Organisation for Economic Co-operation and Development

DELSA/HEA/WD/HWP(2022)15

Unclassified English text only

7 September 2022

DIRECTORATE FOR EMPLOYMENT, LABOUR AND SOCIAL AFFAIRS
HEALTH COMMITTEE

## Health Working Papers

OECD Health Working Papers No.147

# The Economics of Medication Safety

## Improving medication safety through collective, real-time learning

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JEL classification: H51, I11, I18, L86

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JT03501969

The Economics of Patient Safety Part V

# The Economics of Medication Safety

## Improving medication safety through collective, real-time learning

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# Acknowledgements

The work was enabled by a voluntary contribution from the Ministry of Health of Germany (BMG). The authors would especially like to acknowledge Dr. Ingo Härtel for his input and support.

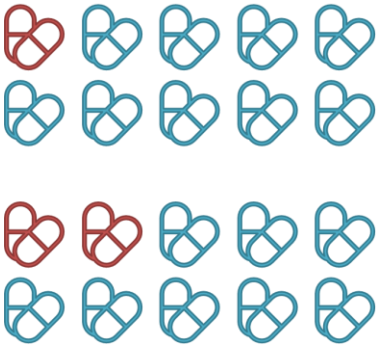
Australia, Belgium, Canada, Czech Republic, Estonia, Germany, Israel, Italy, Japan, Latvia, Luxembourg, Mexico, the Netherlands, Norway, Portugal, Slovenia, Switzerland, Türkiye and the United States. We are extremely grateful to the coordinating leads who are recognized in Annex A.

The authors are grateful for inputs and recommended improvements on the report from Erica Barbazza, Christian Berringer, Neelam Dhingra-Kumar, Dimitrios Florins, Nikhil Prakash Gupta, Helen Haskell, Alpana Mair, Harald Mische, Giuseppa Ottimofiore, Libby Roughead, Hamsini Shankar, and Herbert Sommer.

We would also like to thank Francesca Colombo and Frederico Guanais for their feedback and support.

This work was coordinated and authored by the OECD, including Katherine de Bienassis, Laura Esmail, Ruth Lopert, and Niek Klazinga. Constanza Salas Ramos provide research and drafting support.

# Key messages



As many as **one-in-10 hospitalizations** in OECD countries may be caused by a medication-related harm and…

**One-in-five inpatients** experience medication-related harms during hospitalization

Costs from **avoidable admissions** due to medication-related harms

+

**Added length of stay** due to preventable hospital-acquired medication-related harms

=

**OVER USD 54 billion**

in OECD countries, annually

## To improve medication safety, countries can:

# Executive Summary

This report includes four components; it 1) assess the human impact and economic costs of medication safety events in OECD countries, 2) explores opportunities to improve prescribing practices 3) examines the state-of-the art in systems and policies for improving medication safety, and 4) provides recommendations for improving medication safety at the national level.

## Poor medication safety and sup-optimal prescribing outcomes come at a significant cost

Poor medication practices and inadequate system infrastructure—resulting in poor adherence, medication-related harms, and medication errors—too often results in patient harm. **As many as 1 in 10 hospitalizations in OECD countries may be caused by a medication-related event and as many one in five inpatients experience medication-related harms during hospitalization**. Together, costs from avoidable admissions due to medication-related events and added length of stay due to preventable hospital-acquired medication-related harms **total over USD 54 billion in OECD countries**. This figure is equivalent to 11% of total pharmaceutical spending across 31 OECD countries for which data are available[1].

Beyond medication-related harms, the more rational use of medicines can open significant opportunities to improve patient outcomes. **Almost half of all patients receive prescriptions for medications that do not meet their clinical needs**—medications with inappropriate dosing or duration, or even a completely inappropriate medication altogether or medication when an alternative intervention may be as--or more--effective. Beyond this, estimates suggest that **half of all** medicines (those prescribed, purchased, or dispensed) **are not taken appropriately**[2]. This sub-optimal use of health care resources is accompanied by out-of-pocket costs for consumers and high costs for health systems and needs to be addressed. There exist a number of mechanisms to promote rational use of medicines, for example, use of clinical guidelines, drug and therapeutics committees, digital innovations, and audit and feedback to improve prescribing behaviour. There is also potential for improving rational use of medicines through regulatory and economic interventions, supported by robust evaluation alongside implementation**.**

## Where countries stand in regard to the adoption of medication safety policies

OECD countries have made significant progress in implementing functional tools to monitor and assess medication safety. The next frontier is operationalising these data to make systems safer in real-time. A

1 Total pharmaceutical sales estimated at 478,448.30 Million US$, PPP
2 https://www.who.int/activities/promoting-rational-use-of-medicines

number of countries can be looked to as leaders in the field, and their health information infrastructures can be viewed as a roadmap for improving medication safety.

In 2022 the OECD conducted a survey of 20 OECD countries to determine where countries stood in the adoption of policies to improve medication safety. The role of **health information infrastructure in improving medication safety is key**—and growing evidence suggests that effective **drug utilisation review** (DUR) processes can reduce medication-related harms and improve safety. Findings show that 14 of 20 responding countries now have national drug utilisation systems. The majority of respondent countries note that the data used for DUR are claims data, however an increasing number of countries also utilise data from e-prescribing systems. Three countries—Australia, Japan, and the United States—include electronic health record data in their DUR systems. In seven countries, Estonia, Korea, Norway, the Netherlands, the United States, Latvia and Slovenia, **DUR data are made available in real-time**. The most common use of DUR data is for reimbursement coverage decisions, which reflects the fact that most DUR systems in OECD countries base their data on claims. However, a number of countries are using DUR data to **drive quality improvement in health care delivery** and as a mechanism for **providing clinicians and prescribers with feedback**.

Adoption of **national lists of high-alert medications** can guide healthcare leaders in the implementation of safeguards to reduce the occurrence of medication errors and medication-related harms associated with incorrect use of these medicines. National lists of high alert medications have been developed in in Australia, Belgium, Costa Rica, Estonia, Germany,[3] Israel, Japan, Mexico, Slovenia, Türkiye and United States. Another system-wide intervention that has capacity to help assess the occurrence of medication safety errors—and thus inform policy makers where action needs to be taken—is **novel reporting techniques**, such as trigger tools. Only Estonia, Norway and Costa Rica report currently having national level systems of non-voluntary reporting using trigger tools, but Australia, Israel, the Netherlands, Mexico, Switzerland, and the United States report that trigger tools are used in some settings.

There have been a number of **innovations in digitization** (smart infusion pumps, drug administration systems, e-prescribing) and **data infrastructure** (patient-reports of medication-related harms, post-market surveillance, eHR capacity, bar coding) that have significant potential to improve medication safety at scale. However, **systematic uptake of these interventions is lagging**. Only four countries, Costa Rica, Estonia, Israel and the Netherlands, currently have implemented national programmes using barcodes to track medications for tracking and administration. To date, most digitally related interventions have been adopted by countries only in selected care settings. Seventeen countries use barcode medication administration, 14 use smart infusion pumps, and 13 use automated dispensing cabinets in at least some settings.

## Building medication safety monitoring into the COVID-19 response

The political environment caused by the COVID-19 pandemic has created an opening for meaningful reform, as deficiencies in health sector information systems have led to inadequate information for responding to the COVID crisis. COVID-19 has also provided an opening for countries to leverage COVID-19 related reforms in a way that may also address long-standing barriers in the structures, policies and institutions that have kept OECD countries from fully utilising and benefiting from health-related data. The following opportunities can be undertaken by countries as they look to adapt their health systems to the new normal to build medication safety into their COVID-19 response and recovery activities:

- The COVID-19 vaccine rollout demonstrated the importance of **real-time information sharing**, open-source data repositories and strong communication systems to identify, investigate and

[3] The German Actionplan for improving medication safety (2021 – 2024) there is a measure is currently to create this kind of list and for creating action recommendations.

respond to rare adverse events. These trends are important steps towards **strengthening pharmacovigilance systems** across OECD countries and globally—and a pathway to improving medication safety outcomes. Governments must continue to build upon the gains made in the last two years and ensure health data systems are **high-quality and interoperable; integrate eHRs with information on patient diagnosis and outcomes; and put in place fit for purpose laws and policies** that allow data linkage.

- Investments should continue to build systems that allow **patient access** to information about their medications and **capture patient experience of medication-related harms and medication side-effects**. Patient-reported safety measures related to medication safety (i.e., assessments of patient reports of medical errors) have been adopted at the national level by ten countries (Belgium, Canada, Costa Rica, Estonia, Germany, Italy, Japan, Netherlands, Türkiye, and the United States) and adopted at the sub-national level or in select institutions in six more.
- **Expanding the roles of pharmacies and pharmacists** in clinical care can improve access to medicines and other care services. Pharmacists have begun to serve as the first point of contact for patients in many countries for accessing testing or vaccination. In many countries, pharmacists have taken on new roles renewing prescriptions and helping patients access medication. In Australia, Germany, Israel, Netherlands, Norway and Switzerland, community pharmacists are able to provide emergency prescription refills. Three countries currently report that community pharmacists are permitted to administer medications, including vaccines, by injection. Clinical pharmacists are increasingly included as members of inter-disciplinary care teams in primary and hospital care, with roles including oversight of medication dispensing process and review of prescriptions for high-risk patients at admission.
- There are opportunities to build medication safety into digital advancements that have been made in the health sector. **ePrescribing systems** generate valuable data for use in drug utilisation review, which can then be used to enhance prescriber feedback mechanisms, information to patients, or advise policy makers in real time as to trends in prescribing practices. Linkages with eHRs is the next frontier—where together the **data from ePrescribing and eHRs can be used to monitor outcomes** (including, but not limited to the occurrence of medication-related harms) **in almost real-time** to enhance safe medicines use and rational use of medications.

Just as in other sectors, the process of adopting and implementing new ways of working can lead to safety lapses. **The innovations to improve medication safety in the health sector have great potential,** but require careful evaluation and calibration when implemented by countries to prevent the introduction of new safety risks.

# Résumé

Ce rapport comporte quatre volets : il 1) évalue l'impact humain et les coûts économiques des événements liés à la sécurité des médicaments dans les pays de l'OCDE, 2) explore les possibilités d'améliorer les pratiques de prescription, 3) examine l'état de l'art des systèmes et des politiques visant à améliorer la sécurité des médicaments, et 4) fournit des recommandations pour améliorer la sécurité des médicaments au niveau national.

## Une mauvaise sécurité de la médication et des résultats de prescription supra-optimaux ont un coût important.

Les mauvaises pratiques en matière de médication et l'infrastructure inadéquate du système - qui se traduisent par une mauvaise observance, des préjudices liés à la médication et des erreurs de médication - causent trop souvent des préjudices aux patients. **Dans les pays de l'OCDE, jusqu'à une hospitalisation sur dix peut être causée par un événement lié à la médication et jusqu'à un patient hospitalisé sur cinq subit des préjudices liés à la médication pendant son hospitalisation**. Les coûts liés aux admissions évitables dues à des événements liés à la médication et à l'allongement de la durée de séjour en raison des dommages évitables liés à la médication en milieu hospitalier s'élèvent à **plus de 54 milliards USD dans les pays de l'OCDE**. Ce chiffre équivaut à 11 % des dépenses pharmaceutiques totales dans les 31 pays de l'OCDE pour lesquels des données sont disponibles[4].

Au-delà des effets néfastes des médicaments, l'utilisation plus rationnelle des médicaments peut ouvrir des perspectives importantes d'amélioration des résultats pour les patients**. Près de la moitié des patients se voient prescrire des médicaments qui ne répondent pas à leurs besoins cliniques**, qu'il s'agisse de médicaments dont la posologie ou la durée ne sont pas adaptées, voire de médicaments totalement inappropriés ou de médicaments pour lesquels une autre intervention pourrait être aussi, voire plus, efficace. En outre, on estime que **la moitié de tous les médicaments** (prescrits, achetés ou délivrés) **ne sont pas pris de manière appropriée**[5]. Cette utilisation sous-optimale des ressources de santé, qui s'accompagne de frais à la charge des consommateurs et de coûts élevés pour les systèmes de santé, doit être combattue. Il existe un certain nombre de mécanismes pour promouvoir l'utilisation rationnelle des médicaments, par exemple l'utilisation de directives cliniques, de comités pharmaceutiques et thérapeutiques, d'innovations numériques, d'audits et de retours d'information pour améliorer les comportements de prescription. Il est également possible d'améliorer l'usage rationnel des médicaments par des interventions réglementaires et économiques, soutenues par une évaluation solide parallèlement à la mise en œuvre.

[4] Ventes totales de produits pharmaceutiques estimées à 478 448,30 millions de dollars US, PPA
[5] https://www.who.int/activities/promoting-rational-use-of-medicines

## Où en sont les pays en ce qui concerne l'adoption de politiques de sécurité des médicaments ?

Les pays de l'OCDE ont fait des progrès considérables dans la mise en œuvre d'outils fonctionnels pour surveiller et évaluer la sécurité des médicaments. La prochaine frontière est l'opérationnalisation de ces données pour rendre les systèmes plus sûrs en temps réel. Un certain nombre de pays peuvent être considérés comme des leaders dans ce domaine, et leurs infrastructures d'information sur la santé peuvent être considérées comme une feuille de route pour améliorer la sécurité des médicaments.

En 2022, l'OCDE a mené une enquête auprès de 20 pays de l'OCDE pour déterminer où en étaient les pays dans l'adoption de politiques visant à améliorer la sécurité des médicaments. **Le rôle de l'infrastructure d'information sur la santé dans l'amélioration de la sécurité des médicaments est essentiel** - et de plus en plus de données suggèrent que des processus efficaces d'**examen de l'utilisation des médicaments** (EUM) peuvent réduire les dommages liés aux médicaments et améliorer la sécurité. Les résultats montrent que 14 des 20 pays qui ont répondu ont maintenant des systèmes nationaux d'utilisation des médicaments. La majorité des pays répondants indiquent que les données utilisées pour l'EUM sont des données sur les demandes de remboursement, mais un nombre croissant de pays utilisent également des données provenant de systèmes de prescription électronique. Trois pays - l'Australie, le Japon et les États-Unis - incluent les données des dossiers de santé électroniques dans leurs systèmes d'EUM. Dans sept pays, soit l'Estonie, la Corée, la Norvège, les Pays-Bas, les États-Unis, la Lettonie et la Slovénie, **les données sur l'EUM sont disponibles en temps réel**. L'utilisation la plus courante des données de l'EUM concerne les décisions de couverture de remboursement, ce qui reflète le fait que la plupart des systèmes d'EUM des pays de l'OCDE fondent leurs données sur les demandes de remboursement. Cependant, un certain nombre de pays utilisent les données de l'EUM pour **améliorer la qualité de la prestation des soins de santé** et comme mécanisme pour **fournir un retour d'information aux cliniciens et aux prescripteurs.**

L'adoption de **listes nationales de médicaments de haute alerte** peut guider les responsables des soins de santé dans la mise en œuvre de mesures de protection visant à réduire la survenue d'erreurs de médication et de préjudices liés à la médication associés à une utilisation incorrecte de ces médicaments. Des listes nationales de médicaments de haute alerte ont été élaborées en Allemagne[6], en Australie, en Belgique, au Costa Rica, en Estonie, en Israël, au Japon, au Mexique, en Slovénie, en Turquie et aux États-Unis. Une autre intervention à l'échelle du système qui a la capacité d'aider à évaluer la fréquence des erreurs liées à la sécurité des médicaments - et donc d'informer les décideurs sur les mesures à prendre - consiste en de bbb, telles que les outils de déclenchement. Seuls l'Estonie, la Norvège et le Costa Rica déclarent disposer actuellement de systèmes nationaux de déclaration non volontaire utilisant des outils de déclenchement, mais l'Australie, Israël, les Pays-Bas, le Mexique, la Suisse et les États-Unis indiquent que ces outils sont utilisés dans certains contextes.

Un certain nombre d'**innovations dans le domaine de la numérisation** (pompes à perfusion intelligentes, systèmes d'administration des médicaments, prescription électronique) et de l'**infrastructure des données** (rapports des patients sur les effets nocifs des médicaments, surveillance post-commercialisation, capacité du DSE, codage à barres) offrent un potentiel important pour améliorer la sécurité des médicaments à grande échelle. Cependant, **l'adoption systématique de ces interventions tarde à se concrétiser**. Seuls quatre pays, le Costa Rica, l'Estonie, Israël et les Pays-Bas, ont actuellement mis en œuvre des programmes nationaux utilisant des codes à barres pour le suivi et l'administration des médicaments. À ce jour, la plupart des interventions liées au numérique n'ont été adoptées par les pays que dans certains milieux de soins. Dix-sept pays utilisent l'administration des

[6] Le plan d'action allemand pour l'amélioration de la sécurité des médicaments (2021 - 2024) prévoit actuellement la création de ce type de liste et la formulation de recommandations d'action.

médicaments par code-barres, 14 utilisent des pompes à perfusion intelligentes et 13 utilisent des armoires de distribution automatisées dans au moins certains milieux.

## Intégrer le contrôle de la sécurité des médicaments dans la réponse au COVID-19

L'environnement politique provoqué par la pandémie de COVID-19 a créé une ouverture pour une réforme significative, car les déficiences des systèmes d'information du secteur de la santé ont conduit à une information inadéquate pour répondre à la crise du COVID. La pandémie COVID-19 a également permis aux pays de tirer parti des réformes liées à la pandémie COVID-19 d'une manière qui pourrait également permettre de lever les obstacles de longue date dans les structures, les politiques et les institutions qui ont empêché les pays de l'OCDE d'utiliser pleinement les données relatives à la santé et d'en tirer profit. Les possibilités suivantes peuvent être exploitées par les pays qui cherchent à adapter leurs systèmes de santé à la nouvelle normalité pour intégrer la sécurité des médicaments dans leurs activités d'intervention et de rétablissement liées à COVID-19 :

- Le déploiement du vaccin COVID-19 a démontré l'importance du **partage de l'information en temps réel**, des dépôts de données à source ouverte et des systèmes de communication solides pour identifier, étudier et répondre aux événements indésirables rares. Ces tendances constituent des étapes importantes vers le **renforcement des systèmes de pharmacovigilance** dans les pays de l'OCDE et dans le monde entier - et une voie vers l'amélioration des résultats en matière de sécurité des médicaments. Les gouvernements doivent continuer à s'appuyer sur les progrès réalisés au cours des deux dernières années et s'assurer que les systèmes de données de santé sont de **haute qualité et interopérables, qu'ils intègrent les DSE avec des informations sur le diagnostic et les résultats des patients, et qu'ils mettent en place des lois et des politiques adaptées** qui permettent de relier les données.
- Les investissements devraient se poursuivre pour mettre en place des **systèmes permettant aux patients d'accéder aux informations** sur leurs médicaments et de **saisir l'expérience des patients en matière de dommages et d'effets secondaires des médicaments.** Des mesures de la sécurité des médicaments rapportées par les patients (c'est-à-dire des évaluations des erreurs médicales signalées par les patients) ont été adoptées au niveau national par dix pays (Allemagne, Belgique, Canada, Costa Rica, Estonie, Italie, Japon, Pays-Bas, Turquie et États-Unis) et adoptées au niveau infranational ou dans certains établissements dans six autres.
- **L'élargissement du rôle des pharmacies et des pharmaciens** dans les soins cliniques peut améliorer l'accès aux médicaments et aux autres services de soins. Dans de nombreux pays, les pharmaciens ont commencé à être le premier point de contact des patients pour l'accès aux tests ou à la vaccination. Dans de nombreux pays, les pharmaciens ont assumé de nouveaux rôles en renouvelant les ordonnances et en aidant les patients à accéder aux médicaments. En Australie, en Allemagne, en Israël, aux Pays-Bas, en Norvège et en Suisse, les pharmaciens communautaires sont en mesure de renouveler les ordonnances en urgence. Trois pays indiquent actuellement que les pharmaciens communautaires sont autorisés à administrer des médicaments, y compris des vaccins, par injection. Les pharmaciens cliniques font de plus en plus partie des équipes de soins interdisciplinaires dans le cadre des soins primaires et hospitaliers, leurs rôles comprenant la supervision du processus de délivrance des médicaments et l'examen des ordonnances pour les patients à haut risque lors de leur admission.
- **Les systèmes de prescription électronique** génèrent des données précieuses pour l'examen de l'utilisation des médicaments, qui peuvent ensuite être utilisées pour améliorer les mécanismes de retour d'information des prescripteurs, l'information des patients ou pour conseiller les décideurs en temps réel sur les tendances des pratiques de prescription. La prochaine étape consistera à établir des liens avec les DSE, où **les données provenant de la prescription en ligne et des DSE pourront être utilisées pour surveiller les résultats** (y compris, mais sans s'y limiter,

l'apparition d'effets néfastes liés aux médicaments) **en temps quasi réel** afin d'améliorer l'utilisation sûre et rationnelle des médicaments.

Tout comme dans d'autres secteurs, le processus d'adoption et de mise en œuvre de nouvelles méthodes de travail peut entraîner des lacunes en matière de sécurité. **Les innovations visant à améliorer la sécurité des médicaments dans le secteur de la santé ont un grand potentiel**, mais elles doivent être évaluées et calibrées avec soin lorsqu'elles sont mises en œuvre par les pays afin d'éviter l'introduction de nouveaux risques pour la sécurité.

