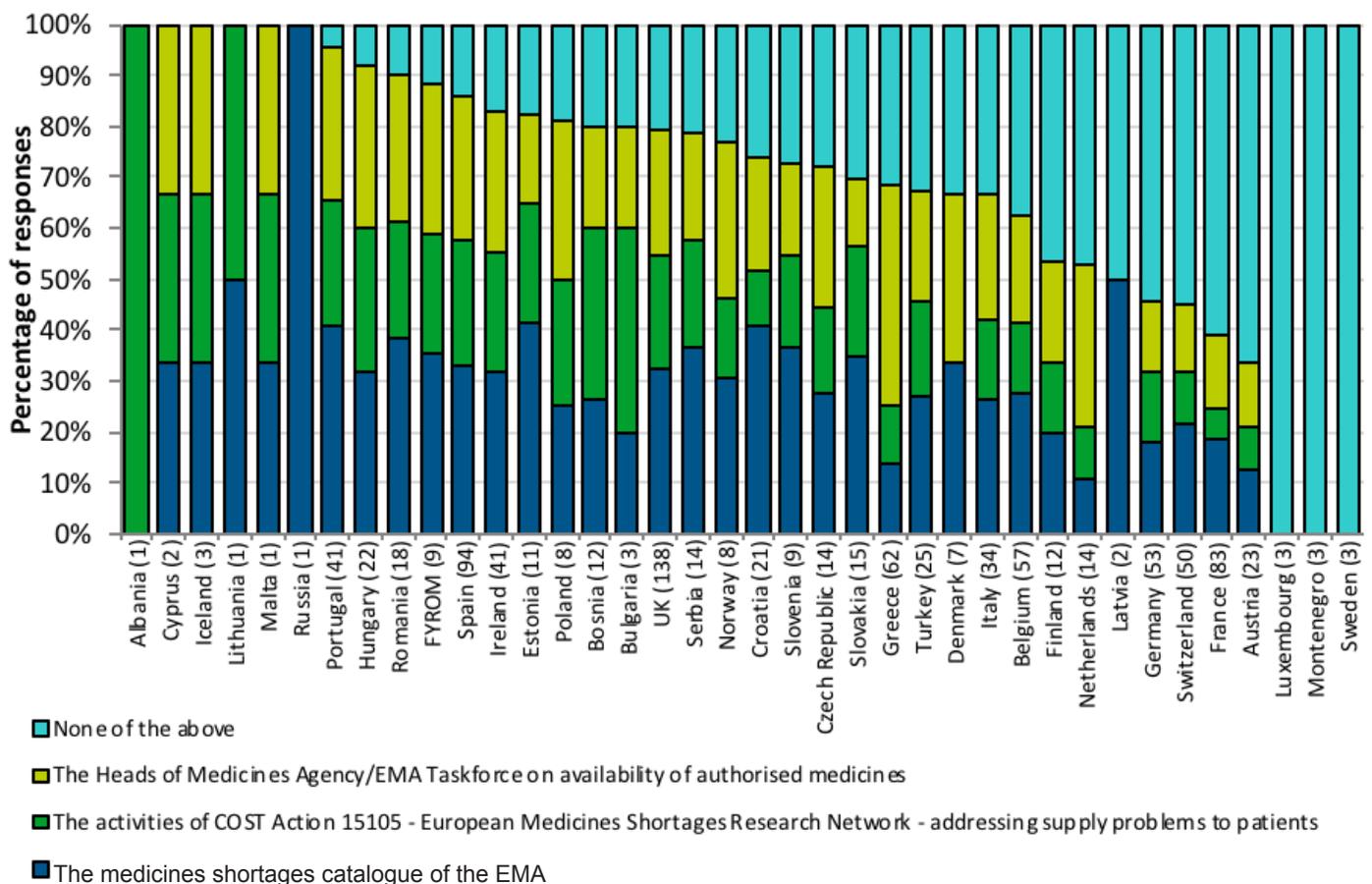


Figure 22 Percentage of responses for question 30 'Which of the following proposed policy solutions on medicines shortages do you personally support? (tick all that apply)', grouped by country. (N=918). Numbers in brackets represent number of responses from that country.