# Zusammenfassung

Der vorliegende Bericht umfasst vier Teile. Im ersten Teil werden die menschlichen und wirtschaftlichen Kosten medikationsbedingter sicherheitsrelevanter Ereignisse im OECD-Raum untersucht. Der zweite Teil beschreibt Möglichkeiten zur Verbesserung der Verordnungspraxis, der dritte Teil befasst sich mit den neusten Systemen und Maßnahmen zur Verbesserung der Arzneimitteltherapiesicherheit und im vierten Teil folgen Empfehlungen zur Verbesserung der Arzneimitteltherapiesicherheit auf nationaler Ebene.

## Defizite bei der Arzneimitteltherapiesicherheit und suboptimale Verordnungen verursachen beträchtliche Kosten

Durch ungeeignete Arzneimitteltherapien und inadäquate Systeminfrastrukturen, die unzureichende Adhärenz, medikationsbedingte Schäden und Medikationsfehler nach sich ziehen, kommen nur allzu oft Patient*innen zu Schaden. **Im OECD-Raum ist möglicherweise ein Zehntel der Krankenhauseinweisungen auf medikationsbedingte Ereignisse zurückzuführen, und bei einem Fünftel der stationär behandelten Patient*innen treten während des Krankenhausaufenthalts medikationsbedingte Schädigungen auf.** Die Kosten der vermeidbaren, auf medikationsbedingte Ereignisse zurückzuführenden Hospitalisierungen sowie der längeren Krankenhausaufenthalte aufgrund von vermeidbaren, im Krankenhaus auftretenden medikationsbedingten Schäden **belaufen sich im OECD-Raum insgesamt auf mehr als 54 Mrd. USD**. Dies entspricht 11 % der gesamten Arzneimittelausgaben in den 31 OECD-Ländern, für die Daten verfügbar sind.[7]

Ein rationalerer Arzneimitteleinsatz verringert nicht nur die medikationsbedingten Schäden, sondern kann auch maßgeblich zur Verbesserung der Patientenergebnisse beitragen. **Fast der Hälfte aller Patient*innen werden Arzneimitteltherapien verordnet, die nicht ihren klinischen Bedürfnissen entsprechen** – sei es durch eine inadäquate Dosierung oder Behandlungsdauer, völlig ungeeignete Arzneimittel oder einen Arzneimitteleinsatz in Fällen, in denen eine alternative Therapie möglicherweise ebenso wirksam – oder wirksamer – wäre. Darüber hinaus wird Schätzungen zufolge **die Hälfte aller** (verordneten, gekauften bzw. ausgegebenen) **Arzneimittel nicht ordnungsgemäß eingenommen.**[8] Durch diesen suboptimalen Einsatz von Gesundheitsressourcen fallen Kosten für Patient*innen und hohe Kosten für Gesundheitssysteme an, daher sollten geeignete Vorbeugungsmaßnahmen ergriffen werden. Zur Förderung eines rationalen Arzneimitteleinsatzes bietet sich eine Reihe von Mechanismen an. Hierzu zählen beispielsweise klinische Leitlinien, Arzneimittel- und Therapiekommissionen, digitale Innovationen sowie Audits und Feedback, um das Verordnungsverhalten zu optimieren. Auch regulatorische und wirtschaftliche Maßnahmen können zu einem rationaleren Arzneimitteleinsatz beitragen, insbesondere wenn die Umsetzung mit einer belastbaren Evaluierung einhergeht.

7 Der Arzneimittelumsatz beträgt Schätzungen zufolge insgesamt 478 448,30 Mio. USD (in KKP).
8 https://www.who.int/activities/promoting-rational-use-of-medicines.

## Welche Maßnahmen zur Verbesserung der Arzneimitteltherapiesicherheit wurden auf Länderebene bereits ergriffen?

Bei der Umsetzung funktionaler Instrumente zur Überwachung und Beurteilung der Arzneimitteltherapiesicherheit haben die OECD-Länder beträchtliche Fortschritte erzielt. Nun geht es darum, die Sicherheit der Systeme mithilfe von Echtzeit-Daten zu erhöhen. Einige Länder können in dieser Hinsicht als Vorreiter gelten. Ihre Gesundheitsdateninfrastrukturen veranschaulichen, wie die Arzneimitteltherapiesicherheit verbessert werden kann.

Die OECD führte 2022 in 20 Mitgliedsländern eine Erhebung durch, um zu ermitteln, inwieweit in diesen Ländern bereits Maßnahmen zur Verbesserung der Arzneimitteltherapiesicherheit umgesetzt wurden. **Die Gesundheitsdateninfrastruktur ist bei der Verbesserung der Arzneimitteltherapiesicherheit von grundlegender Bedeutung.** Immer mehr Befunde zeigen zudem, dass effektive Verfahren zur kritischen Betrachtung des Gebrauchs von Arzneimitteln bzw. **Drug-Utilisation-Reviews** (DUR) die medikationsbedingten Schäden reduzieren und die Arzneimitteltherapiesicherheit erhöhen können. Der OECD-Erhebung zufolge verfügen 14 der 20 teilnehmenden Länder bereits über ein entsprechendes System auf nationaler Ebene. Die meisten Teilnehmerländer berichten, dass für die Drug-Utilisation-Reviews auf Abrechnungsdaten zurückgegriffen wird. Immer mehr Länder beziehen dabei jedoch auch die Daten aus elektronischen Verordnungen mit ein. In drei Ländern – Australien, Japan und den Vereinigten Staaten – werden bei den Drug-Utilisation-Reviews auch die Daten der elektronischen Patientenakten berücksichtigt. In sieben Ländern – Estland, Korea, Norwegen, den Niederlanden, den Vereinigten Staaten, Lettland und Slowenien – **werden die Daten der Drug-Utilisation-Reviews in Echtzeit zur Verfügung gestellt**. Genutzt werden diese Daten vor allem für Erstattungsentscheidungen, was erklärt, warum die DUR-Systeme der meisten OECD-Länder auf Abrechnungsdaten basieren. Einige Länder nutzen die Daten der Drug-Utilisation-Reviews **zur Verbesserung der Versorgungsqualität** und **als Feedback-Mechanismus für medizinische Fachkräfte und Verordner*innen**.

**Nationale Listen von Hochrisikoarzneimitteln** können Entscheidungsträgern in der Gesundheitsversorgung dabei helfen, Sicherheitsmaßnahmen umzusetzen, die die Prävalenz von Medikationsfehlern und medikationsbedingten Schäden aufgrund eines inadäquaten Einsatzes solcher Arzneimittel verringern. Australien, Belgien, Costa Rica, Deutschland,[9] Estland, Israel, Japan, Mexiko, Slowenien, Türkiye und die Vereinigten Staaten verfügen bereits über entsprechende Listen. **Neue Erfassungstechniken** wie Trigger-Tools können auf Systemebene Defizite im Bereich der Arzneimitteltherapiesicherheit ermitteln helfen und Politikverantwortlichen zeigen, wo Handlungsbedarf besteht. Über ein nationales Erfassungssystem mit Trigger-Tools verfügen derzeit lediglich Costa Rica, Estland und Norwegen. In Australien, Israel, Mexiko, den Niederlanden, der Schweiz und den Vereinigten Staaten werden in einigen Settings Trigger-Tools eingesetzt.

Einige **Innovationen in den Bereichen Digitalisierung** (intelligente Infusionspumpen, Arzneimittelverabreichungssysteme, elektronische Verordnungen) und **Dateninfrastruktur** (Patientenberichte über medikationsbedingte Schäden, Überwachung nach Markteinführung, ePA-Fähigkeit, Barcodes) können maßgeblich dazu beitragen, die Arzneimitteltherapiesicherheit umfassend zu verbessern. **Die systemweite Einführung dieser Innovationen geht allerdings nur schleppend voran**. Nationale Programme mit Barcodes für die Nachverfolgung und Verabreichung der Medikation wurden bis dato nur in vier Ländern eingeführt – Costa Rica, Estland, Israel und den Niederlanden. Die meisten digitalisierungsbezogenen Maßnahmen wurden bislang lediglich in ausgewählten Versorgungssettings umgesetzt. So nutzen 17 Länder zumindest in manchen Settings Barcodes bei der Verabreichung von Arzneimitteln, 14 intelligente Infusionspumpen und 13 automatisierte Arzneimittelausgabesysteme.

[9] Deutschlands Aktionsplan zur Verbesserung der Arzneimitteltherapiesicherheit (2021–2024) sieht die Erstellung einer solchen Liste und die Erarbeitung von Handlungsempfehlungen vor.

## Im Rahmen der Covid-19-Maßnahmen ein Monitoring der Arzneimitteltherapie-sicherheit vorsehen

Das durch die Covid-19-Pandemie entstandene Politikumfeld bietet die Chance für eine umfassende Reform, da aufgrund von Defiziten in den Gesundheitsinformationssystemen für Politikmaßnahmen zur Bewältigung der Covid-19-Krise nicht genügend Daten zur Verfügung stehen. Außerdem können die Länder im Zuge der pandemiebedingten Reformen auch seit Langem bestehende Hindernisse in den Strukturen, Maßnahmen und Einrichtungen beseitigen, die die OECD-Länder bislang davon abgehalten haben, Gesundheitsdaten umfassend zu nutzen und auszuschöpfen. Um die Gesundheitssysteme auf die neue Normalität auszurichten und die Arzneimitteltherapiesicherheit bei den Maßnahmen zur Bekämpfung von Covid-19 und zur Unterstützung der wirtschaftlichen Erholung zu berücksichtigen, bieten sich den Ländern folgende Möglichkeiten:

- Die Covid-19-Impfkampagnen haben deutlich gemacht, wie wichtig ein **Informationsaustausch in Echtzeit**, Open-Source-Datenbanken und solide Kommunikationssysteme sind, um selten auftretende unerwünschte Ereignisse zu erkennen, zu untersuchen und entsprechende Maßnahmen zu ergreifen. Die Entwicklungen in diesen Bereichen sind wichtige Schritte zur **Stärkung der Pharmakovigilanzsysteme** im OECD-Raum und auf globaler Ebene – und eine Chance, im Bereich der Arzneimitteltherapiesicherheit bessere Ergebnisse zu erzielen. Dazu müssen die Länder die in den letzten beiden Jahren erzielten Fortschritte weiter ausbauen und sicherstellen, dass die Gesundheitsdatensysteme **hochwertig und interoperabel** sind, **Daten zu Diagnosen und Patientenergebnissen in ePA integrieren** und **geeignete gesetzliche Bestimmungen und Maßnahmen umsetzen**, um die Verknüpfung der Daten zu ermöglichen.
- Es bedarf weiterer Investitionen, um Systeme aufzubauen, in denen die **Patient*innen Zugriff** auf Informationen über ihre Arzneimitteltherapien haben und **Patientenerfahrungen in Bezug auf medikationsbedingte Schäden und Nebenwirkungen von Arzneimitteln** erfasst werden. Zehn Länder haben auf nationaler Ebene auf Patientenberichten beruhende Indikatoren für die Arzneimitteltherapiesicherheit (d. h. die Auswertung von Patient*innen gemeldeter Behandlungsfehler) eingeführt – Belgien, Costa Rica, Deutschland, Estland, Italien, Japan, Kanada, die Niederlande, Türkiye und die Vereinigten Staaten. In sechs weiteren Ländern wurden solche Indikatoren auf subnationaler Ebene oder in ausgewählten Einrichtungen eingeführt.
- Durch eine **Ausweitung der Aufgaben von Apotheken und Apotheker*innen** bei der Patientenversorgung kann der Zugang zu Arzneimitteln und anderen Versorgungsleistungen verbessert werden. In Bezug auf Tests oder Impfungen entwickeln sich die Apotheken in vielen Ländern allmählich zur ersten Anlaufstelle für Patient*innen. In zahlreichen Ländern haben die Apotheker*innen neue Aufgaben übernommen. Sie verlängern Verordnungen und stellen sicher, dass Patient*innen Zugang zu Arzneimitteln haben. In Australien, Deutschland, Israel, den Niederlanden, Norwegen und der Schweiz können Apotheken in Notfällen Verordnungen erneuern. In drei Ländern können Apotheken Injektionen verabreichen, z. B. Impfungen. Klinische Pharmazeut*innen werden in der Primärversorgung und bei der stationären Behandlung zunehmend in die interdisziplinären Versorgungsteams eingebunden und übernehmen Aufgaben wie die Überwachung der Arzneimittelausgabe und die Überprüfung der Verordnungen für Hochrisikopatient*innen bei deren Einweisung.
- Es gibt verschiedene Möglichkeiten, mit digitalen Innovationen im Gesundheitssektor zur Verbesserung der Arzneimitteltherapiesicherheit beizutragen. **Elektronische Verordnungssysteme** etwa generieren wertvolle Daten für Drug-Utilisation-Reviews, mit denen auch die Feedback-Mechanismen für Verordner*innen und die Patienteninformation verbessert und Politikverantwortliche in Echtzeit über Entwicklungstrends bei den Verordnungspraktiken informiert werden können. Der nächste Schritt wäre die Verknüpfung dieser Daten mit den ePA, damit **die Daten aus elektronischen Verordnungen und die Daten aus den ePA fast in Echtzeit zur**

**Überwachung der Ergebnisse** (auch aber nicht ausschließlich im Hinblick auf medikationsbedingte Schäden) verwendet werden können und ein sicherer und rationaler Arzneimitteleinsatz gefördert werden kann.

Die Einführung und Umsetzung neuer Vorgehensweisen kann, wie in anderen Sektoren auch, zu Sicherheitsdefiziten führen. **Die Innovationen zur Verbesserung der Arzneimitteltherapiesicherheit im Gesundheitssektor besitzen großes Potenzial,** müssen bei ihrer Einführung in den einzelnen Ländern jedoch sorgfältig evaluiert und kalibriert werden, um der Entstehung neuer Sicherheitsrisiken vorzubeugen.

# Table of contents

OECD Health Working papers 3

Acknowledgements 4

Key messages 5

Executive Summary 6

Résumé 9

Zusammenfassung 13

The Economics of Patient Safety Series 20

Acronyms 21

1 Medication-related harms and errors are not rare events and have significant economic impact 22

There has been limited progress in improving medication safety due to a number of converging factors 22

The occurrence of medication errors can lead to an erroneous feedback loop—compounding harms 23

Increased medication use is associated with more medication errors and medication-related harms 29

The prevalence of inappropriate prescribing is substantial, and possibly increasing 31

The economic impacts of medication-related harms events on health systems 32

The economic case for improving medication safety 34

2 Reducing inappropriate prescribing and improving the rational use of medicines 37

The irrational use of medicines: prescribing the wrong medication, overuse and underuse 37

Strategies to improve rational use 40

3 Improving medication safety throughout the care pathway—the state of the art in OECD countries 44

National strategies to improve medication safety 44

Pharmacovigilance and Drug Utilisation Review 45

The status of adoption of digitalisation and medication patient safety initiatives 54

4 Building medication safety into the COVID-19 recovery 59
The dynamics created by COVID-19 can be used to accelerate change 59
Improving the functionality of data for monitoring medication safety in real-time 59
Using good patient safety governance and transparency to build public trust 60
Capitalising on COVID-19 related improvements in access, including care in pharmacies and digital health 64
Conclusions 67

References 68

Annex A. National Contact Points for Snapshot Survey 84

Annex B. Assumptions used in modelling the economic burden of unsafe medication practices in OECD countries 85

OECD Health Working Papers 86

Recent related OECD publications 87

## Tables

Table 1.1. Frequency of side-effects with different medication types 29
Table 1.2. Examples of national level estimates of the economic impact of medication-related harms 34
Table 1.3. Recent examples of potential saving assessments by interventions to improve medication safety 36
Table 2.1. Overview of strategies to enhance rational prescribing in primary care in 13 countries 41
Table 3.1. Selected examples of national medication safety regulations or strategies 44
Table 3.2. Use of DUR data for provider feedback, quality improvement, and policy purposes 54

## Figures

Figure 1.1. Factors contributing to increased use of medications have all been on the rise 22
Figure 1.2. Each medication-related harm increases the likelihood of a subsequent event 24
Figure 1.3. Population at age 75 and over taking more than five medications concurrently, 2012, 2019 (or nearest year) and 2020 28
Figure 1.4. Total pharmaceutical spending averages, 2018: Real net pharmaceutical spending as a percentage of healthcare 32
Figure 1.5. Expenditure on retail pharmaceuticals per capita, 2019 (or nearest year) 32
Figure 1.6. Percentage of patients who report that they skipped prescribed medicines due to cost, 2020 or most recent year 33
Figure 1.7. Major pathways of release of human and veterinary pharmaceuticals into the environment 34
Figure 2.1. People with diabetes prescribed recommended anti-hypertensive medication in the past year in primary care, 2019 (or nearest year) and 2020 40
Figure 3.1. Scope of Drug Utilisation Review Systems in OECD Countries 48
Figure 3.2. Information on medicines collected via the above Drug Utilisation Review System 50
Figure 3.3. DUR data sources and access to DUR data by stakeholders 50
Figure 3.4. DUR linkage capacity to other data sets 51
Figure 3.5. Uptake of interventions to improve medication safety related to care coordination 55
Figure 3.6. Status of adoption of digitization and medication safety initiatives by level of adoption by country 57
Figure 4.1. Health Workers perceptions of nonpunitive response to errors, data from latest year by country 62
Figure 4.2. Patients reporting that they experienced a medication-related mistake, 2020 (or nearest year) 63
Figure 4.3. Countries reporting expanded roles for clinical and community pharmacists 66

## Boxes

Box 1.1. Key terms and definitions 26
Box 1.2. Medication safety as a lever of health systems sustainability 34
Box 2.1. *The overuse of sedatives in the treatment of insomnia: the case of the Australian Veterans' MATES Program* 39
Box 3.1. United States FDA Sentinel Initiative 46
Box 3.2. Korea's Drug Utilisation Review Program 49
Box 3.3. Japan's Medical Information Database NETwork (MID-NET®) for improving medication safety monitoring 52

# The Economics of Patient Safety Series

- The Economics of Patient Safety: From analysis to action (2022)
- The Economics of Patient Safety Part IV: Safety in the workplace - Occupational safety as the bedrock of resilient health systems (2021)
- The Economics of Patient Safety Part III: Long-term care - Valuing safety for the long haul (2020)
- The Economics of Patient Safety in Primary and Ambulatory Care: Flying Blind (2018)
- The Economics of Patient Safety: Strengthening a value-based approach to reducing patient harm at national level (2017)

# Acronyms

| | |
|---|---|
| ACE | Angiotensin-converting enzyme |
| AMR | Antimicrobial resistance |
| AME | Adverse medication event |
| AE | Adverse event |
| AIFA | Italian Medicines Agency |
| CIHI | Canadian Institute for Health Information |
| CMS | Center for Medicare and Medicaid Services (United States) |
| CME | Continuing Medical Education |
| COVID-19 | Coronavirus Disease 2019 |
| DUR | Drug Utilisation Review |
| ED | Emergency department |
| eHR | Electronic health record |
| eMP | Electronic medication treatment plan (Germany) |
| EU | European Union |
| EVDAS | EudraVigilance data analysis system |
| GIPGenees- en | Hulpmiddelen Informatie Project (Drug Information System, Netherlands) |
| HHS | Health and Human Services (United States) |
| HIRA | Health Insurance Review and Assessment Service (Korea) |
| ICU | Intensive care unit |
| KIDS | Korea Institute of Drug Safety and Risk Management |
| LOS | Length of stay |
| LTC | Long-term care |
| MFDS | Ministry of Food and Drug Safety (Republic of Korea) |
| MOHW | Ministry of Health and Welfare (Republic of Korea) |
| MRAEs | Medication-related adverse events |
| NNH | Number needed to harm |
| NNT | Number needed to treat |
| NorPD | Norwegian Prescription Database |
| NPDUIS | National Prescription Drug Utilization Information System (Canada) |
| NSAIDs | Non-steroidal anti-inflammatory drugs |
| OECD | Organisation for Economic Cooperation and Development |
| pDDI | potential drug-drug interaction |
| PHC | Primary Health Care |
| PIMs | Potentially inappropriate medications |
| PS | Patient Safety |
| PSC | Patient Safety Culture |
| SFK | Stichting Farmaceutische Kengetallen (Foundation for Pharmaceutical Statistics Netherlands) |
| TGA | Therapeutic Goods Administration (Australia) |
| WHO | World Health Organisation |
| ZIN | National Health Care Institute (Netherlands) |

# 1 Medication-related harms and errors are not rare events and have significant economic impact

## There has been limited progress in improving medication safety due to a number of converging factors

The use of prescription medicines is so prevalent in OECD countries that both clinicians and patients alike may at times lose sight of their potential harms. Pharmaceutical consumption has been increasing for decades, driven in part by a growing demand for treatment of age-related and chronic diseases, and by evolution in clinical practice. Global consumption of pharmaceuticals was estimated to be as high as 4.5 trillion doses in 2020 (IMS, 2015[1]) The use of medicines continues to increase and has been estimated to have increased globally by one-third over the last decade (IQVIA, 2021[2]).

As the use of medicines has increased, so has the number of medications approved for use. Between 2009 and 2017, the US FDA approved 302 new drugs, up from 209 over the previous 8-year period representing a 44% increase (Batta, Kalra and Khirasaria, 2020[3]). Over 20,000 prescription pharmaceutical products are currently approved for marketing by the US FDA (FDA, 2020[4]). Across the European Economic Area (EEA), there are over 85,000 approved pharmaceutical products across authorising agencies, using over 13,000 active ingredients (European Medicines Agency, 2021[5]).

### Figure 1.1. Factors contributing to increased use of medications have all been on the rise


Source: Authors

Increases in pharmaceutical availability have converged with demographic changes in recent decades, as the number of people living with chronic conditions has grown as OECD country populations age. These patients often have complex needs, including complex medication regimens to control multiple conditions. Most medications for chronic health conditions are designed for ongoing use, as opposed to time limited use. As of 2019, over 45% of people over age 75 in OECD countries are taking five or more medications concurrently (OECD, 2021[6]). While medicines are intended to benefit patients, inappropriate prescribing and multiple medicine use, also described as polypharmacy, exerts a considerable burden on both patients and health systems. All of these factors together have resulted in an increase in medications use, which in turn increases the likelihood of medication-related harms (see Figure 1.1).

The availability of over-the-counter (OTC) medications, often without prescriber or pharmacist oversight or counselling, further complicates health systems' capacity to ensure medication safety. Information on a patient's OTC medicine use may often be lacking or incomplete, patient counselling may not be available at point-of-sale, and patients may be unaware of the potential risks of products that they are taking or administering, particularly those arising from interactions with prescription medications. Across OECD countries in 2019, 21% of pharmaceutical expenditures was directed to OTC products (OECD, 2021[6]). This estimate varies widely from country to country, largely due to differences in the coverage of prescription medicines, but also to prices and availability of different medicines. At the population level, the use of OTC medicines is highly prevalent. For example, in Germany, the 7-day prevalence of use of at least one OTC medicine was 40% (Eickhoff et al., 2012[7]).

Despite increasing awareness of medication safety issues over the last two decades, progress in improving medicine use has stalled. Healthcare systems generally lack robust mechanisms to measure medication safety events (Pronovost et al., 2016[8]). Different indicators are used to measure medication safety problems and there remains limited investment in harmonizing these measures and creating infrastructure to monitor the problems routinely. Moreover, despite the development of and evidence to support effective interventions for improving medication safety, implementation varies widely (Bates and Singh, 2018[9]). For example, staff may find work-around solutions when faced with digital technologies that don't fit their work-flow (e.g., omitted steps, incorrect sequence, and unauthorized steps in bar coding), which negate the potential benefits (Koppel et al., 2008[10]). Healthcare providers need to be involved in the adaptation and implementation of medication safety interventions to ensure that contextual issues such as clinical workflow, training, human factors, and organization are taken into account. Their engagement facilitates intervention uptake and effectiveness (Jeffries et al., 2017[11]).

Health data infrastructure and monitoring systems to ensure safe medication use have not kept up with the demands placed on systems as medication use has proliferated (OECD, 2019[12]). There are numerous opportunities to improve care that remain untapped—from the political level down to individual interactions between patients and providers.

This report includes four components; it 1) assess the human impact and economic costs of medication safety events in OECD countries, 2) explores opportunities to improve prescribing practices 3) examines the state-of-the art in systems and policies for improving medication safety, and 4) provides recommendations for improving medication safety at the national level.

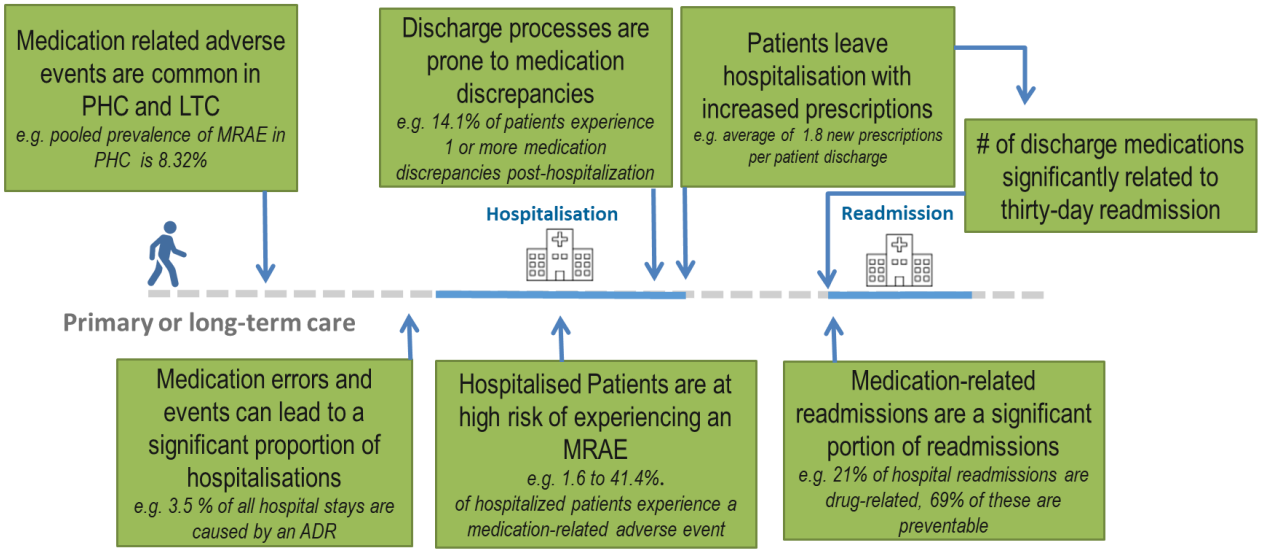
## The occurrence of medication errors can lead to an erroneous feedback loop—compounding harms

Medication-related harms events are common in all settings of care. A systematic review of thirty-three studies in primary care, with a total study population of 1.5 million individuals, found that the pooled prevalence of medication-related harms was 8% (Insani et al., 2021[13]). Research in long-term care facilities has revealed that overall rates of medication-related harms reach nearly 1 per 10 resident months (Gurwitz et al., 2005[14]).

Medication use outside the hospital is a common factor contributing to hospital admissions. More than 1 in 10 hospitalisations in OECD countries is likely caused by a medication-related event. A systematic review assessing rates of medication-related hospital admissions in 12 countries, the majority relating to unplanned hospital admissions or admissions in the older population, found that over 15% of hospital admissions were associated with medication-related problems (Ayalew, Tegegn and Abdela, 2019[15]). To put this in perspective, the number of medication-related admissions may be higher than some of the most common reasons for hospital admission, such as pneumonia or heart disease (Salah et al., 2021[16]).

While medication-related harms may lead to admissions, they are also commonly experienced while patients are in the hospital. A systematic review including studies from the UK, US, Netherlands, Finland and New Zealand found that medication-related harms affect approximately 19% of inpatients during hospitalisation (Laatikainen et al., 2017[17]). As many as two out of three patients may experience a medication error during the hospital admission process, prescribing errors occur at the rate of almost one per patient, and administration errors at approximately one-in-ten. Compounding this is that the risk of experiencing a MRAE increases by 0.5% with each additional night of a hospital stay (Roughead, Semple and Rosenfeld, 2016[18]; Tran et al., 2019[19]). Given that the occurrence of an MRAE typically results in an increased length of stay, the risk of experiencing a subsequent MRAE is also increased. Hospitalisations not only de facto raise the risk of anti-microbial resistant infections (AMR), they also increase rates of polypharmacy, which in turn increase the risk of AMRs. Findings from Italy looking at more than one thousand patients 65 and older found that the prevalence of polypharmacy was 52% at hospital admission and 67% at discharge (Nobili et al., 2011[20]). Up to two errors per patient have been reported in medication documentation in discharge summaries in Australia (Roughead, Semple and Rosenfeld, 2016[18]). And when patients leave the hospital, they often do so with additional prescribed medications—each of which increases the likelihood of readmission (See Figure 1.2).

## Figure 1.2. Each medication-related harm increases the likelihood of a subsequent event



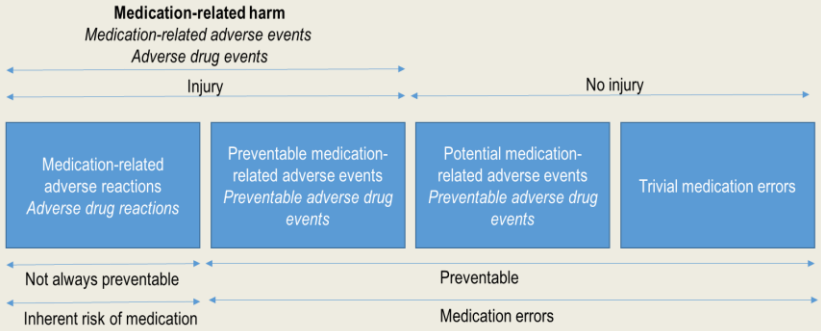

Source: Authors using data from (Cano and Rozenfeld, 2009[21]; Bouvy, De Bruin and Koopmanschap, 2015[22]; Wolfe et al., 2018[23]; El Morabet et al., 2018[24]; Coleman et al., 2005[25]; Picker et al., 2015[26]; Elson, Cook and Blenkinsopp, 2017[27]; Gurwitz et al., 2005[14]). Inspired by similar figure in (Roughead, Semple and Rosenfeld, 2016[18]) and based on a template developed by Eliana Barrenho.

Failure to identify medication-related harms can also trigger a cascade of inappropriate prescribing, particularly when a new medicine is prescribed to treat an anti-microbial resistant infections associated with another medicine, or where the adverse outcome is mistaken for a new medical condition requiring treatment (Kalisch et al., 2011[28]). Both recognised and unrecognised AMEs can contribute to

inappropriate prescribing, setting off prescribing cascades that can further threaten patient safety (McCarthy, Visentin and Rochon, 2019[29]). Medications commonly associated with prescribing cascades include those for dementia, as well as antihypertensives, sedatives, opioids, NSAIDs, anticonvulsants, antibiotics, and antiemetics) (Kalisch et al., 2011[28]).

### Box 1.1. Key terms and definitions[10]

- **Patient safety incident**: An event or circumstance which could have resulted, or did result, in unnecessary harm to a patient
- **Medication error**: An unintended failure of a medication that leads to, or has the potential to lead to, harm to the patient [EU-GVP Annex I].
- **Medication-related harm/ Adverse medication event (AME)/ Medication-related adverse event (MRAE)**: An injury or harm caused by the use of medicine (also referred to as an adverse drug event) (Laatikainen, Sneck and Turpeinen, 2022[30]; IOM, 2007[31]). In definitions used by the EU, the experienced harm does not necessarily have a causal relationship with this treatment. [Regulation (EU) No 536/2014 Art 2(2)(32)].




Source: adapted from (US HHS, 2014[32]; WHO, 2019[33])

- **Side effect:** A harmful or unpleasant secondary effect which occurs in addition to the desired therapeutic effect of a medication.
- **Adherence:** the extent to which a person's behaviour (e.g. taking medication) corresponds with agreed recommendations from a health care provider (WHO, 2003[34])
- **Drug utilisation review**: An authorised, structured, ongoing review of prescribing, dispensing and use of medication (AMCP, 2019[35]).
- **Medication review:** A structured review of a patient's medication conducted between a clinician and a patient.
- **Potentially inappropriate medication**: Medications that have side effects that outweigh the clinical benefits, particularly when there are safer or more effective alternatives (Thorell et al., 2019[36]).
- **Potentially inappropriate medication combination**: The influence of a medication on the efficacy of another medication simultaneously taken, putting the patient at risk of drug-drug interactions (Migliazza et al., 2021[37]).
- **Polypharmacy**: The usage of multiple medications. The most commonly reported numerical definition is five or more medications used daily (Masnoon et al., 2017[38]).

## *Medicines for chronic conditions are increasingly widely used*

In 2019, on average more than one-third of people aged 16 and over across 26 OECD countries reported living with a longstanding illness or health problem (OECD, 2021[6]). This has led to significant increases in the consumption of medications used to treat common chronic health conditions, including anti-hypertensives, lipid-modifying agents (such as cholesterol-lowering medicines), anti-diabetic agents and anti-depressants. Consumption of anti-hypertensive medications, for example, increased by 65% on average between 2000 and 2019. Even greater growth was observed in the use of lipid-modifying agents,

[10] **Disclaimer**: Due to variation in the use and application of definitions and terminology between and within countries, cited works in this report require careful interpretation due to potential differences in the interpretation and use of terms.

with consumption in OECD countries increasing by a factor of nearly four between 2000 and 2019. Anti-diabetic and anti-depressant medication use also doubled over the same period.

A person-centred approach to medications use must consider that the effects of medications are typically heterogeneous, and benefit some patients more than others. Data on which subgroups of patients are likely to derive the greatest benefit from a specific therapy are often lacking, which can make individual prescribing decisions challenging. Further complicating the issue, clinical trials continue to report findings in terms of relative effects, which tend to exaggerate findings of modest benefit and are more difficult to interpret (Elliott et al., 2021[39]).

When clinical trial results are expressed in terms of absolute effects–such as number needed to treat (NNT) or number needed to harm (NNH)–clinicians, patients and policy makers can gain a much more clinically meaningful picture of the balance of benefits and harms of a medication. For example, the use of statins for the primary prevention of cardiovascular events in the elderly has been a controversial issue. An individual patient-level data meta-analysis of the effects of statins a significant reduction in major vascular events in all age groups (Armitage et al., 2019[40]). However, in a separate analysis, when the data were compiled to reflect the absolute effects, the NNT for major vascular events in patients over 75 without vascular disease was 446 people per good outcome (whereas out of every 223 people one bad outcome is expected) (Heneghan and Mahtani, 2019[41]). Reporting these data in terms of absolute effects revealed that patients over 75 years of age with no vascular disease are unlikely to benefit from statin therapy.

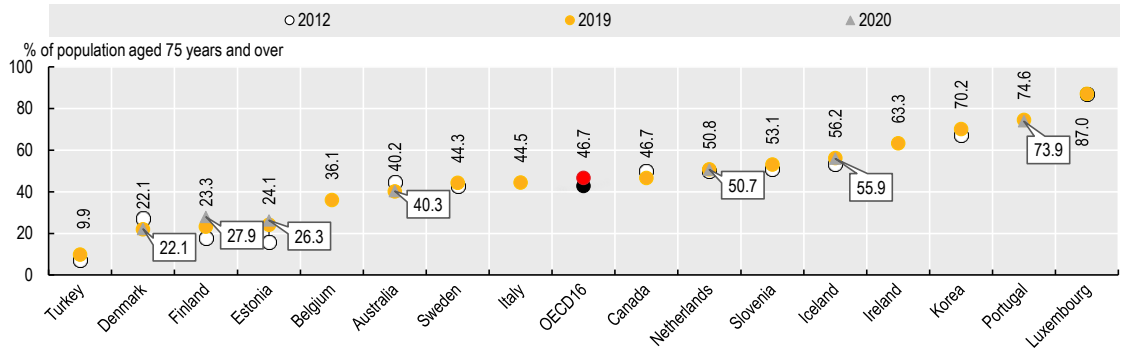
### *Non-pharmacological treatment alternatives are underused despite their demonstrated effectiveness to treat several chronic conditions*

The healthcare system is largely structured around the use of medicines to treat and manage disease. While for some conditions, medications are the only effective treatment available, relying on medication as the initial or sole approach to disease management exposes patients to excessive risk. Across some conditions, an emerging evidence base is pointing towards non-pharmacologic interventions that are equally effective and pose less risk to patients. For example, clinical guidelines for the treatment of chronic low back pain recommend initial treatment with non-pharmacologic interventions such as exercise, physical rehabilitation, and cognitive behavioural therapy (AAFP, 2017[42]). Yet, for many patients the treatment remains solely pharmacological. Barriers to the uptake and use of non-pharmacological interventions exist at all levels and must be addressed to make access to and use of these options more frequent and reduce overall exposure to unnecessary medication (Becker et al., 2017[43]) .

### *Increasing use of pharmacological treatment for chronic conditions is a contributing factor to potentially dangerous polypharmacy*

A significant proportion of the OECD population suffers from multiple chronic conditions, often necessitating the use of multiple medications. As a result, the proportion of patients taking five or more medications has been increasing—and in some countries (i.e. Korea, Portugal, and Luxembourg) over 70% of those 75 and older take more than five medications concurrently (Figure 1.3). In Sweden, excessive polypharmacy (>10 medicines per person) was reported in 12% of patients (Morin et al., 2018[44]). The considerable safety risks associated with polypharmacy increase with each additional medication (Scott and Jayathissa, 2010[45]; Viktil et al., 2007[46]). While polypharmacy may be justified for the management of multiple comorbidities, inappropriate polypharmacy—such as the use of inappropriate medications, medication overuse and duplication—is common (Masnoon et al., 2017[47]).

**Figure 1.3. Population at age 75 and over taking more than five medications concurrently, 2012, 2019 (or nearest year) and 2020**




Source: OECD Health Statistics 2021.

### *Some patient groups are particularly at risk*

Some patient groups are at higher risk of experiencing medication-related harms, including psychiatric patients and older adults. These groups may be particularly vulnerable due to high rates of polypharmacy and difficulty in accessing coordinated care. Older adults also experience changes in there physiology, which can affect both the absorption, distribution and excretion of medicines (pharmacokinetics) and effect of the medicines (pharmacodynamics) which put them at greater risk of developing MRAEs. Changes in pharmacokinetics—the absorption, distribution, metabolism and excretion of medication are affected by both the ageing process and by diseases commonly associated with ageing. Changes in pharmacodynamics—the degree to which a medication generates a pharmacological effect—depend upon a range of factors (Drenth-van Maanen, Wilting and Jansen, 2020[48]). Lastly, older persons experience changes in body functions, including visual acuity, motor functions and cognition, all of which can pose challenges to the correct use of a medication.

Use of multiple anti-psychotic medications is particularly high risk due to potential medication-to-medication interactions, and medication practices that lead to additive prescribing, rather than substitution. Findings from studies of hospitalised psychiatric patients in Mexico found that, on average, patients were taking eight medicines, including four psychiatric medications. Within this group, patients taking six or more medications were more than five times more likely to suffer negative secondary effects, and for each additional psychiatric medication, hospital stays increased by 7 days (Carmona-Huerta et al., 2019[49]).

Medication-related harms have been found to be particularly common in older adults with dementia (Sakiris et al., 2021[50]). High rates of adverse events have also been observed in paediatric populations due to challenges in dosing, and use of the medication for conditions where it has not been well studied or is not approved, (the latter known as off-label use) (Rieder, 2019[51]; Dubrall et al., 2021[52]). Reported incidences of AMEs requiring ICU admission have been found to range between 0.4 and 27% (Jolivot et al., 2014[53]). In addition, intensive care unit patients have been found to be at particularly high risk of experiencing medication-related harms, with these events associated with illness severity and increased nursing workload (Seynaeve et al., 2011[54]).

## Increased medication use is associated with more medication errors and medication-related harms

### *Poor medication-related outcomes are surprisingly common*

#### *Medication-related hospital admissions and mortality can have a significant human toll*

Medications frequently reported as associated with hospital admissions include commonly prescribed medications, such as anti-coagulants, anti-hypertensives, analgesics, anti-diabetics, anti-psychotics, and anti-neoplastic medications. Hospital admissions due to these medicines are frequently preventable. A 2019 systematic review using data from 11 countries found that approximately one-third of medication-related hospital admissions were preventable and another 40% were potentially preventable (Ayalew, Tegegn and Abdela, 2019[15]).

Findings from the US suggest that medication-related harms are among the most common adverse patient safety events occurring in hospitals —impacting approximately 2 million patients annually in the US alone. This comes at significant human and financial cost. Estimates suggest that each hospital acquired AME increases hospital length-of-stay from between 2 to 5 days (US HHS, 2014[32]). Serious harms associated with medication-related harms include bleeding, hypotension, delirium or confusion, constipation, volume overload or electrolyte imbalance, and cardiac events or arrhythmias (Robb et al., 2017[55]). In addition to increasing length of stay and harms, in-hospital AMEs are associated with poorer health outcomes, including higher mortality rates (Vitorino, Aguiar and Sousa, 2020[56]). Studies looking at the mortality associated with medication-related harms report varying results. Findings from Spain and Finland suggest the prevalence of hospital-acquired fatal adverse medication-related events ranges from 5 and -18 % of all medication-related adverse events (Laatikainen et al., 2017[17]). Population-based research in Sweden suggests that fatal adverse medication reactions may account for approximately 3% of all deaths in the general population (Wester et al., 2008[57]).

#### *Medication-related side-effects*

Medication-related side-effects can vary significantly across the population in their frequency and severity—but are commonly experienced even with frequently taken medications (see Table 1.1). The experience of side-effects has been linked to poorer adherence and health outcomes. Side-effects of commonly prescribed medications span a wide range, but commonly include drowsiness, allergic reactions, gastrointestinal problems and heart problems.