The responses grouped by country can be seen in **Figure 22**, where they are sorted by the proportion of responses answering 'None of the above' to see the variation of support across countries for the policy solutions.

Q31. Which of the following proposed policy solutions on medicines shortages would you personally support? (tick all that apply)

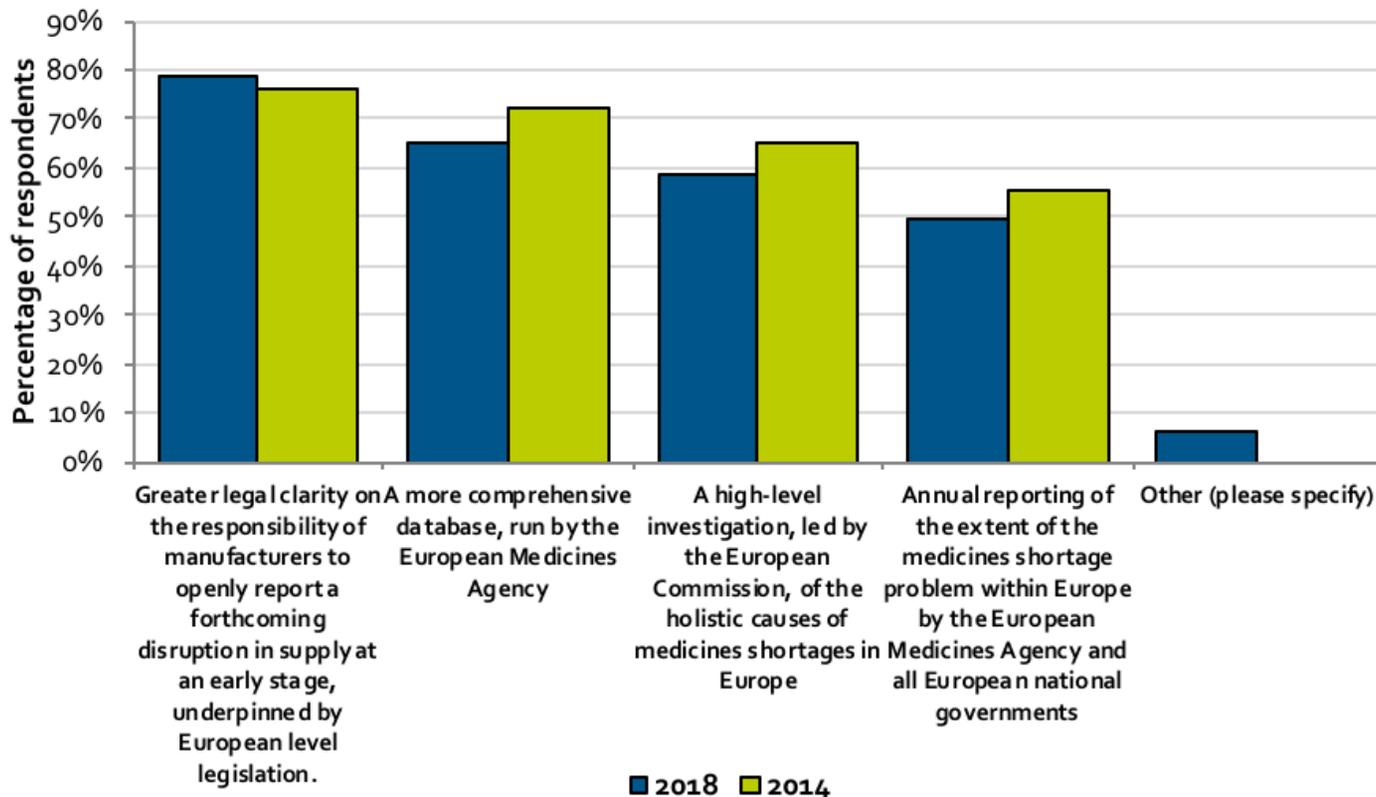


Figure 23 Percentage of participants in the 2018 and 2014 surveys who supported this proposed policy solution. (N2018=918, N2014=319) (Note that this was a tick all that apply question in both surveys)

It is not surprising to see that 79% of the 918 respondents to this question support greater legal clarity on the responsibility of manufacturers to report upcoming supply chain issues at an early stage; in question 10 many comments were observed regarding pharmacists not being aware of supply issues until a delivery did not show up and in question 14 it was observed that the reporting system for medication shortages was weakened by a lack of obligation for manufacturers to share information on supply issues.

A comprehensive database run by EMA was also a popular choice with 65% of respondents supporting the proposal, followed by a high level investigation on the causes for shortages and annual reporting on the extent of the problem with 58% and 50% respectively. This is the same order the proposals were ranked in the 2014 survey. The proportion of responses for 3 of the 4 proposed options is slightly lower in 2018 compared to 2014, but this may be partially due to the fact that respondents were given an 'Other' option in 2018 which was not available in the 2014 survey.

The most common theme from the 'Other' comments is for an increased legal clarity on manufacturers. This obligation should not just cover the reporting of potential shortages, but also help to ensure supply of medicines and maintain sufficient stock levels. Some examples of this are: "clear responsibility for pharmaceutical companies in the continuity of medicines supply. Discontinuity should have legal and extensive financial consequences for registration holders" – Netherlands, "place obligations on manufacturers/ MA holder where they are the sole suppliers of that drug i.e. where there is not an alternative" – Ireland and "why not experience sanctions against pharmaceutical industry who cannot provide the medicine during a signed binding?" – France.

15. Recommendations (Q32)

Q32. Please use the comment box below to make any further comments that might be helpful to EAHP's policy and advocacy activity on the topic of medicines shortages, including reflections on causation, reports of impacts, proposed solutions, and sources of evidence

There were 92 useable freetext responses to this question, which contains recommendations from respondents on how they would like to see the shortages issue managed. Some common themes which emerged from the responses are listed below:

Responses wanting more timely and accurate information from suppliers/manufacturers on shortages (10 responses)

- *"I beg for more effectiveness, more often in our countries, we have to deal with shortages far before authorities are aware of it."* – France
- *"Information on early state by manufacturer (to hospital, ministry of health) is most effective preventing measure."* – Poland
- *"I have ticked the box stating we would like clarity, as I don't think that the actual problem, and /or the replenishment date of the drug is truthful. I say this all the time to suppliers (please be honest) patient care hasn't been affected because of the massive resource we have put in place to manage these shortages."* – United Kingdom

Responses calling for suppliers/manufacturers to be legally obliged to maintain stock levels and ensure supply (8 responses)

- *"Policy resp. the government's should have more legal handle to obligate companies to increase their Stock in the countries of delivering. I miss the serious care of the governments about this problem."* – Germany
- *"More responsibility of producers to assure the presence of their medicines in commerce, even if they have other countries where they commerce these medicines, perhaps where they gain more."* – Italy
- *"Greater legal clarity on the responsibility of manufacturers to organize their own sufficient stock keeping."* – Austria

Responses calling for increased communication/collaboration, either nationally between hospitals, or internationally across Europe (7 responses)

- *"A better information network should be initiated so that information about shortages and availability of medicines among European countries."* – Bulgaria
- *"Better national connection, information exchange and drug distribution between hospitals."* – Croatia
- *"Collaboration between countries is very useful."* – Iceland

Responses calling for a central lead/agency to work on the problem to reduce duplication of efforts (at European, EU, or national level) (8 responses)