**Table 1.1. Frequency of side-effects with different medication types**

| | Medication | Sample | % that experienced side-effects or AMEs | Source |
|---|---|---|---|---|
| Cancer | Chemotherapy | 150 patients | 72% | (Mazzotti et al., 2012[58]) |
| Depression | SSRI/SNRI | 700 patients | 38% | (Cascade, Kalali and Kennedy, 2009[59]). |
| Diabetes | Metformin | 1259 patients | 26% | (Flory et al., 2018[60]) |
| Hypertension | Antihypertensive medication | 175 patients | 85% | (Tedla and Bautista, 2016[61]) |
| Infection | Hospital administered antibiotics | 1,488 adult inpatients | 20% | (Tamma et al., 2017[62]) |
| Schizophrenia | Second-generation antipsychotics | 435 survey participants | 83% | (Tandon et al., 2020[63]) |
| Cardiovascular | Anticoagulants | 42,585 patients | 18% | (Shehab et al., 2016[64]) |

Literature suggests that patients may be unlikely to disclose that they are experiencing medication side-effects with their care providers. For example, in a 2009 web-based study of patients taking anti-

depressants, only 40% of those who experienced side-effects reported them to their prescribing physicians (Cascade, Kalali and Kennedy, 2009[59]).

Side-effects of medications can have significant effects on quality of life. Research looking at older patients with polypharmacy found that 81% agreed that their health depended on their medicines and 78% agreed that the medicines protected their health from declining; 25% patients were concerned about the danger of dependence and 11% were concerned about the side-effects of medication (Mortelmans, Goossens and Dilles, 2022[65]). A number of studies have found that patients often are not provided with recommended information on medication side-effects. Findings from the UK's 2020 adult inpatient survey from the Care Quality Commission for example, found that many patients did not receive adequate information at the time of discharge about the medicines they were meant to take after their stay. Specifically, the survey found that only 28% of respondents were told about their medications' possible medications' side-effects, and nearly half were not provided with an explanation of how to take their medicines (CQC, 2022[66]). In surveys of other patient groups, there were also high proportions of patients who reported not receiving information on side-effects, including 24% of people who used community mental health services and 40% of patients requiring urgent and emergency care (Nuffield Trust, 2021[67]).

### *Drug interactions are increasing with increasing polypharmacy*

Harmful medication-to-medication interactions appear to have increased significantly in the past decades in parallel with increases in polypharmacy (Guthrie et al., 2015[68]). A population-based study in the UK found that one in four patients prescribed the common diabetes medication, metformin, had contraindications to its use (Emslie-Smith et al., 2001[69]). A study drawing on a national dataset on medication dispensing in Poland found that 6% of the general population was at risk of experiencing a medication-to-medication interaction. A similar study in France, in a random sample of 100,000 patients in the French health insurance system found co-dispensing of contraindicated medications was high—over one-in-ten patients—one case of potentially interacting combinations per patient (Létinier et al., 2019[70]).

A meta-analysis of 27 studies in 10 countries showed that approximately one third of general practice patients and over two thirds of intensive care patients experienced a preventable medication-to-medication interaction during their hospital stay (Zheng et al., 2018[71]). A 2015 study of medication-to-medication interactions in an intensive care unit of a teaching hospital in Brazil found the mean number of drug-drug interactions per patient taking an antimicrobial was 2.6 and 98% of patients experienced clinically significant interactions (Alvim et al., 2015[72]).

### *Poor adherence and compliance also contribute to poor safety outcomes*

Medication adherence describes the degree to which patients take prescribed medications appropriately. Between 4 and 31% of patients commenced on treatment for three common conditions (diabetes, hypercholesterolaemia, or hypertension) never fill their first prescription. For those who do fill their prescription, only 50 to 70% ultimately take their medications regularly (i.e. at least 80% of the time) *and more than half discontinue within two years of the initial prescription* (Khan and Socha-Dietrich, 2018[73]). A 2012 study assessing the avoidable costs of medications as well as the costs of providing care to patients as their conditions deteriorated, estimated that non-adherence contributed to more than half the avoidable spending on suboptimal medicines use globally (IMS Institute, 2012[74]). Lack of medication adherence also increases the likelihood of medication-related harms in the future. Recent research from Canada has found that, for example, non-adherence to medication following hospital discharge is associated with an increased risk of medication-related harms (Weir et al., 2020[75]).

*The impact of medication use on long-term costs and health outcomes needs further analysis*

Less studied are the long-term harmful impacts of medication use, including harms may result from chronic use, or there may be delayed medication-related harms or impacts. A number of commonly-used medications—including antibiotics, steroids, anticoagulants and diabetes medications--have been found to be associated with risks of adverse outcomes in the long term, such as organ failure, vision problems, increase risk or fractures, mental ill-health, and poorer cardiovascular outcomes among others (Rice et al., 2017[76]; Duong et al., 2022[77]; Paul and Doogue, 2016[78]). Population studies in Denmark have found that hormonal birth control is associated with risk of depression in the longer term (Skovlund et al., 2016[79]). Chronic use of steroids can lead to steroid-induced glaucoma, and preventable blindness (Roberti et al., 2020[80]). Antibiotic exposure in childhood has been found to be associated with increased occurrence of asthma, allergies, and obesity among other poor outcomes (Duong et al., 2022[77]). The harmful impact of medication use on long-term health outcomes requires further study in order to more accurately assess the impact on population health and health expenditure.

## The prevalence of inappropriate prescribing is substantial, and possibly increasing

The impact of inappropriate prescribing on medication safety is significant. A recent meta-analysis that included 5 million older patients across 27 different countries found that as many as one third experienced a potentially inappropriate prescription in the primary care setting (Liew et al., 2020[81]). Inappropriate prescribing is also highly prevalent in the hospital setting. In one tertiary emergency care facility in Japan, potentially inappropriate medications were identified in as many as 55% of admissions to hospital and 28% discharges (Aida et al., 2021[82]). Another study from Switzerland found that more than 80% of older, hospitalised patients received at least one potentially inappropriate medication or medication combination. The same study found potentially inappropriate medication combinations (PIMCs) in 47% of patients prior to hospitalisation, in 21% during hospitalisation, and in 25% of patients after discharge (Migliazza et al., 2021[37]). This is complemented by research from Chile, which found that the prescription of potentially inappropriate medications (PIMs) was common and increased with age; patients aged 80 or older were three times as likely to be prescribed a PIM as younger patients (65–70 years old) (Arellano et al., 2016[83]).

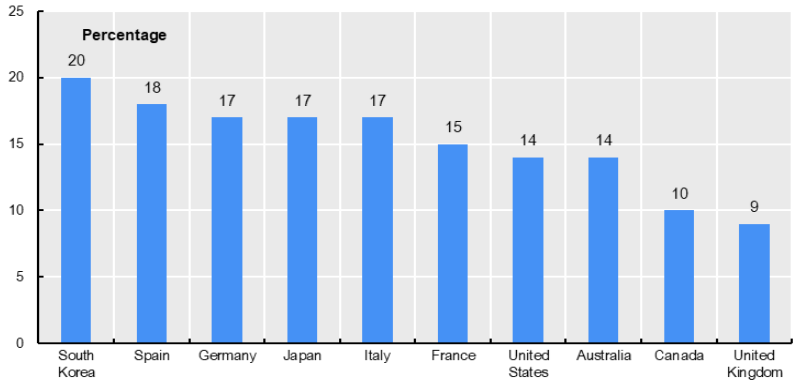
Irrational medication use puts patients at significant risk of harm and is on the rise. A recent meta-analysis found that studies published before 2011 reported a pooled prevalence of 25%, with the proportion consistently increasing over the years to 44% for studies published from 2016 onwards (Liew et al., 2020[81]). Between 8 to 17% of medication-related harms occurring in older persons in primary care may be due to inappropriate prescribing (Liew et al., 2020[81]). These adverse outcomes included emergency room visits, medication-related harms, functional decline, poorer quality of life and hospitalisations (Liew et al., 2020[81]). Other studies support these findings. A retrospective cohort study of over one million adults in Italy found a 16% increased risk of hospitalisation during periods of exposure to potentially inappropriate medication use (Varga et al., 2017[84]). In Ireland, hospital admission was independently associated with a higher rate of having being prescribed potentially inappropriate medicines (adjusted hazard ratio 1.24 (95% confidence interval 1.20 to 1.28) (Pérez et al., 2018[85]).

## The economic impacts of medication-related harms events on health systems

### *Trends in pharmaceuticals as a share of health expenditure*

One aspect that makes medication safety so important to policy makers is the impact that it has on health spending. There are significant opportunities for governments to improve medication use—to promote better prescribing, improve adherence, reduce waste, and achieve better patient outcomes. The amount of money that OECD countries spend on pharmaceuticals is substantial. In 2019, spending on retail pharmaceuticals (that is, excluding those used during hospital treatment) accounted for one-sixth of overall health care expenditure in OECD countries—the third largest component of health spending after inpatient and outpatient care. In a number of countries, including Korea, Spain, Germany, Japan, and Italy, pharmaceuticals accounted for more than 15% of net healthcare spending in 2018 (Figure 1.4).

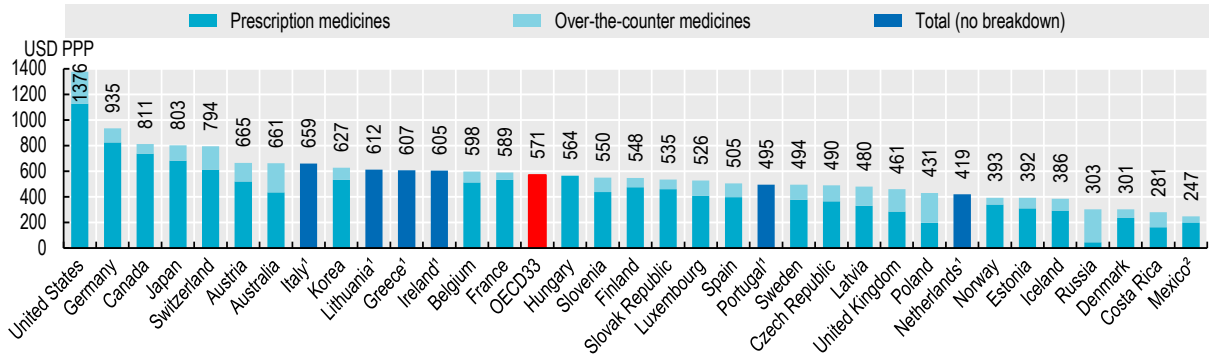
**Figure 1.4. Total pharmaceutical spending averages, 2018: Real net pharmaceutical spending as a percentage of healthcare**




Source: (IQVIA, 2021[2])

A variety of factors influence the level of per capita spending on retail pharmaceuticals, including distribution, prescribing and dispensing; formulary selection, pricing and procurement policies; and patterns of uptake of novel and generic medicines. In 2019, per capita retail pharmaceutical expenditure in OECD countries averaged USD 571 (adjusted for differences in purchasing power) (Figure 1.5). Spending in the United States was more than double the OECD average, while the majority of OECD countries fell within a relatively narrow spending band of ±15% from the average.

**Figure 1.5. Expenditure on retail pharmaceuticals per capita, 2019 (or nearest year)**



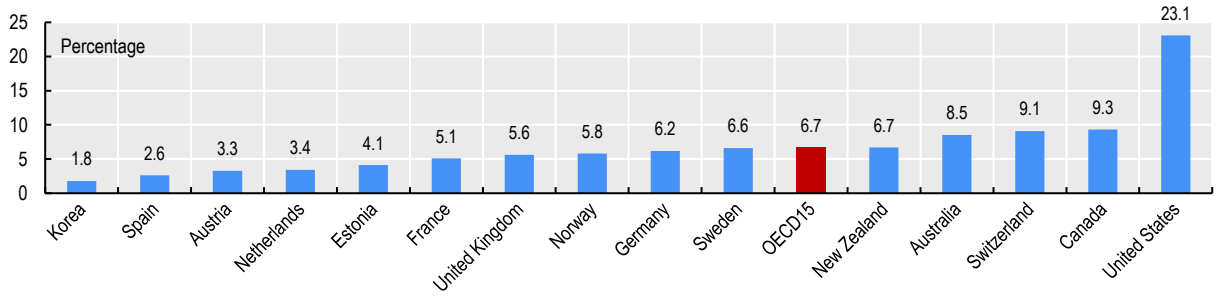
1. Includes medical non-durables (resulting in an overestimation of around 5-10%). 2. Only includes private expenditure.
Source: OECD Health Statistics 2021.

Assessments of retail pharmaceutical spending are not completely representative of the costs of pharmaceuticals to the health system. Spending on medicines for use in hospitals can be substantial – typically accounting for one-in-five dollars spent on top of retail spending. Over the last decade, hospital pharmaceutical spending has increased significantly, in part driven by the introduction of new high-cost treatments, including those in oncology and immunology (OECD, 2021[6]). In most countries, total spending on pharmaceuticals in hospitals increased at a faster pace than that on retail medicines.

### *There is also a direct financial burden on patients*

Pharmaceutical costs are experienced both by payers and patients—the latter may experience substantial out-of-pocket costs. The financial burden of polypharmacy and irrational prescribing also weighs on patients. Findings from the WHO on financial protection for health show that out-of-pocket payments incurred by households with catastrophic health spending are largely due to spending on outpatient medicines (WHO Barcelona Office, 2019[86]). Although most health benefit packages cover prescribed medicines, the low-income elderly may struggle to make the required patient contributions, or pay for supplemental over-the-counter products. Substantial out-of-pocket payments have been found to contribute to non-adherence, prompting some patients to ration medicines in order to make them last longer (Zivin et al., 2010[87]; Warth et al., 2019[88]). On average, 7% of survey respondents in OECD countries say that they skipped prescribed medicines due to cost—ranging from almost 1-in-5 people in the United States to 1-in-50 in Korea (Figure 1.6). In the long run, skipped medications can lead to loss of disease control resulting in higher rates of high-cost services, such as emergency and inpatient care.

**Figure 1.6. Percentage of patients who report that they skipped prescribed medicines due to cost, 2020 or most recent year**




Source: OECD Health Statistics Database 2021

Small increases in out-of-pocket costs can lead to significant decreases in adherence. A study from the US Bureau of Economic Research using data from the US's Medicare's prescription medication benefit program found that increasing patient out-of-pocket costs by one-third would cause a 20% reduction in medication consumption, thus causing a more than 30% increase in monthly mortality, primarily due to cutbacks in use of medicines to treat cardiovascular disease, like statins and anti-hypertensives (Chandra et al., 2021[89]).

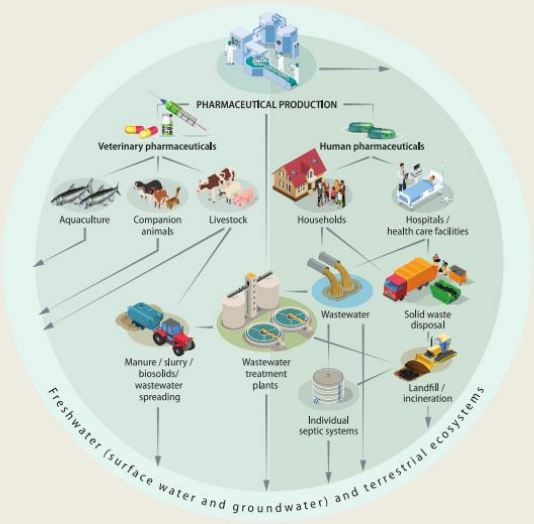
### Box 1.2. Medication safety as a lever of health systems sustainability

**Appropriate use of medicines can reduce the impact that health systems have on the environment**

The misuse of pharmaceuticals not only has direct costs and harms to patients—but increasing attention has been paid to the impact that pharmaceutical use has on the environment, leading to additional long-term costs and human harms. Pharmaceutical production has been assessed to have a sizable carbon footprint, having been found to be significantly more emission-intensive than the automotive industry (Belkhir and Elmeligi, 2019[90]).

Evidence has also been growing of the negative environmental impacts related to the use or release of pharmaceuticals into the environment. For example, the misuse and over-use of antibiotics is an important contributing factor of the emergence and spread of antimicrobial resistance - a global health crisis with the potential for enormous health, food security and economic consequences. Pharmaceuticals can disperse through the environment via multiple pathways as illustrated in Figure 1.7.

#### Figure 1.7. Major pathways of release of human and veterinary pharmaceuticals into the environment




Source: (OECD, 2019[91]).

## The economic case for improving medication safety

A number of national level analyses have assessed the impact of medication errors or medication-related hospital admissions, and have demonstrated significant costs to national health systems in managing these (Table 1.2). National-level estimates have ranged from EUR 94 million in the Netherlands to almost USD 2 billion in the United States.

### Table 1.2. Examples of national level estimates of the economic impact of medication-related harms

| | Estimated national health impact | Assessment | Estimated National Cost | Source |
|---|---|---|---|---|
| Australia | 275,000 hospital admissions annually | Annual cost of medication-related admissions | AUD 1.4 billion | (Lim et al., 2022[92]) |
| Canada | Preventable medication hospitalisations | | CAD 140 million | (Canadian Patient Safety Institute, 2018[93]) |

| | | | | |
|---|---|---|---|---|
| Germany | 2 million adults ingesting medications have will have an AME | Annual economic burden related to AMEs | EUR 816 million | (Stark, John and Leidl, 2011[94]) |
| Japan | | direct costs of managing adverse medication-related events | JPY 804.53 billion and JPY 597.19 billion (EUR 6,269 million and EUR 4,653 million) | (Katsuno et al., 2021[95]) |
| Netherlands | | total costs associated with preventable medication-related hospital admissions | EUR 94 million | (Leendertse et al., 2011[96]) |
| Spain | 350,835 ADR-related hospitalisations (almost 1.7% of all hospitalisations) in Spain between 2001 and 2006 | cost to the health system caused by ADR-related hospitalisation | EUR 272 million in 2006 | (Carrasco-Garrido et al., 2010[97]) |
| United Kingdom | 237 million medication errors annually | Definitely avoidable AMEs | GBP 98 462 582 per year | (Elliott et al., 2021[98]) |
| United States | 196 600 AMEs | Cost of treating preventable inpatient AMEs | USD 871 million and USD $1.8 billion | (Slight et al., 2018[99]) |

Source: Authors

At the global level, in 2012 IMS estimated that the costs associated with medication errors were USD 42 billion annually (IMS Institute, 2012[74]). This estimate has not been revised over the last 10 years,

Using available research, we estimate that **over six million hospital admissions annually are the result of medication-related harms**. Using 2019 OECD data from 37 OECD countries to determine the crude average cost of a hospital admission (approximately USD 8,300), this puts the aggregate cost of avoidable hospital admissions due to medication-related harms at **USD 51 billion**[11], annually. **This figure is equivalent to 3% of all spending on hospital inpatient care.** Once in inpatient care, the likelihood of experiencing a medication-related harm only increases. **Each year, more than one million**[12] **hospitalised patients in OECD countries experience a preventable medication-related harm in hospital.** In addition to patient harm this increases the costs of hospitalisation. The impact of hospital-acquired medication-related harms on length of stay is estimated at approximately 3 million avoidable hospital days across OECD countries annually—or a total of an **additional USD 3.4 billion**.

Together, **costs from avoidable admissions due to medication-related events and added length of stay due to hospital acquired medication-related harms total USD 54.3 billion** in OECD countries. This estimate does not take into account out-of-pocket spending on unnecessary pharmaceuticals and corrective treatment, lost productivity and litigation costs, or the costs of MRAEs addressed in primary, ambulatory, emergency, and long-term care. This figure is equivalent to **11% of total pharmaceutical spending** across 31 OECD countries for which data are available[13]. Additional information on the sources and assumptions used can be found in Annex A

The estimated USD 54 billion that is spent annually on avoidable care due to adverse medication events are funds that could be better spent on improving medication monitoring systems, staff training, quality improvement initiatives, appropriate primary or ambulatory care and efforts that would improve the quality of life by better aligning medication use with need. In addition to the costs, it is important to remember that experiencing a medication safety event can be a **traumatic, painful, and debilitating experience** that can have **serious impacts on patient outcomes**.

11 50,900,000,000. US Dollars, Current prices, current PPPs

12 OECD modelling estimates over 1,000,000 events per year across OECD Countries. Costs of increased length of stay due to preventable adverse medication event in hospital (estimated at 3.4 billion) have been subtracted from total hospitalisation costs to avoid double counting.

13 Total pharmaceutical sales estimated at 478,448.30 Million US$, PPP

### Table 1.3. Recent examples of potential saving assessments by interventions to improve medication safety

| | Setting/Population | Intervention | Estimated Savings | Source |
|---|---|---|---|---|
| France | Adult orthopaedic and trauma surgery unit | Clinical pharmacist services | Cost-benefit ratio of €1.94 in savings for every €1 invested | (Renaudin et al., 2021[100]) |
| Netherlands | All hospital patients | Medication review program | Positive cost–benefit ratio of 9.7 | (Wilkes et al., 2021[101]) |
| United Kingdom (Scotland) | Patients with high risk medicines | Polypharmacy reviews | Up to 155 GBP per patient | (Mair et al., 2017[102]) |
| United States | Pharmacy-based intervention | Medication review program | $218 for likely AMEs and $319 for likely and possible AMEs; 3.6-5.3 times the pharmacists' time and salary cost | (Fernández et al., 2020[103]) |
| United States | Kidney transplant recipients | Pharmacist-led mobile health program | 49% lower hospitalization charges for intervention arm | (Taber et al., 2021[104]) |

Source: Authors

### *The costs of inappropriate prescribing—beyond harms—are likely underestimated*

Beyond medication-related harms, the extent and cost of inappropriate prescribing is more difficult to measure, but may dwarf the costs of medication-related adverse events alone (safe prescribing is further discussed in Section 2). In Canada, it has been estimated that in 2013 $419 million ($75 per older Canadian) was spent on potentially inappropriate medications outside the hospital setting. Benzodiazepines and other hypnotics were the leading contributors to both frequency and cost of potentially inappropriate prescriptions. In the United States, a study of the extent and cost of potentially inappropriate prescribing of medications used by persons enrolled in the Medicare Part D Prescription Drug Program between 2014 and 2018 found that 43 billion doses of potentially inappropriate medications were dispensed, at a cost of over $25 billion (Fralick et al., 2020[105]).

The costs of inappropriate prescribing, together with those of longer term adverse outcomes, indirect costs of medication-related harms (e.g. lost productivity, sick leave), and direct costs of hospitalisations and extended length of stay (LOS) due to medication-related harms are likely to far exceed the estimates presented in the previous section.

# 2 Reducing inappropriate prescribing and improving the rational use of medicines

## The rational use of medicines: the right medicine at the right dose and duration for the right patient

The rational use of medicines concerns the entire care pathway and implies using the right medication, for the right patient, at the right time. More broadly, rational use of medications must recognize that medicines are used within a care and therapeutic continuum where non-pharmacological strategies and systems solutions are often required, sometimes first line approaches, and support appropriate medicine use. It includes enabling patients to understand and use medicines well supported by prescribers and dispensers within a robust care pathway and health system infrastructure that also enables the evaluation of interventions at the patient and system level (WHO, 2012[106]). More recently, the concept of rational use has been incorporated into the concept of "high-value care", which specifies that the components of appropriate medicines' selection be: safe (i.e. do not harm), effective, cost-effective, valuable (compared with alternative expenditures) and wanted by informed patients (Elshaug et al., 2017[107]). This concept of value adds in the societal dimension of allocating resources across a population with different medical needs, which needs to be considered to ensure that national, regional or non-governmental health care systems remain economically sustainable.

## The irrational use of medicines: prescribing the wrong medication, overuse and underuse

With respect to prescribing, irrational or inappropriate use can take many forms: inappropriate medication (either the wrong medication for the wrong indication or a medication with questionable efficacy), dosage form, dose, route, dosage interval and treatment duration (Hepler and Strand, 1990[108]). Inappropriate prescribing can also be viewed as an issue of overuse (Brownlee et al., 2017[109]) or underuse (Glasziou et al., 2017[110]).

### *Overuse: the most common form of irrational use*

The overuse of medication can be defined as medication that is unnecessary, and is more likely to cause harm than do good (MSH, 2012[111]; Brownlee et al., 2017[109]). In practice, however, defining overuse is more complex and should be considered along a continuum. At one end, there are medications that have clear and universal benefit, for example, the use of insulin in patients with Type I diabetes (Brownlee et al., 2017[109]). On the other end are medications that have been shown to be ineffective or pose high risk of harm. Most medications fall somewhere in between these two extremes, where clinical judgment and

individual patient characteristics and preferences play a large role. Since each therapeutic option has its side-effects, benefits and costs, patient preferences must play a role in the appropriate selection of therapeutic options (Mulley, Trimble and Elwyn, 2012[112]).

### *Polypharmacy: a classic case of overuse*

Polypharmacy can be defined as the concurrent use of multiple medicines by an individual patient, which is either appropriate (when it is therapeutically beneficial) or inappropriate (when it is not) (Mair et al., 2017[102]). A large proportion of patients with multiple chronic illnesses are prescribed complex, multiple-drug regimens that raise the risk of inappropriate polypharmacy. In Scotland, among patients with two or more chronic illnesses, a study found more than 20% were taking four to nine medicines a day and 1% were taking 10 or more (Payne et al., 2014[113]). The hazards associated with polypharmacy are substantial and include increased risks of medication related harms, drug-drug or drug-disease interactions, falls, and cognitive impairment (NIH, 2021[114]). The treatment burden of polypharmacy is also a problem, as patients and families must understand, refill and administer multiple medications and monitor for side effects.

### *The Overprescribing of Opioids and the Opioid Crisis*

The use of opioid analgesics has increased substantially over the last decade, and this has led to a steep increase in hospitalisations and emergency department visits arising from unintended overdoses. The public health crisis that continues to unfold in some countries has placed opioid use as a major policy priority for many governments (OECD, 2019[115]).

In general, opioid analgesics are often prescribed for acute pain management, which frequently leads to inappropriate long term opioid use. In the context of long term use, doses may escalate and prescription of higher doses can lead to dependence and overdose. For example, the prescription of higher doses of opioids is correlated with a 32% to 188% increased risk of unintended overdose and opioid related morbidity and mortality (Chou et al., 2015[116]). As many as 1 in 16 surgical patients in the US who use opioids become chronic opioid users (Brummett et al., 2017[117]). Another study by Higgins et al (2018) found that 5% of patients receiving an opioid analgesic prescription for the treatment of pain became opioid dependent. In North America, commonly prescribed opioid analgesics can lead to inappropriate non-prescription use, including hydrocodone, oxycodone, codeine and tramadol. In Europe, misused opioids include methadone, buprenorphine and fentanyl (UNODC, 2018[118]).

### Box 2.1. *The overuse of sedatives in the treatment of insomnia: the case of the Australian Veterans' MATES Program*

The treatment of insomnia is commonly associated with the overuse of sedatives, and insomnia is a common problem among the elderly. The Australian Veterans' MATES (Medicines Advice and Therapeutics Education Services) is a program that aims to optimise the use of medicines and health services through targeted education and prescriber feedback to veterans and their health professionals. The program found that one third of veterans living in residential aged care were using benzodiazepines at least eight months per year, despite guidance that these medications should be stopped after one month of use. The risks associated with the overuse of sedatives are well-known, and include increased risk of hospitalization from falls, confusion, delirium and dementia. Furthermore, prolonged use of hypnotics can lead to tolerance and dependence. Meanwhile, effective non-pharmacological alternatives for the treatment of insomnia exist (e.g. cognitive behavioural therapy, CBT).

The Australian Veterans MATES program developed an Insomnia Treatment Program to address this issue. General practitioners guided patients to use a sleep diary and therapy selection guide, and prescribed the use of CBT as an alternative to hypnotics. The program identified at risk patients for GPs and educated and supported GPs to review the risks associated with hypnotics and provided guidance on how to reduce and discontinue these medicines. Similarly, educational materials were provided to patients. The impact of this program, implemented in two phases (2009 and 2012) was significant; the program resulted in a reduction in the use of hypnotic medicines (116,000 fewer patient months of treatment) and a reduction in the number of hospitalisations for hip fracture (43 avoided) after 12 months follow-up (Kalisch Ellett et al., 2018[119]).

Source: (Australian Government Department of Veterans' Affairs, 2021[120])

*The inappropriate use of antibiotics has led to a growing crisis of antimicrobial resistance*

One of the most commonly cited examples of overuse of medicines is in relation to antibiotics, which has led to a crisis of antimicrobial resistance, a major policy priority for OECD member countries. Inappropriate use of antimicrobials is prevalent but differs across types of health care specialties (. It is estimated that without action, AMR could lead to up to 2.4 million deaths in Europe between 2015 and 2050, and could cost health systems as much as $ 3.5 billion annually (OECD, 2022[121]).

The increase in antimicrobial resistance is a direct consequence of the irrational use of antibiotics (both first and second line) and the problem is exacerbated by a decline in new antimicrobials being developed and brought to market (OECD, 2022[121]). The use of second-line agents should be limited to severe cases and only when indicated. A number of factors contribute to antibiotic overuse, including systems approaches to reduce spread of infectious diseases, lack of public knowledge and awareness; access to antibiotics without prescription and use of leftover antibiotics; the knowledge, attitudes and perception of prescribers and dispensers; inadequate medical training; pharmaceutical promotion; lack of rapid and sufficient diagnostic tests; patient-doctor interaction; and community-based infection control procedures.

### *Underuse has received much less attention but also contributes significantly to global morbidity and mortality*

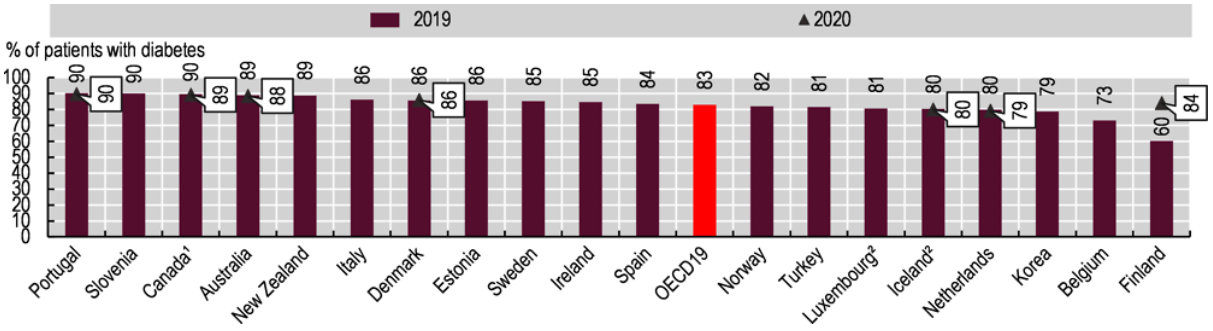
Underuse of medicines is the failure to initiate effective and affordable treatment for patients with a condition where one or several medication classes have demonstrated their efficacy ( (Piau et al., 2012[122]; Glasziou et al., 2017[110]). It is a common issue in secondary prevention (Pratt et al., 2015[123]). A study in Belgium found that even when controlling for polypharmacy, older patients were frequently under-prescribed certain medications (Wauters et al., 2016[124]). Polypharmacy, underuse and misuse were correlated and were coexistent in almost half of community-dwelling adults aged 80 or older. The study

found that for each additional underused medication at baseline, there was a 39% increased risk of death and a 26% increased risk for being hospitalised.

*The underuse of anti-hypertensives – the case of diabetes*

The use of anti-hypertensive medications to regulate the blood pressure of diabetic patients is a cornerstone of treatment. Still, it remains an area where underuse or inappropriate use of medications is a problem. One study found that over half of all diabetic patients received a potentially inappropriate anti-hypertensive (28% over-prescription and 35% under-prescription). Of these, angiotensin-converting enzyme (ACE) inhibitors and beta-blockers were the most frequently under-prescribed (Márquez et al., 2017[125]). The underuse of ACE inhibitors and beta-blockers was independently associated with increased hospital admissions for heart failure. The OECD collects data on the volume of anti-hypertensives prescribed to patients with diabetes; variation exists between countries but there is a paucity of data on which medications are being prescribed (see Figure 2.1).

**Figure 2.1. People with diabetes prescribed recommended anti-hypertensive medication in the past year in primary care, 2019 (or nearest year) and 2020**




1. 2020 estimate based on provisional 1 April to 30 September data from all jurisdictions except Quebec. 2. Three-year average. Source: OECD Health Statistics 2021.

## Strategies to improve rational use

### *Improving prescribing often requires a multi-modal approach but the decision-maker's toolbox is vast*

Several interventions have been developed to target or improve rational medication use. In general, these strategies can be categorised as macro-level or micro-level strategies (MSH 2012). Rotar and colleagues expanded and summarised these strategies illustrated in the Table below (Rotar, Van Den Berg and Klazinga, 2020[126]).

## Table 2.1. Overview of strategies to enhance rational prescribing in primary care in 13 countries

| | | | | Austria | BH | France | Germany | Greece | Italy | Netherlands | Norway | Romania | Scotland | Slovenia | Spain | Sweden |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TARGETED APPROACHES | Continuous medical education and professional development | Training of prescribers | Formal CME | √ | | √ | | | √ | √ | √ | √ | | √ | √ | √ |
| | | | Supervisory visits | | | √ | | | | | √ | | | √ | √ | |
| | | | Group lectures | √ | | √ | √ | | √ | √ | √ | | √ | √ | √ | |
| | | | Seminars | √ | | √ | √ | | √ | √ | √ | | √ | √ | √ | √ |
| | | | Workshops | √ | | √ | √ | | √ | √ | √ | | √ | √ | √ | √ |
| | | Printed materials | Clinical literature and newsletters | √ | | √ | √ | | √ | √ | √ | | √ | √ | √ | √ |
| | | | Treatment guidelines and medicine formularies | √ | | √ | √ | | √ | √ | √ | | √ | √ | √ | √ |
| | | | Illustrated materials (flyers, leaflets) | √ | | √ | √ | | √ | √ | √ | | √ | √ | √ | √ |
| | | Approach based on face 2 face contact | Educational outreach | √ | | √ | √ | | √ | √ | √ | | √ | √ | √ | √ |
| | | | Influencing opinion leaders | | | | √ | | √ | | | | √ | √ | √ | √ |
| | Management of health services | Supervision, monitoring and feed-back | Limited procurement lists | √ | √ | | | | √ | √ | √ | | | | √ | |
| | | | Drug use review and feedback – performance reporting, quality improvement programmes | √ | | √ | √ | √ | √ | √ | √ | | √ | | √ | √ |
| | | | Regional drug and therapeutics committees | | | √ | | | √ | | | | √ | | √ | √ |
| | | | Cost information | √ | | √ | √ | | √ | √ | | √ | √ | √ | √ | √ |
| | | Prescribing and dispensing approaches | Structured medication order forms | | | | | | √ | √ | √ | | | | √ | √ |
| | | | Standard diagnostics and treatment guidelines | | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ | √ |
| | | | Therapy packaging | | | | √ | | √ | √ | √ | | √ | | | √ |
| SYSTEM ORIENTED APPROACHES | Economic interventions | Price setting and fees | Dispensing fee | | | √ | √ | | √ | √ | | | | | | |
| | | | IRP | √ | | √ | | √ | √ | √ | | √ | | √ | | |
| | | | Tenders | | √ | | √ | | √ | √ | | | | √ | | √ |
| | | Insurance | Generic substitution | | √ | √ | √ | √ | √ | √ | √ | | | √ | √ | √ |
| | | | Therapeutic reference pricing | | | | √ | | | √ | | √ | | √ | | √ |
| | | | Molecular reference pricing | √ | | √ | √ | | | √ | | √ | | √ | | √ |
| | | Capitation-based reimbursement | | | | | | | √ | √ | | √ | | | √ | √ |
| | | Medicine sales by prescribers | | √ | | | | | | √ | | | | | | |
| | Regulatory interventions | Pharmaceutical registration | | √ | √ | √ | √ | | √ | √ | | √ | √ | √ | √ | √ |
| | | Limited medicines lists (formularies) | | √ | √ | √ | | | √ | √ | | √ | | | √ | |
| | | Prescribing restrictions | Prescription fill limits, caps of number of pills/month, Rx/month: pressure on physicians to prioritise (explicitly) | √ | | | | √ | √ | | | √ | | √ | | |
| | | | Prescribing restricted to specialists | √ | | √ | | √ | √ | √ | √ | √ | √ | √ | √ | |
| | | Dispensing limitations | Dispensing centres | | | | | | √ | | | √ | √ | √ | √ | |
| | | | Dispensing timeframes | √ | | | | √ | √ | √ | | √ | | √ | √ | √ |

Source: Reprinted with authors' permission (Rotar, Van Den Berg and Klazinga, 2020[126]).

As Table 2.1 illustrates, some countries use particular approaches more than others. All countries use a multi-modal strategy (i.e. two approaches or more) and each approach has been implemented in at least one country. While this work illustrates the distribution of different strategies, there are limited data on which combinations of strategies might be more effective than others. We need better evidence on the effectiveness and implementation of multi-modal approaches to inform decision-makers on which are likely to work best and under what circumstances.

Macro-level strategies ("systems oriented") can be understood as either regulatory or economic. Regulatory interventions are laws or policies that aim to affect prescribing patterns through restrictions or incentives (Suleman and Movik, 2019[127]). Examples include pharmaceutical registration and approval, prescribing restrictions (e.g., prescription fill limits, prescribing restricted to specialists) and dispensing

limitations (e.g., specific timeframes, dispensing centres) (MSH, 2012[111]; Rotar, Van Den Berg and Klazinga, 2020[126]). Economic interventions include financial incentives or reimbursement-based mechanisms intended to influence prescribers, dispensers, or consumers to make specific medication choices. Examples include capitation-based reimbursement, gainsharing, insurance-based interventions (e.g., reference pricing, generic substitution policies), price setting and fees (dispensing fees, international reference pricing, tenders) and restrictions on medicines sales by prescribers (e.g. "buy and bill") (Rotar, Van Den Berg and Klazinga, 2020[126]) (see Table 2.1).

### *Making "right-prescribing" a bigger focus for prescribers and health systems*

Encouraging "right-prescribing," including the de-prescribing of medicines that have low clinical value, is an obvious way to reduce inappropriate polypharmacy, particularly among the oldest patients, who often experience an increase in polypharmacy in the last year of life. In Sweden, the proportion of patients exposed to ten or more medications in their last year of life rose from 30% to 47% between 2007 and 2013 (Morin et al., 2017[128]). Prescribers need to consider the added clinical value of preventive treatments in this cohort and whether continued treatment is justified (Dubois et al., 2018[129]).

Some health systems have implemented digital prescribing tools for assessing and reducing the occurrence of polypharmacy. Australia and Canada have established 'de-prescribing networks' consisting of researchers, pharmacists, doctors and patient advocates who together develop strategies and raise awareness about medication safety and promote de-prescribing of medications that may no longer be of benefit or may cause harm to patients (Canadian Deprescribing Network, 2019[130]). SPIDER (Structured Process Informed by Data, Evidence and Research) is an ongoing project in Canada, which aims to improve care for elderly patients living with polypharmacy in primary care (Greiver et al., 2019[131]). At the international level, the EU created a consortium of experts in the project called Stimulating Innovation Management of Polypharmacy and Adherence in The Elderly (SIMPATHY). The project is funded under the European Union's Health Programme (2014-2020) and seeks to explore how management programmes can be implemented to improve medication safety and prevent patient harm by addressing the appropriate use of polypharmacy (European Union, 2019[132]). Continuing work via iSIMPATHY is implementing and delivering patient centred approach to review medications for patients of all age groups[14].

Different initiatives have demonstrated that reducing inappropriate polypharmacy is possible. Greater capacity for data linkage across settings and involvement of pharmacists in care and regular collaborative medicine review can reduce inappropriate prescribing and the frequency of AMEs (Garcia and Joseph, 2006[133]). The implementation of medication review and closer follow-up of patients by community pharmacists has been associated with lower hospitalisation rates due to AMEs, as well as reductions in hospital costs in some studies (Trygstad et al., 2009[134]) (Malet-Larrea et al., 2016[135]).

### *Regulatory and economic interventions can improve medication utilisation and reduce costs but require robust evaluation alongside implementation*

Research suggests that many regulatory and economic interventions reduce medication utilisation and costs, but the impact on reducing inappropriate prescribing and improving patient outcomes is less clear and more context dependent.

Financial incentives have been used by several jurisdictions influence prescribers' behavior. These incentives can include laws, regulations or orders made by public or private payers, NGOs or insurers (Suleman and Movik, 2019[127]). Although a number of countries employ economic strategies, evidence is lacking on whether or not they are effective and if so, what harms might accrue (Rotar, Van Den Berg and Klazinga, 2020[126]). A systematic review examined 18 studies of pharmaceutical policies from six high-

[14] https://www.isimpathy.eu/

income countries (UK, Germany, Ireland, Sweden, Taiwan and the Netherlands) and concluded that pharmaceutical budget caps or targets can lead to modest reductions in medication utilization, with uncertain effects on pharmaceutical costs, healthcare utilisation or health outcomes (Rashidian et al., 2015[136]).

There are also policies such as the monitoring and enforcement of restrictions, generic prescribing, programmes to implement treatment guidelines, and system-wide policies regarding monitoring medicine safety (Suleman and Movik, 2019[127]). Given the uncertainty in the positive and negative effects of many pharmaceutical policies outlined above, governments must ensure robust evaluation is embedded into any policy implementation to assess impacts on patient outcomes, medication utilisation and health care expenditure. Micro-level interventions, including digital solutions, audit/feedback mechanisms, and continuing education, can be accessed by prescribers through the management of health services or through continuing professional development of physicians and other prescribers. Multi-component interventions addressing both the patient and clinician roles appear to have the greatest potential, particularly in reducing overuse (Colla et al., 2017[137]).

One of the difficulties in determining the real world effectiveness of interventions to improve rational medication use is the fact that they are often context dependent. Observed lack of effectiveness may be due to a lack of efficacy of the intervention or due to variation in implementation. For example, the implementation of a clinical decision support system in a clinical setting should account for clinical workflow and professional culture. This underscores the need for evaluation to be a core component of any new program being developed to help inform leadership on whether or not the program is being implemented as intended, to assess the intervention's effectiveness, and to direct resources to approaches that work given the national and local context.