- *"A common framework in European level (SOP) could be useful."* – Greece
- *"A record at European level"* – Romania
- *"Every hospital in the UK has pharmacists dealing with the same problem. Valuable loss of time. If one person did it & the rest comply/tweak would be time effective."* – United Kingdom
- *"At the moment we seem to have no National System in Ireland and we rely on information that is drip-fed from Pharmaceutical Reps. The EU needs to lead on this. Also I have serious concerns on how the EU Falsified Medicines Directive will impact on Ireland, as a peripheral EU English Speaking country in the context of Brexit."* – Ireland

Responses relating to importing medicines from other countries and comments on price difference for the same product (11 responses, 4 specifically referring parallel trade)

- *“I don’t understand that one product in a country is not available but we can buy the same product in a foreign country in that case the firm should be obligated to import it itself out of the foreign country instead of we have to buy it in the foreign country.” – Belgium*
- *“It would be useful if there could be regulation to prevent companies charging significantly higher prices for a very similar medicine imported unlicensed from UK. This can be very costly in regularly prescribed items and must be profitable for these companies.” – Ireland*
- *“The cause of medicines shortages is often re-exports from countries where the drug is cheaper- restrictions on the re- export of drugs.” – Czech Republic*

Responses with specific mentions of parallel trade (4 responses)

- *“We need an initiative by the European Commission: API must produced in Europe. The production of medicines must be hold in Europe and not in far East. Parallel Imports have to be forbidden.” – Austria*
- *“I think EU could ask for a report from every Ministry of Health in EU member countries about this topic (to be compulsory and maybe verifiable, being known that some countries like Romania tend to make fake reports in order to not give explanations about shortages). And parallel export policies with harsh consequences if the regulations are not respected.” – Romania*
- *“More actions to control parallel trade.” – Spain*

Responses related to identifying the specific causes of shortages (10 responses)

- *“More needs to be done to investigate the root cause of these shortages. I believe the medicines are available, they are just being funnelled to where the manufacturer can make most profit rather than keeping up supply with their regular customers.” – Ireland*
- *“I think it would be useful to get information about why are there shortages in general, and about the specific cause in every shortage.” – Spain*
- *“A more holistic review needs to be undertaken to understand why shortages occur and try and prevent them. Currently most shortages are managed reactively instead of proactively.” – United Kingdom*

Responses with suggestions specifically for the EAHP (3 responses)

- *“The EAHP activity must be more connect with reality of European member states.” – Italy*
- *“The same evidence of this problem, for all the hospitals in Europe. I suppose that EAHP can do it.” – Romania*
- *“There needs to be a more joined up approach to medicines shortages e.g. FIP, COST, EAHP, EMA. Also needs to be open information on the number of API manufacturers globally.” – United Kingdom*

16. References

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Appendix A: Reporting system for shortages & national approaches in place (Q14/Q26)

The table below gives a summary of each country's reporting system and other national approaches to the shortages problem. All text are direct quotes from respondent's free text responses. Also included are data from Q13 and Q15 (% respondents in country saying there is a reporting system / % respondents in country judging it to be effective). (These quotes have not been altered)

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/working/functional? (%yes)	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Albania	100%	100%	-	-	-
Austria	70%	25%	www.basg.gv.at	BASG (Bundesamt für Sicherheit im Gesundheitswesen): voluntary list provided by pharmaceutical companies regarding shortages of their products, managed by the public health institution.	AAHP Mailing list of Austrian Hospital Pharmacists: E-Mail discussion Forum concerning drug shortages and strategies to cope with.
Belgium	70%	62%	www.afmps.be	Also FAGG and BCFI publish an overview of out of stock medication.	Working group with the authorities in which the pharmacists are involved. New laws are being drawn to help with solutions on a national level. Industries have to report by law any shortage that will last for 2 weeks. This is under change, a working group has started and it will be changed to 3 days. There will also be an evaluation for each drug shortage, to look for alternatives more quickly and give nationwide advice when a shortage occurs.
Bosnia & Herzegovina	38%	40%	http://www.almbih.gov.ba/	Manufacturers or wholesalers inform medicine agency which provides information on their website.	There is no national level for the medicines shortage problem.
Bulgaria	0%	-	-	-	-
Croatia	59%	46%	www.halmed.hr	There is a list available for download at HALMED (Agency for Medicinal Products and Medical Devices of Croatia). There are no proposed solutions for therapy substitution. Not sure how often is list being updated.	

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/working/functional? (%yes)	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Cyprus	50%	100%	Created a forum in the common hospital purchasing database (SAP) .	We have just created a forum in the common hospital purchasing database (SAP) where every hospital facing a drug shortage can notify other hospitals and seek for help.	-
Czech Republic	80%	50%	www.sukl.cz	There are information about shortages and (if available) possible reimbursement. Additionally, www.epin.phoenix.cz - wholesaler - information about current shortages and sometimes solutions for therapy substitution.	-
Denmark	38%	100%	Amgros (the national Danish buyer for medicines for public hospitals) has a database "Amro".	The Danish medicines Agency has a reporting system, besides that Amgros has at internal self reporting system together with til Danish Hospital Pharmacy.	Initiatives for at national taskforce Group to handle medicines shortage problems, there is a person at Amgros who is dedicated to shortage situations.
Estonia	73%	38%	http://www.ravimiamet.ee/en/node/1403	Republic of Estonian Agency of medicines have lists for shortages of medicines. It changes with new information every day.	We also consult with Agency of Medicines about our problems and how to solve it.
Finland	57%	29%	http://www.fimea.fi/tietoa_fimeasta/ajankohtaista/saatavuushairiotiedotteet	FIMEA (Finnish medicine agency) has websites where medicine company can inform about common shortages and proposed solutions, and where pharmacy can get the information.	We also get information from "pharmacists unions" and medicine companies e-mail.
France	78%	47%	www.ansm.fr	In France there is just ANSM that lists medicine shortages and sometimes by what replace the drug. But not really efficient because shortage information is not given early enough (sometimes several weeks without news) and advice are not always direct equivalent.	Some clinical societies give guidelines to switch medicin in shortage (Oxacilin, Amoxicilin/Ac clavulanic, Normal immunoglobulin human).
FYROM	18%	100%	malmed.gov.mk	In my country we address problems to MalMed healthcare services LTD.	-
Germany	88%	8%	www.bfarm.de	The companies report shortages to different institutions which list them in the internet. The list is often not up to date, and not all shortages are listed here because it is not mandatory and there are different limitations (just shortages > 2 weeks etc.).	Also, The drug shortage list for the vaccines is a lot better: https://www.pei.de/DE/arzneimittel/impfstoff-impfstoffe-fuer-den-menschen/lieferengpaesse/informationen-lieferengpaesse-impfstoffe-node.html . recommendation by the German Society of Hospital Pharmacists, disseminated via email.

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/working/functional?	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Greece	68%	59%	www.eof.gr	There is an on-line reporting system for medicine shortages in the website of the National Organization for Medicines (EOF). The tool is supervised by EOF and hospital pharmacists can report any relevant problem. We get quick response by e-mail or phone call from EOF that informs us about the level of information that the National Organization for Medicines already has about the specific shortage problem we reported.	Proposed alternatives are rarely listed in this website.
Hungary	82%	50%	Ogyei.gov.hu	There is a list that's being updated frequently, it's run by the governing body and it's based by the manufacturer's notice. We have a national website where they propose solution for substitutions.	-
Iceland	50%	0%	Medicinal Agency - report	-	-
Ireland	18%	38%	www.HPRA.ie	There is very little that I am aware of in Ireland. On occasion we have contacted the Health Product Regulatory Authority only to find out that they were not aware of the shortage.	Currently there aren't any but I believe the HPRA are setting some centralised procedure, however, no concrete evidence of its existence yet.
Italy	88%	91%	www.aifa.it	AIFA detailed all shortages of medicines in the website after the declaration of the companies, specially if they are brand companies. Information about therapy substitutions are lacking.	-
Latvia	67%	100%	https://www.zva.gov	Anyone (hospital, pharmacy, patient) could use this website to make our medicines agency know about shortage. But there is a lot of cases when drug isn't mentioned there, because no one applied this issue.	-
Lithuania	0%	-		-	-
Luxembourg	33%	0%	The authorities inform us of some shortages via email.	-	Not of my knowledge.