# 3 Improving medication safety throughout the care pathway—the state of the art in OECD countries

## National strategies to improve medication safety

Good patient safety governance entails the creation and implementation of coherent strategy to ensure that patient safety measures are not stand-alone elements but interlinked and incorporated into a strategic approach across all levels of health care (Auraaen, Saar and Klazinga, 2020[138]; McIntosh et al., 2017[139]) Centralised strategic oversight of patient safety measures can be ensured through the development of a national level patient safety strategy or an agency dedicated to safety and quality. In specific reference to medication safety, national plans, strategies, or regulations to address and improve medication safety can be a mechanism to indicate priorities and align efforts between government and leadership actors. This chapter documents the state of uptake of interventions and policies to improve medication safety related outcomes using data compiled from the 2022 OECD Survey: ***Assessment of the Adoption of Systems and Interventions to Improve Medication Safety***. Information on country respondents can be found in Annex A.

Most countries surveyed noted the existence of a medication safety regulation or strategy (see Table 3.1). In **Belgium**, while there is not a specific national policy on medication safety, there are a number of initiatives supported by the authorities that aim at reducing harms related to the use of medicines. These initiatives are often integrated into programmes that aim to improve patient safety and promote the use of incident reporting in healthcare, including medicines (FPS, 2022[140]). Similar constructs—where medication safety aspects are embedded in national patient safety strategies—exist in **Israel**, **Norway**, **Mexico**, and **Latvia**.

### Table 3.1. Selected examples of national medication safety regulations or strategies

| | National Strategy | Purpose | Involved organizations/source |
|---|---|---|---|
| Australia | National Medicines Policy | • Timely access to the medicines that Australians need, at a cost individuals and the community can afford;<br>• Medicines meeting appropriate standards of quality, safety and efficacy;<br>• Quality use of medicines; and<br>• Maintaining a responsible and viable medicines industry. | Australian Government Department of Health (Australian Government Department of Health, 2020[141]) |
| Costa Rica | Regulation of Good Pharmacovigilance Practices Executive decree No. 39417-S | • Defines the bases that contribute to establishing a quality assurance system in the activities of the National Pharmacovigilance System, by establishing the obligations and responsibilities that must be fulfilled by the different agents that comprise it, in order to guarantee uniform criteria to carry out the evaluation of notifications, the generation of alerts and promote the understanding and teaching of Pharmacovigilance. | (SCIJ, 2015[142]) |

| | | | |
|---|---|---|---|
| Germany | Actionplan for improving medication safety | • Raising awareness among patients, physicians, pharmacists, nurses and the public for avoidable risks of drug therapy<br>• Improvement of information on drugs, labelling of drugs<br>• Documentation of drug therapy and measurement of medication safety<br>• Strategies to improve the safety of the medication safety process<br>• Research in the field of medication safety<br>• Organization of the implementation and continuation of the action plan | Federal ministry of Health and doctor's organizations (German Medical Association, 2022[143]). |
| Japan | The Medical Information for Risk Assessment Initiative (MIHARI) | • Utilising large-scale electronic health information databases as novel information sources for pharmaco-epidemiological drug safety assessments in Japan | (Ishiguro et al., 2016[144]) |
| Korea | Korea Comprehensive Drug Safety Management Plan | • Advancement of post-market safety management and adverse event analysis system utilizing real-word data<br>• Operation and improvement of the Relief of Injury caused by adverse events.<br>• Strengthen the provision of safe drug use services and safety information to patients<br>• Promote international cooperation and harmonization of adverse evebt reporting and management system | Korea Institute of Drug Safety and Risk Management (Pharmaceuticals Affairs Act, 2012) |
| Netherlands | Farmacotherapeutisch Kompas (Pharmaceutical Compass)[15] | • Improves appropriate prescribing of medicines by (primary care) physicians and nurses. | National Health Care Institute (ZIN) |
| Türkiye | Quality Standards in Health Section on Drug Management | • Aim is to effectively manage all the steps that include drug management and diminish risks towards patients and health care professionals. | (Sağlık Hizmetleri Genel Müdürlüğü, 2020[145]) |
| United States | National Action Plan for Adverse Drug Event Prevention | • Identifies common, preventable, and measurable AMEs that cause significant patient harm and aligns efforts of Federal Agencies to reduce harms from identified AMEs nationally | Health and Human Services (HHS) (US HHS, 2014[32]) |

Note: Not an exhaustive list. Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022

## Pharmacovigilance and Drug Utilisation Review

### *Pharmacovigilance*

Pharmacovigilance is the process of detecting, reporting, and addressing adverse medication events, and is a key component of a safe care pathway. In the context of a learning healthcare system, pharmacovigilance activities should include the collection of data to inform and refine our understanding of the effectiveness of treatments and to identify potential subpopulations that may be at increased risk of medication-related harm. Pharmacovigilance activities should ensure seamless communication of the evolving evidence to patients, their caregivers, and healthcare providers. The extent to which countries and health systems are capable of fulfilling these functions largely depends upon the scope and quality of existing health information infrastructure and the extent to which this is linked to end-users. Two main types of surveillance systems generally exist and are often combined: passive surveillance systems which rely on spontaneous reporting of AMEs, and active surveillance systems which are specifically designed for

15 Additional initiatives in the Netherlands are being implemented by the Medicines Evaluation Board, Netherlands Pharmacovigilance Centre Lareb, Health and Youth Care Inspectorate (IGJ), National Institute for Public Health and the Environment, The National Health Care Institute, EudraVigilance, Dutch Foundation for Pharmaceutical Statistics (SFK), Geneesmiddelenbulletin Foundation, patient safety research team of the Netherlands Institute for Health Services Research (Nivel), GIC, Health Base, G-Standaard, Guidelines (written by the scientific associations, The Netherlands Organisation for Health Research and Development), and ththe Informatieberaad Zorg (IB).

post-marketing surveillance, use real-world data to generate drug safety information, and do not rely on individuals to initiate adverse event reports (Huang, Moon and Segal, 2014[146]).

### Box 3.1. United States FDA Sentinel Initiative

Sentinel is the FDA's national electronic system for monitoring the safety of FDA-regulated medical products, including medicines, vaccines, biologics, and medical devices. It was launched in 2008 following the passage of legislation requiring the development of a system for active post-marketing risk assessment and analysis for medical products. Development took place in collaboration with public, academic, and private entities to establish procedures for obtaining access to disparate data sources and validate methods for the creation of a system to link and analyse data from multiple sources. The project harnesses information from multiple eHR systems, administrative data and insurance claim records – these data include demographics, enrolment history, medication dispensing, encounters, vital signs, lab results, diagnoses, procedures, and mortality.

For many years, various parts of the FDA have gathered risk information about medications and other medical products through programs that rely on external sources (such as product manufacturers, consumers, patients, and health care professionals) to report suspected adverse reactions to its Adverse Event Reporting System. This type of safety monitoring is known as "passive surveillance." In contrast, the Sentinel System has been designed as an "active surveillance" system, because the FDA can initiate its own safety evaluations that use available electronic health care data to investigate the safety of medical products. The Sentinel infrastructure is expanding beyond medication safety surveillance, for example to studying the effects of switching between branded and generic medicines, and to the surveillance of the safety of medical devices.

Source: OECD (2019[147]), "Using Routinely Collected Data to Inform Pharmaceutical Policies: Analytical Report for OECD and EU countries", https://www.oecd.org/health/health-systems/Using-Routinely-Collected-Data-to-Inform-Pharmaceutical-Policies-Analytical-Report-2019; FDA (2019[148]), "FDA Sentinel Initiative", https://www.fda.gov/safety/fdas-sentinel-initiative.

Most (13 out of 21) countries indicated that they have an active system for tracking medication events for all medicines. A significant number of countries also indicated the existence of passive systems (11 out 20). Five countries note active systems for selected medicines. In **Costa Rica** there is an active system only for biological medicines; in **Korea** for new drugs and drugs requiring submission of risk management plan; in **Estonia** for novel tuberculosis medications; while in **Belgium** active systems apply only to COVID-19 vaccines.

The structure and governance of pharmacovigilance structures vary by country. For example:

- In **Italy**, since 2007, the Italian Medicines Agency annually provides funding to Regions for active pharmacovigilance initiatives. The Italian Medicines Agency provides guidelines for research areas; approves the projects submitted by the Regions; and manages and monitors the projects. The main areas of interest identified in the active pharmacovigilance programs are studies of adverse medication-related events, and medication information and training interventions directed to health professionals to stimulate spontaneous reporting.
- The Canada Vigilance Program is Health **Canada's** post-market surveillance program that collects and assesses reports of suspected adverse reactions to health products marketed in Canada. Adverse reaction reports are submitted by health professionals and consumers on a voluntary basis, and by manufacturers, distributors and hospitals on a mandatory basis. Monitored health products include prescription and non-prescription medications; natural health products; biologics (includes biotechnology products, vaccines, fractionated blood products, human blood and blood components, as well as human cells, tissues and organs); radiopharmaceuticals; and disinfectants and sanitisers with disinfectant claims.

- In **Australia**, the Therapeutic Goods Administration monitors the safety of therapeutic goods to contribute to a better understanding of their possible adverse events when they are used outside the controlled conditions of clinical trials. Medicine and vaccine adverse event reports that the Therapeutic Goods Administration receives are entered into the Adverse Event Management System. If the Therapeutic Goods Administration identifies a safety concern relating to a therapeutic good, it can take regulatory action to ensure that the product continues to have acceptable safety, efficacy/performance and quality for its intended use.
- In **Costa Rica**, the Ministry of Health manages the National Pharmacovigilance System and the National Pharmacovigilance Center, and is responsible for promulgating policies related to medication safety (Ministerio de Salud, n.d.[149]). As part of the work instruments, the Ministry has an online system for the timely notification of suspected adverse reactions and therapeutic failures of medications. The public health services of the Social Security, in turn, have internal regulations for dealing with adverse reactions and therapeutic failure of medications, which are consistent with the guidelines of the Ministry of Health. There is also an institutional liaison officer to the National Pharmacovigilance Center of the Ministry, who supports actions on medication safety.
- In **Mexico** the National Centre for Pharmacovigilance, overseen by Federal Commission for Protection against Health Risks, was established in 2017 and is in charge of surveillance of adverse medication events, adverse medication reactions and suspected adverse reactions post-vaccination. The CNFV has been implementing notification systems including the e-Reporting[16] and VigiFlow platforms, including a portal enabling the submission of adverse event reports by patients, pharma companies and health care providers (Uppsala Reports, 2020[150]).
- In **Korea** marketing approval is managed by the Ministry of Food and Drug Safety, which collects reports of post-market medication-related adverse events from consumers, hospitals and clinics, pharmacies, drug manufacturers (importers), and Regional Pharmacovigilance Centres. Further, post-marketing safety management systems have been implemented, including mandatory designation and training of drug safety manager/supervisor, and reporting of AMEs among others. In addition, the Korea Institute of Drug Safety and Risk Management, collects, analyses, and manages drug safety data systems that have been implemented in community pharmacies and hospitals to facilitate AME reporting and communication pertaining to safe use of drugs. Many actors collaborate to develop information regarding drug-drug interactions, age-related contraindications, and contraindications in pregnancy, and to provide drug utilisation review, a real-time service for prescribing and drug dispensing by physicians and pharmacists respectively. To promote medication safety at the healthcare facility level, in 2001 the Ministry of Health and Welfare and the Health Insurance Review and Assessment Service (HIRA) launched the quality assessment of pharmaceutical benefits to comparatively analyse the prescription trends of selected medicines (e.g., antibiotics) with significant impact on public health, and provide feedback to prescribers. The goal of this assessment is to reduce drug misuse and abuse, and to facilitate appropriate drug use through voluntary drug management and quality improvement in healthcare facilities.

In Europe, national-level pharmacovigilance are complemented by the activities of the European Medicines Agency (EMA) (EMA, n.d.[151]). EU legislation requires information on medication errors to be collected and reported via national pharmacovigilance systems, this is supported through EMA resources for good practice guidance and pharmacovigilance tasks, and collaborative activities such as the Operating Pharmacovigilance in Europe (SCOPE) Joint Action and planned activities related to the (EMA, 2019[152]; EMA, n.d.[153]; Radecka et al., 2018[154]).

[16] https://www.gob.mx/cofepris/acciones-y-programas/pacientes-consumidores-profesionales-de-la-salud?state=published

### *Drug Utilisation Review*

*Scope of drug utilisation review systems across OECD countries*

Drug utilisation review (DUR) is any system that collects information on the volume and type of medication use. The quality, granularity and linkage of this data with other databases determines the extent to which it is useful at the clinical level and policy level and improves both policy implementation and the quality of care. Drug utilisation review data are equally valuable to local, regional and national administrators through the monitoring and identification of pharmaco-epidemiological patterns that may require targeted intervention, thus contributing to the functioning of a learning health system. Countries vary widely with respect to the national DUR systems in place (see Figure 3.1). Most countries indicate that there are systems in place to conduct drug utilisation review on a national level.

## Figure 3.1. Scope of Drug Utilisation Review Systems in OECD Countries


Note: N=21 responding countries and input from national expert in United Kingdom (Scotland), countries may be counted in multiple categories. In Canada, there is national coverage, but the DUR is implemented and managed at the provincial/territorial level. In Israel, there are DUR is performed by each of the 4 HMOs covering the total population.
Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022 and expert inputs.

In **Australia**, the Drug Utilisation Sub-Committee (DUSC) of the Pharmaceutical Benefits Advisory Committee (PBAC) undertakes data driven assessments of the utilisation of medicines listed on Australia's Pharmaceutical Benefits Scheme (PBS). DUSC monitors the expenditure and patterns of use of PBS-listed medicines including use in accordance with PBS restrictions and quality use of medicines (QUM) principles. In some countries, however, the scope of the DUR is more limited. For example, **Luxembourg** only covers reimbursed medications and patients from the NHS in its DUR, and **Slovenia's** DUR is limited to antimicrobial medicines. In the **United States** there is no national system for DUR. There are state-based systems for utilisation review of prescriptions of controlled substances, including opioid analgesics. These Prescription Drug Monitoring Programs (PDMPs) vary from state to state in terms of the specific mechanisms of data collection, dissemination, and use for intervention[17]. Other systems for DUR are based upon and vary by the payer of healthcare (e.g. Medicare, Medicaid, Veterans Health Administration, Indian Health Service, Department of Defense).

In **Canada**, the CIHI National Prescription Drug Utilization Information System (NPDUIS) contains claims data, formulary data, medication product information and plan information. It provides standardised, comparative information on public pharmaceutical programs and analytical studies on medication use and

[17] https://www.cdc.gov/drugoverdose/pdmp/index.html

spending in Canada. Its data supports sound pharmaceutical policies in the management of Canada's public pharmaceutical benefit program.

The **Netherlands** has two publicly available databases with information on the dispensing of medicines on a national level[18]. These databases are used for research, monitoring, and quality improvement (audit, feedback to pharmacists and prescribing physicians). The first is the Drug Information System (GIP - Genees- en Hulpmiddelen Informatie Project[19]) of the National Health Care Institute (ZIN). GIP which contains information on expenditure on medications in the Netherlands and the degree to which they are used, with coverage reaching 97% of the compulsory insured persons. The register includes dispensing-related data on medicines that are: (1) prescribed by general practitioners, specialists and nurse specialists and (2) dispensed by community pharmacists, dispensing general practitioners and other facilities and (3) being reimbursed under the Health Care Insurance Act. The second is the SFK, Stichting Farmaceutische Kengetallen (Foundation for Pharmaceutical Statistics). SFK is a panel of community pharmacists that registers dispensed medications, covering approximately 95% of all community pharmacists. The registry includes pharmaceutical or medical aids that are prescribed by general practitioners, specialists and nurse specialists and are dispensed by community pharmacists. In **Mexico**, there is no DUR currently implemented. Information regarding the existence and availability of sources of information for establishing a DUR system are currently being explored (Lopes et al., 2022[155]; Salas et al., 2020[156]).

### Box 3.2. Korea's Drug Utilisation Review Program

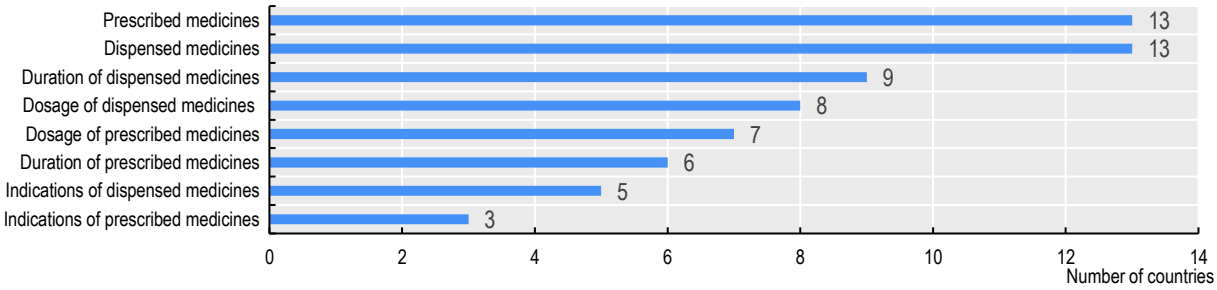
In 2010, HIRA established a drug utilisation review (DUR) system, which uses HIRA's real-time data on Korean patients to provide real-time alerts to clinicians and pharmacists regarding contra-indicated medications due to pregnancy, medication-to-medication interactions, and contra-indications due to age. The DUR is a prospective, real-time review of each prescription before the medication is prescribed and dispensed to the individual patient to minimise the risk of harm due to, for example, medication-to-medication interactions or ingredient duplication. The DUR is enabled electronically by HIRA and is a good demonstration of the scope for using a combination of existing and new data to improve health outcomes using administrative health analyses. A review of the DUR found that it has lowered the prescription of contraindicated medications and lowered pharmaceutical expenditures by reducing over-utilisation (Lee, 2019[157]).

#### *Scope and access to DUR data*

The information collected via DURs varies across countries (see Figure 3.2). Most countries (13/21) report that information on prescribed or dispensed medicines is available in the system. Fewer collect information on the dosage and duration of dispensed medications, and fewer than five countries report including the dosage of prescribed medicines, indications of prescribed medicines, duration of prescribed medicines, and indications of dispensed medicines.

[18] In addition to these systems, a pDUR is used during direct care service to individual patients to detect high risk situations. The system includes medication safety control by prescribing physicians (by their eHR), by pharmacists (by their pharmacy information system) and the more advanced system of Medical Pharmaceutical Decision Rules. Variables included are age, sex, education, income, profession, medical conditions (like impaired renal function and indication for a limited number of high risk drugs mentioned in the Medication Act), and medication use. In general, indications (diagnoses) are not included in the e-prescriptions (apart from the indications for a limited number of high risk drugs).
[19] www.gipdatabank.nl

## Figure 3.2. Information on medicines collected via the above Drug Utilisation Review System

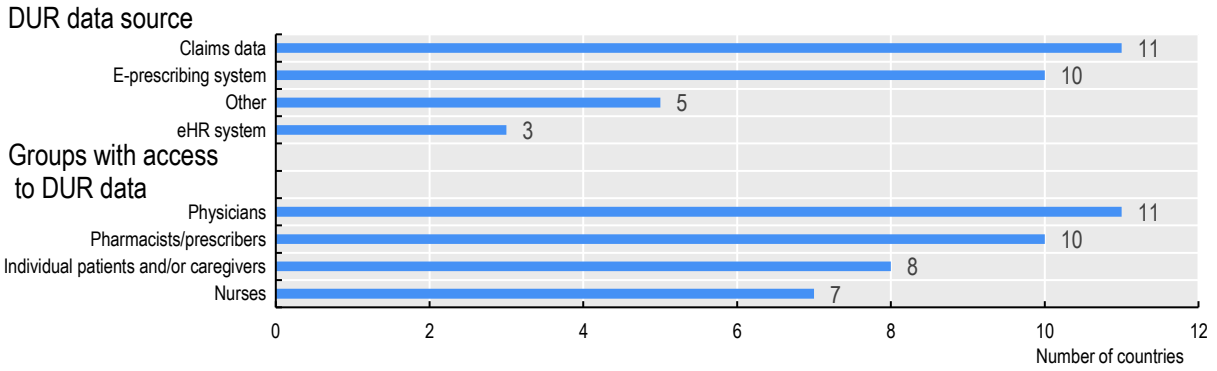



Note: N=21 responding countries, Countries may be counted in multiple categories.
Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022

The majority of respondent countries note that the data used for DUR are claims data, however an increasing number of countries also utilise data from e-prescribing systems (see Figure 3.3). Three countries—**Australia**, **Japan**, and the **United States—**include eHR data in their DUR systems. Four countries include other data sources. **Norway**, for example, includes written prescribing data; the **Netherlands** includes data from its pharmacy dispensing system; **Italy** includes data from Italian Medicines Agency monitoring registries, and **Belgium** includes data from industry. In **Germany,** data are derived from statutory Health Insurance claims.

For medical professionals and pharmacists to use DUR to its fullest potential the DUR advice should be integrated into the clinical workflow to support clinical decision-making. For this reason, in addition to being used by policy makers and key stakeholder organizations, a number of countries make DUR data available to clinicians, including doctors, nurses, and pharmacists to inform their care. **Norway, Italy, Japan, Netherlands, United States,** and **Australia** note that there are mechanisms for the general public to access DUR data. In these countries and in **Latvia,** individual patients or caregivers can access this information (see Figure 3.3). The Norwegian Prescription Database (NorPD) contains data about dispensed medications but does not currently include medications purchased without prescription (over the counter) or supplied to hospitals and nursing homes. Due to these technical limitations, NorPD is not widely used by health personal in clinical practice, however, the register is currently being further developed to enable better institutional use[20].