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/working/functional?	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Malta	0%	-	-	-	-
Montenegro	67%	100%	-	-	-
Netherlands	100%	94%	https://farmanco.knmp.nl	Run by the Royal Dutch Society of Pharmacy. Manufacturers and wholesalers can report shortages to this website.	There is a new regulation in place (since January 1st) allowing to import medication from other EU countries in case of shortage that could help (but has to be tested first).
Norway	100%	89%	www.legemiddelverket.no	Both NOMA and the national centre of shortage of drugs in hospital (https://oslo-universitetssykehus.no/fag-og-forskning/nasjonale-og-regionale-tjenester/nasjonalt-senter-for-legemiddelmangel-og-legemiddelberedskap-i-spesialisthelsetjenesten) has webpages open to everyone.	There are websites, newsletters, a national centre for hospitals which gives recommendations for handling shortages, recommends alternative therapy and has the right to give priority to patients when there are shortages.
Poland	100%	22%	http://wif.waw.pl/zglaszanie-brakow-produktow-leczniczych/	Chef Pharmaceutical Inspectorate collects data reported by pharmacies regarding drug shortages and produces a list of medicines at risk of being illegally exported. Pharmacists are obliged to report shortages online giving details of nature of shortage. Shortages are underreported due to pharmacy staff and time shortages. The reporting system is web based but considered by many not user friendly which may hinder the reporting system.	There is a plan to introduce by October 2018 a national system that will require all pharmacies (community and hospital), wholesalers and manufacturers to report all stock movements daily to the central database. There are several technical difficulties in introducing a complex reporting system. At this stage it is not clear how the uploaded data will be analysed and what actions will be taken to prevent shortages.
Portugal	54%	50%	www.infarmed.pt	-	INFARMED Sometimes proposes solutions for therapy substitution.
Romania	89%	38%	-	Health professionals and patients can use this site to report medicine shortages. This site is correlated with a daily stock reporting system for pharmacies and medical wholesalers. Unfortunately, medicines reported missing are inexplicably found in daily stock reports, but they are not actually available for patients, but rather meant for parallel export. However, this makes government officials say there are no medicine shortages.	ANMDM (https://www.anm.ro/) offers us information about current shortages without linked proposed solutions for therapy substitution.
Russia	0%	-	-	-	-

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/working/functional? (%yes)	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Serbia	67%	40%	www.rfzo.rs	National insurance fund runs website where pharmacists can report shortage. But we cannot see data base with all reported shortages from other institutions.	-
Slovakia	63%	40%	sukl.sk	website with information is available but with no solutions, manufacturers often don't want to inform about the length of shortage of the drug with is not in the list from the website.	-
Slovenia	33%	0%	http://www.jazmp.si	System exists, but manufacturers don't report consistently to the system.	-
Spain	79%	70%	https://cima.aemps.es/cima/publico/home.html	provides information via e-mail and website, and there is a webpage in which it is possible for hospital to get medicines from abroad.	When we have the option to import the medicine, we have the information at: https://mse.aemps.es/mse/documentoSearch.do?metodo=buscarDocumentos . It is here where we create the order to import the drug.
Sweden	33%	0%	www.mpa.se	-	-
Switzerland	78%	56%	https://www.bwl.admin.ch/bwl/de/home.html	Information System is too dull/slow. most of time we already run out of stock when the official Information reaches us. . Additionally, a hospital pharmacist launched the site http://www.drugshortage.ch/index.php to provide the manufacturer a place to voluntarily report shortages. Other health care professionals can also report shortages.	For certain essential groups of drug like f.e. vaccines or antibiotics... there is a federal office taking care of the situation and managing the situation together with the pharmacy. companies.
Turkey	47%	87%	http://www.titck.gov	-	The Ministry of Health set up a whatsapp group with all pharmacist - officer for medical depot stock control -and we share our problems in there.
UK	60%	72%	Commercial Medicines Unit run by DoH. (email responses)	CMU sends out shortage list on monthly basis. PMSG also provide shortage list.	Trusts get together and share / Info via national and regional networks.

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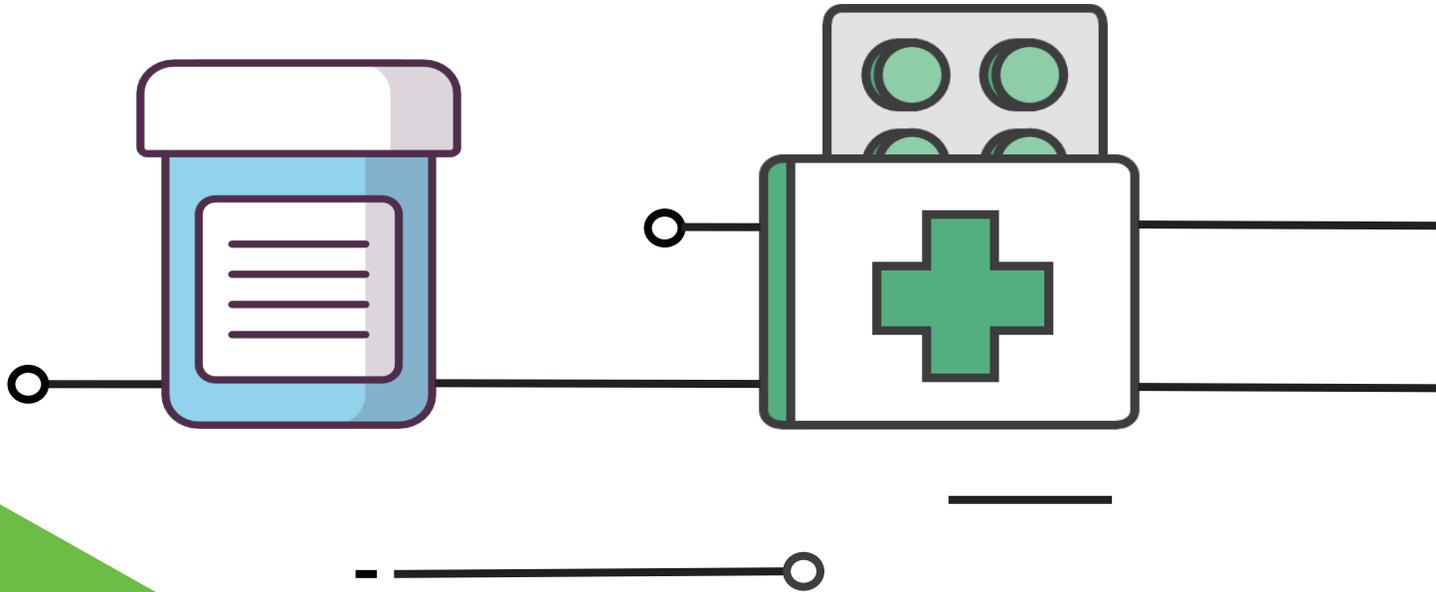


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2018 EAHP Medicines Shortages Report



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