## Figure 3.3. DUR data sources and access to DUR data by stakeholders

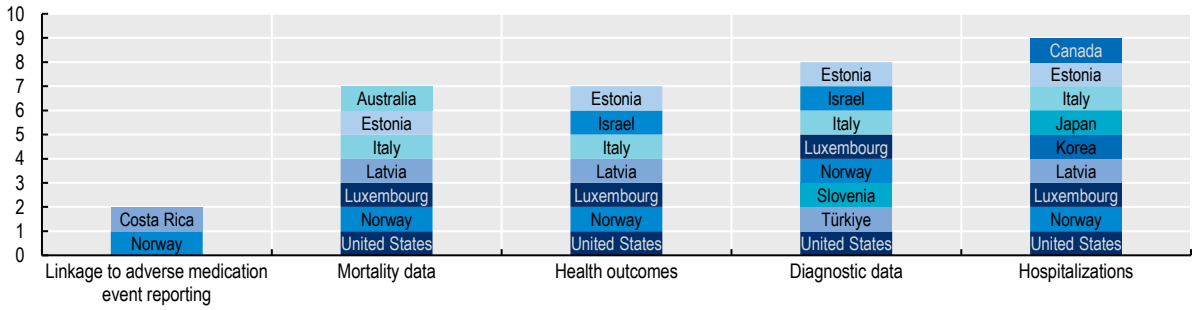



[20] http://www.norpd.no/

Note: N=21 responding countries, Countries may be counted in multiple categories.
Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022

The ability of DUR pharmaceutical data to be linked to other key datasets is important for producing meaningful information for providers and policymakers. A number of countries are able to link their DUR systems with data on hospitalisations, mortality, diagnostics, and health outcomes (see Figure 3.4). Only **Norway** and **Costa Rica** report currently being able to link DUR system data to adverse medication event reporting. In **Korea**, DUR and adverse event reports are available only for some individuals that have already experienced a medication related harm to ensure that the patient is not given the same drug that caused the ADR. DUR data are also linkable to real-time information on drugs contraindicated for blood donation, and to epidemiological data related to emergencies, such as communicable disease data for monitoring outbreaks[21].In the **Netherlands**, pharmaceutical data are linked to diagnosis in secondary and tertiary care, laboratory findings, socio-economic status, education. It is also linkable to the GP information system within a primary care database, in which 10% of the Dutch GP practices. To monitor the safety of individual patients, Medical Pharmaceutical Decision Rules (Medisch Farmaceutische Beslisregels) are used during and after the dispensing of medicines.

## Figure 3.4. DUR linkage capacity to other data sets




Note: N=2 responding countries, Countries may be counted in multiple categories. In Italy data are linkable at the regional level only.
Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022

Countries also cite linkages to other contextual and environmental data—including economic or cost data (**Norway and Luxembourg**) or national insurance benefits schedule (MBS) data (**Australia**). Data from DUR are linkable to eHR system in **Slovenia**, **Luxembourg**, **Türkiye**, **Italy, Estonia, Israel, Norway**, and **Japan**. In **Portugal**, it is possible in some settings to link prescribing and dispensing data to diagnosis or outcomes—but the analysis must be done manually. In **Estonia**, while there are no direct links to the contextual data, the national implementation of personal identification codes creates the possibility of linking additional databases.

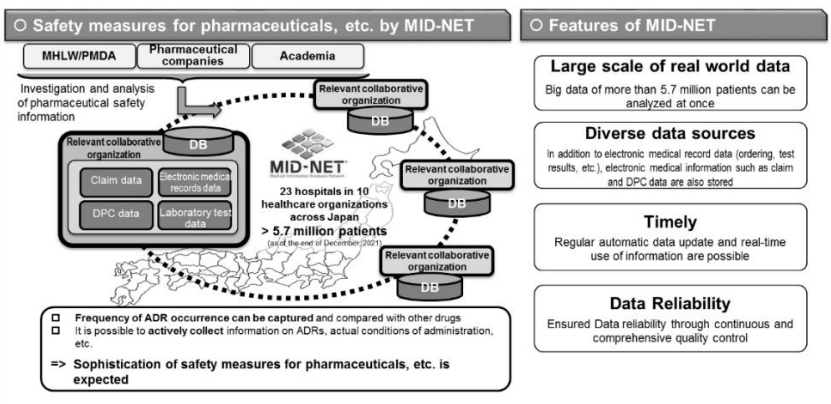
21

| Category | | Time | Organization | Year |
|---|---|---|---|---|
| Medication deferral list for blood donation | | Every day (once) | Korean Red Cross | 2014~ |
| Infectious disease | MERS | Real-time | Korea Disease Control and Prevention Agency (KDCA) | 2015~ |
| | Zika virus | | | 2016~ |
| | Ebola, Lassa, Pest | | | 2017~ |
| | COVID-19 contact history | | | 2020.1~ |
| | COVID-19 vaccination | | | 2021.5~ |

Further, the DUR system provides data on prescription status of infectious disease therapeutics to MFDS to assist supply and demand management of infectious disease drugs and respond to quarantine.

### Box 3.3. Japan's Medical Information Database NETwork (MID-NET®) for improving medication safety monitoring

In Japan, the Pharmaceuticals and Medical Devices Agency (PMDA) manages the medical information database "MID-NET®" (Medical Information Database NETwork) (Yamaguchi et al., 2019[158]). Through collaboration with 10 healthcare organizations including 23 hospitals across Japan, MID-NET® is capable of collecting and analysing medical information (electronic medical record data, administrative claims data, etc.) with a coverage of over 5.7 million patients. The data are used by government agencies, pharmaceutical companies, and academia and the analytical results are used in considering safety measures. MID-NET® functions by linking medical information database systems from healthcare organizations with data from administrative claims, Diagnosis Procedure Combination (DPC) and electronic medical records including laboratory test results. In addition to the diagnoses and prescribing information from claims data, MID-NET® has capacity to link to laboratory tests, allowing the possibility to detect ADRs from changes in the laboratory test results and to combine multiple types of information thereby allowing evaluation of a greater diversity of ADRs. MID-NET® is also used to perform routine monitoring of early medication safety signals before the accumulation of safety information from literature reports and reports of medication-related adverse events.




Partly modified from the original source: (PMDA, 2021[159])

In the **United States**, the FDA leverages multiple commercially available data sources to understand how pharmaceuticals are used at the national and subnational levels. In addition, FDA has created the Sentinel system to allow the agency to conduct drug utilisation analyses and safety studies using a distributed network that consists of data aggregators, health provider systems with eHR data, and insurer claims records (see Box 3.1). Together, these resources give the agency insight into retail pharmacy dispensing, physician prescribing, inpatient medication utilisation, eHR data, and insurance claims data. In-hospital mortality data are generally available, but linkage to the national death certificate registry is done on an ad-hoc basis. FDA also maintains agreements with federal partners that have epidemiology research programmes (Department of Defence, Veterans Affairs, etc.), and utilises several contracting mechanisms to support regulatory research at academic centres.

In **Estonia**, the State Agency of Medicines undertakes (pre- and post-authorisation) medication safety assessment; provides up-to date information on medication safety for health care providers and patients; responds to safety inquiries; collects, assesses and transmits data to the EudraVigilance data analysis system (EVDAS); reports on adverse drug reactions; and assesses the effectiveness of risk minimisation measures (using wholesale statistics and Health Insurance Fund database). Additionally, Estonia has a

Drug Prescription Registry (including dispensed medications), a drug-drug interaction database (INXBASE), and the Synbase database which is used in Primary care[22].

### *Timeliness of data availability in DUR systems varies*

The timeliness of data available in the Drug Utilisation Review System is another characteristic that influences its usefulness for policy making and clinical use. In seven countries, **Estonia, Korea**, **Norway, the Netherlands, the United States, Latvia and Slovenia,** DUR data are made available in real time. In **Korea,** physicians send patient prescriptions to the HIRA DUR service (see box 3.2), and HIRA reviews the data against patient's medication history and DUR standards, and alerts the physician within 0.5 seconds through a pop-up message if any of the prescriptions are found to be problematic. Pharmacists receive similar alerts during drug dispensing. For drugs with a warning message, pharmacists can check with the prescribing doctor whether the prescription should be changed, and if the physician approves a change, the changed prescription can be dispensed. In both cases, the final prescribed and dispensed information is sent back to HIRA. Similar alters are present in the Scottish DUR system, and are being implemented in such a way as to avoid 'alert fatigue,' whereby clinicians turn off alerts or override them on a regular basis.

Twelve countries indicated that data were made available with a delay, ranging from 1 week (**Japan**), between one and six months (**Canada, Costa Rica, Germany, Israel, Portugal, Luxembourg),** or on an annual or ad hoc basis (**Norway, Belgium**). **Italy** and the **United States** indicated that the timing depended on the data source, citing the distributed DUR structure.

### *Use of DUR data for monitoring and improving care*

The most common use of DUR data are for reimbursement coverage decisions, which reflects the fact that most DUR systems in OECD countries base their data on claims. However, a number of countries are using DUR data to drive quality improvement in health care delivery and as a mechanism for providing clinicians and prescribers with feedback (see Table 3.2).

[22] https://synbase.eu/tutvustus

### Table 3.2. Use of DUR data for provider feedback, quality improvement, and policy purposes

| Domain | Use of DUR data | Implementing Countries |
|---|---|---|
| **Clinician or prescriber feedback** | DUR data are **linked with clinician-level alert system** | Estonia, Israel, Netherlands, Republic of Korea, United Kingdom (Scotland), United States, |
| | DUR data **informs practice prescribing** | Costa Rica, Luxembourg, Netherlands, Portugal, Türkiye, United Kingdom (Scotland), United States |
| | DUR data **informs individual clinician prescribing** | Australia, Estonia, Japan, Netherlands, Republic of Korea, Türkiye, United Kingdom (Scotland), United States |
| | DUR data used to provide **real time dispensing decision support** for pharmacists | Estonia, Netherlands, Republic of Korea, United Kingdom (Scotland), United States |
| | DUR data used to **facilitate interactions between clinicians and pharmacists/others** (e.g. academic detailing, group audit and feedback) | Estonia, Netherlands, Portugal, United Kingdom (Scotland), United States |
| **Quality improvement** | DUR data used to **inform local practice guidelines** for prescribing | Costa Rica, Estonia, Israel, Netherlands, Portugal, United Kingdom (Scotland) |
| | DUR data used to **inform professional standards** | Luxembourg, Netherlands, Portugal, United Kingdom (Scotland) |
| | DUR data used to **inform practice performance indicators** | Estonia, Italy, Netherlands, Norway, Republic of Korea[23], Portugal, Türkiye, United Kingdom (Scotland), United States, |
| | DUR data used to **inform audit studies** | Estonia, Netherlands, Portugal, United Kingdom (Scotland) |
| | DUR data used to inform **structured dialogue** between clinicians and pharmacists | Netherlands, Portugal, United Kingdom (Scotland), United States |
| | DUR data linked to **clinical care guideline development and evaluation** | Estonia, Israel, Netherlands, Norway, Portugal, United Kingdom (Scotland), United States |
| **Policy Purposes** | DUR data used for **reimbursement coverage decisions** | Australia, Estonia, Germany, Israel, Italy, Luxembourg, Norway, Portugal, Republic of Korea[24], Switzerland, United Kingdom (Scotland) |
| | DUR data used for **formulary inclusion** | Costa Rica, Israel, Italy, Japan, Luxembourg, Portugal |

Note: Some countries have been included as implementing if the intervention has been implemented at the sub-national level.
Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022 and expert consultation.

## The status of adoption of digitalisation and medication patient safety initiatives

Countries show varying uptake of medication patient safety initiatives—including those related to adoption of new technologies, interventions aimed at patients and prescribers, and systems-level interventions (see Figure 3.6).

### *Supporting healthcare providers in medication safety and care coordination strategies*

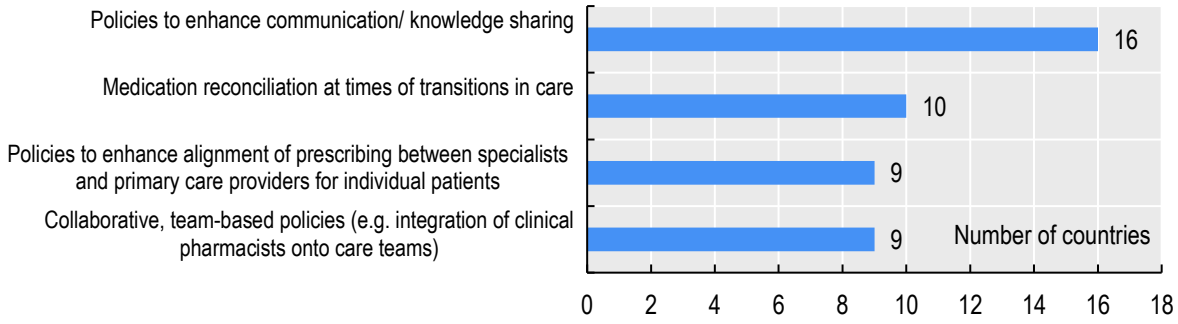
Health care providers have a clear role in improving medication safety outcomes, and countries have adopted numerous approaches to improve safety-related care coordination from the provider perspective, including strategies related to change management practices and vision setting around patient (Stewart et al., 2017[160]). Most surveyed countries (13 of 19) have implemented policies to enhance communication and knowledge sharing (see Figure 3.5). There are a range of possible educational interventions that vary in their form and intensity. Continued medical education and professional development can range from interventions to train prescribers (formal CME, supervisory visits, group lectures, seminars, workshops), to

[23] The "rate of prevention of overlapping prescription" was implemented in 2020 as a patient safety indicator from Indicators for the Healthcare Quality Evaluation Grant initiative of Korea National Health Insurance Program. This indicator is calculated based on DUR data.
[24] In principle, prescription of drugs with drug-drug interactions and age and pregnancy contraindications are not reimbursed (under the NHI). If these drugs were medically necessary, the reasons for prescription and dispensing must be specified on the claim, and the appropriateness of the claims are reviewed.

disseminating printed materials (e.g., clinical literature, newsletters, treatment guidelines and medicine formularies, illustrated materials), to more intense face to face interventions (e.g. educational outreach, use of local opinion leaders, academic detailing). Economic evaluations of continuing professional education for prescribing found them to be associated with reduced drug costs (Cook et al., 2022[161]).

Good care coordination between primary care and specialist care is key to ensuring synchronous, consistent care, but there is often poor understanding of respective roles and responsibilities between care providers (Vimalananda et al., 2018[162]). A 2017 study from the Netherlands, for example, found that one third of in-hospital prescription changes were either not documented or incorrectly documented in primary care providers records—putting patients at risk of medication-related harms (Poldervaart et al., 2017[163]). In addressing this, several countries (including **Australia, Belgium, the Czech Republic, Latvia, Luxembourg, Mexico,** the **Netherlands, Norway**, and the **United States**) have implemented policies to enhance alignment of prescribing practices between specialist and primary care providers for individual patients.

### Figure 3.5. Uptake of interventions to improve medication safety related to care coordination




Note: N=21 responding countries, Countries may be counted in multiple categories.
Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022

Medication reconciliation at time of transition of care is another intervention that has been adopted by many countries to improve medication safety and person-centred care. This activity often involves developing a complete list of a person's medications, reviewing them for accuracy, and assessing and documenting any changes. Even though reconciliation is recognised as a key mechanism to improve patient safety, recent systematic reviews have noted a lack of consensus and evidence on the most effective ways of conducting systematic reconciliations (Redmond et al., 2018[164]). Ten countries report medication reconciliation occurs at times of transition in care. Team-based policy approaches—including the integration of clinical pharmacists onto care teams—have also been adopted in a number of cases. Collaborative transdisciplinary team-based approaches involving physicians, nurses and pharmacists have been found to be effective in improving medication safety (Håkansson Lindqvist, Gustafsson and Gallego, 2019[165]).

Another important—and widely adopted—intervention involves prescriber access to patients' medical history, including past prescribed or de-prescribed medicines, with **Australia, Costa, Rica, the Czech Republic, Estonia, Germany, Israel, Luxembourg the Netherlands, Norway, Slovenia** and **Türkiye** reporting that policies to enable this have been adopted at the national level. Improved integration of prescription medication monitoring programs and eHRs is a particular area that has been identified for improving prescribing practices by increasing the availability of past prescription information (Freeman et al., 2019[166]).

Policies for providing clinician decision support and performance feedback are promising strategies for improving prescribing practice and reducing low-value care, particularly when paired with other strategies (Colla et al., 2017[137]). Mechanisms to monitor the volume of prescriptions at the system level can be linked

to the prescriber level to optimise prescribing, encourage behavior change, and ultimately improve patient safety and outcomes. As discussed previously in this section, DUR systems have been used by a number of countries with the objective of changing the behaviour of individual clinicians (see Table 3.2). This should occur at multiple levels, starting with the individual prescriber who gets feedback on their prescribing patterns. The feedback loop ideally continues at the practice level, regional level and national level to help inform a clearer picture of what's going on and to help target specific interventions to change patterns and behavior. Countries reporting national systems for audit or feedback mechanisms for prescribers include **Australia, Belgium, Costa Rica, Estonia, Japan, the Netherlands, Norway, Slovenia, Türkiye, Scotland in the United Kingdom** and **the United States**.

### *Patient-focused medication safety initiatives*

Patient-related safety strategies, those that involve education and access to medication information, patient-reported experiences, and targeted interventions to vulnerable populations, have been adopted by a significant proportion of responding countries. Examples include **Korea's** 'knowing medicine correctly' project by MFDS, which was initiated to increase the public's understanding of medications, including the right administration of medications, and is continuously providing medication safety education for children, adolescents, pregnant women, and older adults.

Shared-decision making between a physician and a patient is an element of the care process that is important to emphasize and understand in order to improve medication use. The patient is an active participant in their care decisions and thus, any interventions to improve pharmaceutical therapy decision making needs to ensure that patient preferences and values are adequately addressed. A key component to this involves ensuring that patients have access to information about the medicines they are prescribed (e.g. though an online portal or physical medicines passport). Countries that have policies in place to ensure patient access to information about their medicines are **Australia, Costa Rica, the Czech Republic, Estonia, Germany, Israel, Japan, the Netherlands, Norway** and **Türkiye**. In **Korea**, the 'My prescription medicine" at a glance' service by HIRA utilizing DUR grants patients access to the information about the list of drugs dispensed to the patient at a hospital or pharmacy in the past 1-year. However, access is not universal, but is limited to those who have consented to the provision of personal information. In the **United Kingdom (Scotland)** a patient mobile application has been developed to allow patients shared access with clinicians to decision making tools for managing medications.

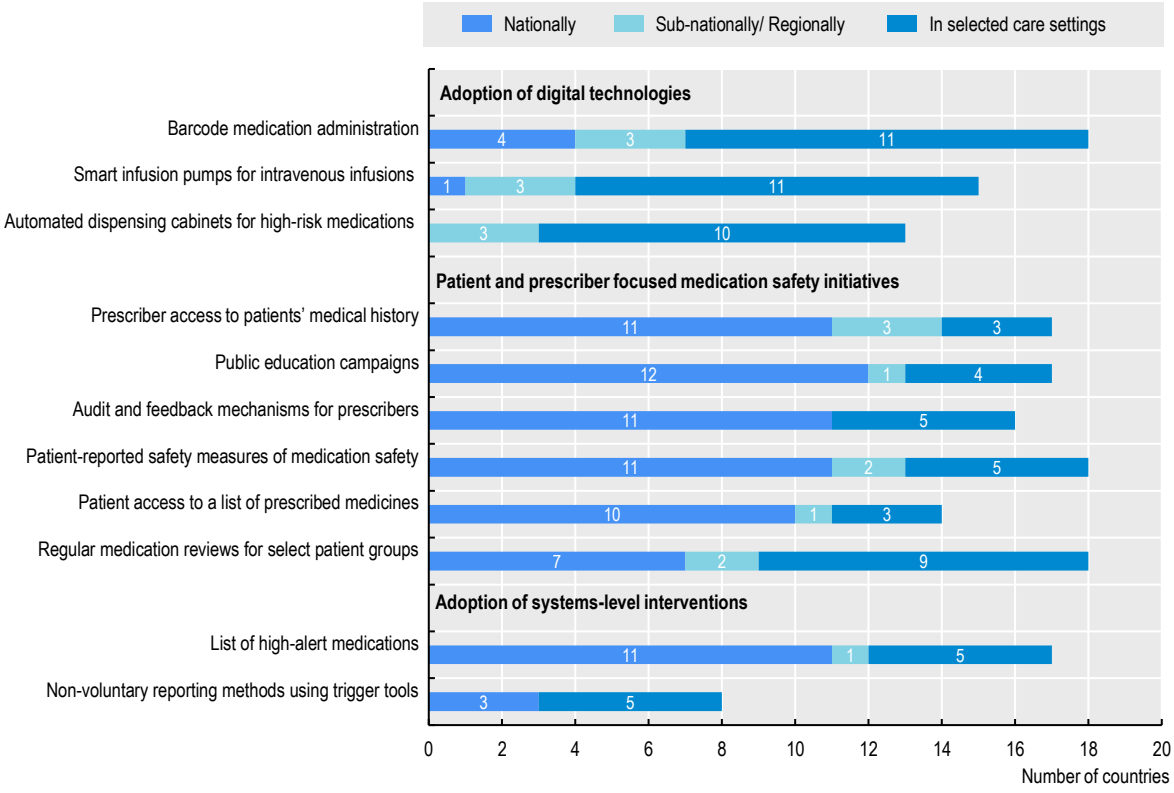
Patient-reported safety measures related to medication safety (i.e. assessments of patient reports of medical errors) have been adopted at the national level by ten countries (**Belgium, Canada, Costa Rica, Estonia, Germany, Italy, Japan, Netherlands, Türkiye, and the United States**) and adopted at the sub-national level or in select institutions in six more. As discussed in Section 1, patients are a key source of information on the prevalence of medication-related harms Data may be collected via dedicated data portals (as is done in **Costa Rica**—where there is a shared online portal to allow citizens and health providers to report suspected medication-related adverse events[25]) or via population-based surveys, as is done in Belgium. Measures of patient safety from the perspective of patients can be used, along with traditional patient safety indicators, health outcome indicators, and measures of patient safety culture reported by health care workers to give a holistic perspective of the state of safety in health systems (de Bienassis and Klazinga, 2022[167]). As countries build out their patient-reported safety measures, there are opportunities to harmonise internationally and use the information for benchmarking purposes (OECD, 2019[168]).

Regular review of medications was also nationally implemented in seven countries (**Belgium, Australia, Costa Rica, Japan, Netherlands, Norway,** and **Luxembourg**)—with sub-national or institution-based implementation in an additional (nine). In **Germany**, patients who use three or more medicines

[25] http://www.notificacentroamerica.net/n/Pages/mapa.aspx#no-back-button

simultaneously are entitled access to an electronic medication treatment plan (eMP), which contains information about the patient's medication (previous medication, prescribed and over-the-counter medications), medication-related data (e.g. allergies, intolerances or pre-existing conditions) and information about usage (dose, administration method, etc.). In **Korea**, the National Health Insurance Service launched the Pilot Project for Polypharmacy Management, including providing assistance to use drugs appropriately, reviewing overlap of similar drugs, monitoring ADEs/ADRs, and assessing health status, for patients with hypertension, diabetes, or heart disease who regularly take 10 or more drugs (for ≥ 60 days in a 6-month period).

## Figure 3.6. Status of adoption of digitization and medication safety initiatives by level of adoption by country




Note: N=21 responding countries, Countries may be counted in multiple categories.
Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022

### *Adoption of digital technologies to improve patient safety*

Digital technologies and automated systems—such as barcode medication administration, smart infusion pumps, and automated cabinets for high-risk medications—hold great potential for improving medication safety outcomes (Truitt et al., 2016[169]; Zheng et al., 2021[170]). However, systematic uptake of these interventions is lagging. Only four countries, **Costa Rica, Estonia**, **Israel** and the **Netherlands**, currently have implemented national programmes using barcodes to track medications for administration—and only **Germany** and **Norway** report that barcode systems are used systematically at the sub-national/regional level. No countries reported national adoption of automated dispensing cabinets for high-risk and other medications, though **Germany** and **Norway** reported their use at sub-national/regional level. Only **Türkiye** reported national adoption of Smart infusion pumps for intravenous infusions. To date, most digitally related interventions have been adopted by countries only in selected care settings. Seventeen countries use

barcode medication administration, 14 use smart infusion pumps, and 13 use automated dispensing cabinets in at least some settings.

### *Adoption of systems-level interventions*

High-alert medications are medicines that present particularly high risk of causing severe patient harm if subject to a medication error (ISMP, 2018[171]). Adoption of national lists of high-alert medications can guide healthcare leaders in the implementation of safeguards to reduce the occurrence of medication errors and harms associated with incorrect use of these medicines. National lists of high alert medications have been developed in in **Australia, Belgium, Costa Rica, Estonia, Germany,[26] Israel, Japan, Mexico, Slovenia, Türkiye,** and **United States**. In **Korea** 'High-risk drug safety guidelines for pharmacies' were announced at the Regional Patient Safety Centre of the Patient Safety Management Headquarters of the Korean Pharmaceutical Association in January 2020. This includes safety management standards in inventory management, storage, dispensing, administration, patient safety events reporting, monitoring, analysis, and prevention education for high-risk medications in pharmacies. Also, medical institution accreditation standards implemented by the Korea Institute for Healthcare Accreditation include "Storage and Management of High-Risk Medications", requiring medical institutions to set and manage this list of high-risk medications.

Another system-wide intervention that has capacity to help assess the occurrence of medication safety errors—and thus inform policy makers where action needs to be taken—is novel reporting techniques. Trigger tools, for example, involve a retrospective review of random samples of hospital records using predetermined codes, or "triggers," to identify possible medication-related harms. These tools have the benefit of not relying on spontaneous reporting of adverse events, which require health care providers to actively report safety incidents and have been found to significantly underestimate the occurrence of events (IHI, 2018[172]). Only **Estonia, Norway** and **Costa Rica** report currently having national level systems of non-voluntary reporting using trigger tools, but **Australia, Israel, the Netherlands, Mexico, Switzerland,** and **the United States** report that trigger tools are used in some settings.

[26] The German Actionplan for improving medication safety (2021 – 2024) there is a measure is currently to create this kind of list and for creating action recommendations.

# 4 Building medication safety into the COVID-19 recovery

## The dynamics created by COVID-19 can be used to accelerate change

The coronavirus pandemic has placed substantial strains on the health care workforce and resources, revealing and exacerbating the real patient safety risks that come with health care. The experience of this significant crisis has served as a mechanism for significant changes in terms of regulation, governance, and structural resources for health care safety. This section assesses the opportunities that can be taken by countries as they look to adapt their health systems to the new normal to build medication safety into their COVID-19 response and recovery activities.

## Improving the functionality of data for monitoring medication safety in real-time

The COVID-19 pandemic has made apparent the need for solutions to address long-standing deficits in health system information and communication systems in OECD countries. The pandemic has a major impact on future operations of healthcare, the need for communication and transparency, and other public trust measures, increased digitalisation, and the need for rapid and robust pharmacovigilance.

Many countries found that they lacked basic, timely data for decision making—such as information on health workforce, resources, hospitalisations, and mortality. Moreover, **the political environment caused by the COVID-19 pandemic has created an opening for meaningful reform**, as deficiencies in health sector information systems have led to inadequate information for responding to the COVID crisis. COVID-19 has also provided an opening for countries to leverage COVID-19 related reforms in a way that may also address long-standing barriers in the structures, policies and institutions that have kept OECD countries from fully utilising and benefiting from health-related data.

A health system's capacity to support rational medication use is largely related to the quality and linkage of the data that are collected. Missing information about a patient's current treatment regimen or diagnosis through poorly coordinated information systems can result in a prescriber making a medication therapy decision that they might have otherwise avoided (Cresswell et al., 2017[173]). Information friction is common in highly segmented health systems like the United States[27], but occurs across many OECD countries where diagnosis, outcomes, hospital admissions, dispensing and prescribing information are not readily available to both the patient and prescribing provider (Oderkirk, 2017[174]). This often happens during transitions of care, which has been identified by the WHO as one of the high-risk situations for medication safety events (WHO, 2017[175]). Integrated data systems, with **linkages between key datasets**, including

[27] Segmentation in general may be caused by duplication and lack of harmonization in regard to formats of data entry and data owners/stewards, as well as limitations or lack of mandates/coordination for data linkage or sharing.

prescription databases, eHRs, administrative databases, and adverse-event reporting systems, can help countries responsively or pro-actively identify and address medication safety issues.

In a 2021 OECD survey, 15 of 24 responding countries indicated that there had been legal, regulatory, or policy reforms in 2020 and 2021 to improve health data availability, accessibility, or sharing. In conjunction with efforts to increase data sharing, 9 of 24 countries had made reforms to improve privacy or security protections—with a number of countries strengthening both data sharing and data privacy simultaneously (de Bienassis et al., 2022[176]). Data sharing improved significantly within the public sector, sometimes through automated processes. Most OECD countries linked different data sources to monitor the COVID-19 pandemic and open data policies were promoted. Not surprisingly, timeliness of key national datasets was an area where countries almost universally drove data advancements as a result of the COVID-19 pandemic. In addition, the need for improved data quality was, and continues to be, essential to informing countries' COVID-19 related policies. Improvements in the quality, coverage, and completeness of existing national personal health datasets were widely made among OECD countries in response to COVID-19 (de Bienassis et al., 2022[176]). These regulatory reforms and enhanced **data sharing** capacity, including new internationally oriented projects such as the European Health Data Space[28], can potentially be further leveraged to inform systems for monitoring medication safety—for example through standardized coding and harmonization of patient safety terminology.

The COVID-19 vaccine rollout demonstrated the importance of **real-time information sharing**, open-source data repositories and strong communication systems to identify, investigate and respond to rare adverse events. These trends are important steps towards strengthening pharmacovigilance systems across OECD countries and globally—and a pathway to improving medication safety outcomes. Governments must continue to build upon the gains made in the last two years and ensure health data systems are high-quality and interoperable; integrate eHRs with information on patient diagnosis and outcomes; and put in place fit for purpose laws and policies that allow data linkage (Naniche et al., 2021[177]).

Section 3 illustrated the increasing number of countries that are collecting data on prescribed or dispensed medications and using it both prospectively and retrospectively to learn about and improve the rational use of medicines. The accelerated approval of medicines for the treatment of COVID-19 underscored the necessity of robust data collection on medication utilization and outcomes to inform prescribers on the evolving benefit-risk profile of these medications. Ideally, countries adopt or strengthen systems that link **individual-level prescription data with other data to follow the pathway of care and observe patient outcomes** to allow for the feedback loops in the system to both change behaviour and inform patient safety.

## Using good patient safety governance and transparency to build public trust

The COVID-19 pandemic has highlighted how a lack of clear information and timely data can cause uncertainty in decision-making and foster mistrust among the population. Ensuring the availability of timely and granular open-source data on key issues, such as the number of people vaccinated, the number of doses administered, geographical coverage, and the number of people experiencing adverse reactions, has been used to facilitate data analysis and dissemination (OECD, 2021[178]).

Over the course of the coronavirus pandemic, countries have observed increasing levels of distrust in government capacity to handle the crisis and implement coherent policies. More broadly, the pandemic has triggered widespread disinformation that has undermined both understanding and acceptance of science and public policy (de Figueiredo et al., 2020[179]). For example, despite widespread recognition

[28] https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en

among experts that COVID-19 vaccination can reduce the occurrence of serious COVID-19 related complications, significant portions of the population were unwilling to be vaccinated—in part due to the influence of misinformation. Data from seven OECD countries showed that in January 2021 a quarter of the population in France, Germany and the United States stated that they would refuse COVID-19 vaccination, and an even higher proportion among younger population cohorts. More than 50% of French 25- to 34-year-olds, and one-third of Dutch 25- to 34-year-olds, said they would probably or definitely not get vaccinated (Kantar, 2021[180]).

To improve transparency and public communications, many countries have **increased capacity for communicating data with the public**, for example through dashboards or other online systems. The pandemic increased the need for timely data including new systems to analyse and report data so that information could be quickly communicated and utilised by policy makers and stakeholders, including the public (Barbazza et al., 2021[181]). All 24 countries that responded to the 2021 survey reported that new mechanisms for reporting and analysing timely personal health data were established (de Bienassis et al., 2022[176]).

Proactively releasing information that is up-to-date, reliable and easy to understand about medication safety, in compliance with access to information laws, is also crucial for people outside government to have confidence in the effectiveness of government regulation and policies. In the context of the COVID-19 pandemic, trust in the safety of vaccines, for example, was tested by reports of rare, but serious, adverse events with a probable causal link to the Oxford/AstraZeneca vaccine. Both the safety signal and the different responses of public health bodies around the world undermined public confidence. In order to promote public trust in new and existing medicinal products (including vaccines), it is essential that governments demonstrate that no quality or safety standards were compromised for the sake of speedy development and approval processes (OECD, 2021[178]). As part of this, regulatory bodies have shown increased openness and capacity to conduct rapid assessment of patient-reported suspected adverse reactions after vaccination.

To respond to increasing public demands for immediate, easily understandable information, dashboards have been used as a key communication tool for sharing COVID-19 related data to the public in most OECD countries and these are generally updated daily and accessible to the public (de Bienassis et al., 2022[176]; Ivanković et al., 2021[182]) In COVID dashboards, countries usually report tests, cases and deaths but in some cases, other indicators are also reported. **Canada** developed a COVID dashboard and interactive tool on excess mortality, and an international interactive data map of COVID-19 cases by country for international benchmarking. A Health Inequalities Improvement Dashboard in **England (United Kingdom)** will contain expanded datasets where there is currently a relative scarcity of information, e.g. for people experiencing post-COVID syndrome (NHS, 2021[183]).

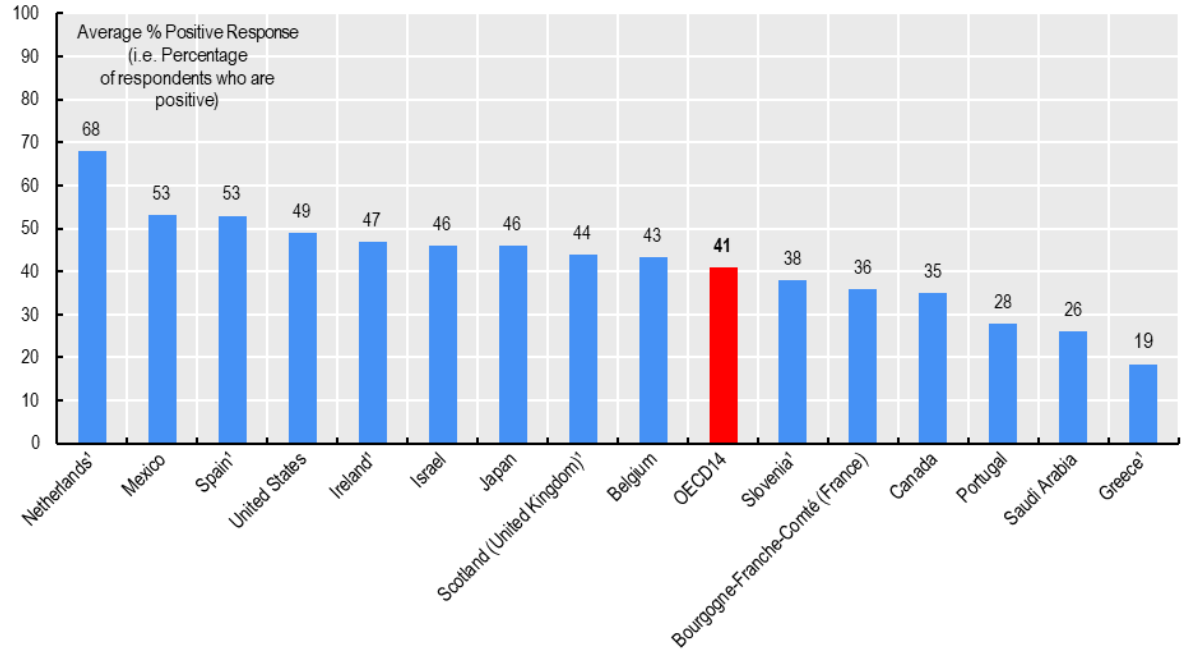
As countries work to **restore trust in and strengthen the regulatory systems** that may have been affected by COVID-19, there are opportunities to improve governance practices at all levels of health care delivery. Moreover, there is a need for comprehensive monitoring and reporting of both the benefits, harms, and levels of uncertainty. Research has increasingly dismissed the notion that presenting evidence as uncertain or being open about what is not yet known leads to a loss in trust (van der Bles et al., 2020[184]). Moreover, withholding information, however tentative, has been shown to lead to mistrust, as documented widely during the pandemic and other crises. Communicating uncertainty is therefore important and necessary to prevent and curb misinformation. In this respect, trust can be rebuilt through good communications strategies, **while dually transparent about the degree of certainty about any claims, levels of risk, and margins of errors** of shared data on safety. Finally, lessons learned in relation to communicating about COVID-19 can be applied to medication safety—including **access to publicly available data and transparent reporting**.

### *Governance should promote a safety culture that enables reporting and learning*

Most medication safety surveillance systems rely on voluntary reports of medication errors and adverse events, however, there remain major barriers in creating an environment where clinical care providers, health care institutions, and patients alike feel comfortable (and supported) in bringing forward reports of adverse events and near-misses. Findings from recent work assessing patient safety culture in the hospital setting have found that only 42% of staff on average across OECD countries feel that their mistakes and event reports are not held against them and that mistakes are not kept in their personnel file (see Figure 4.1). Concerns about punishment, blame and legal consequences can impact reporting practices. Just over half of surveyed health workers in OECD countries feel that near-misses and other types of medication errors are appropriately reported in their care setting (de Bienassis and Klazinga, 2022[167]).

## Figure 4.1. Health Workers perceptions of nonpunitive response to errors, data from latest year by country

Less than half of health care workers on average in OECD countries report that their mistakes and event reports are not held against them and that mistakes are not kept in their personnel file




1. Data older than 2015. Note: The size and composition sample of patients and hospitals may vary from year to year. Please see (de Bienassis and Klazinga, 2022[167])for more information on the included surveys.

Source: OECD Patient Safety Culture Pilot Data Collection, 2020-21

Establishing a reporting-culture across health care settings is a key aspect to creating systems that can benefit from organizational learning and continuous improvement so that mistakes can lead to positive changes and changes evaluated for effectiveness. Commitment on the part of leadership and management is crucial to establishing and maintaining a safe, people-centred environment that enables reporting to medication safety surveillance systems. Healthcare leaders play a key role in fostering communication and creating enabling atmospheres where health care workers feel able to raise concerns and submit error reports without fear of personal retribution. Finally, patients must be actively engaged and included in the development of a safety culture that promotes safe medication use.

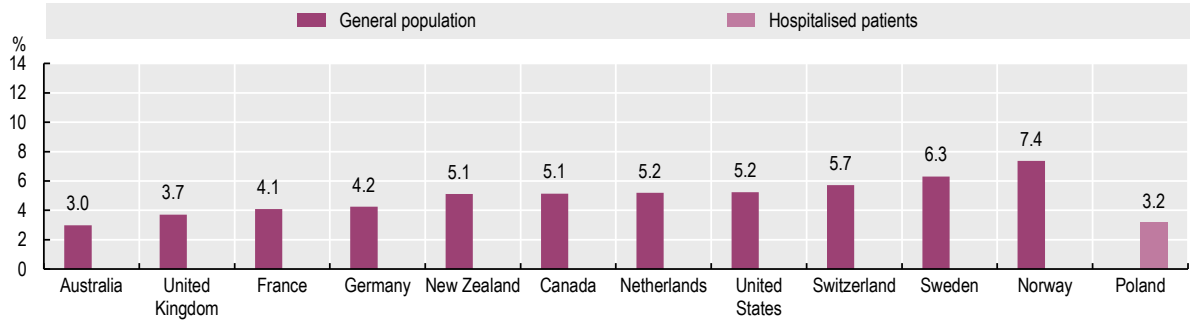
## Investing in person-centred medication and addressing the behavioural aspect of improving mediation safety outcomes

The 2020 and 2021 health systems responses to the COVID-19 pandemic with testing and vaccination policies have largely **lacked patient-centeredness**, revealing a lack of embedded people-centred care policies into OECD health care systems. The absence of formal patient representation in health decision making was largely absent while countries made rapid decisions to contain the virus's spread, such as measures restricting mobility and measures implemented in hospitals and long-term care settings. Among 57 patient organisations in Europe, nearly two-thirds indicated that there was no patient involvement or consultation in management and decision making processes during the pandemic (OECD, 2021[185]). Beyond the moral imperative, the collective action required for the Covid-19 response suggests that countries would have benefited from public engagement to shore up trust in the institutions, evidence generated and decisions made (Bernheim, 2016[186]; Lancaster, Rhodes and Rosengarten, 2020[187]). Similar findings on limited public engagement have been described in relation to the development of new public reporting mechanisms and dashboards (Barbazza et al., 2021[181]). Governments can leverage existing strategies for efficient and active community participation under public health emergencies and integrate them into existing medication safety systems (Dick, Moodie and Greiner, 2022[188]).

### *Investments should continue to build systems that capture patient experience of medication-related harms and medication side-effects*

Patient perspectives are critical to make health systems more safe and people-centred—and patients are a key source of information about the prevalence of medication-related harms. Measurement of patient experience and outcomes is far from systematic in most countries, and international comparability remains limited. Patient experience of medication-related harms can provide important information about the status of medication safety. Capturing patients' experience directly is an avenue to increase the rate of adverse event reporting and to improve signal detection (Weigmann, 2016[189]). Among a number of patient safety incidents for which patient-reported data has been collected, medication-related incidents are the most frequently reported across countries. The proportion of people who reported wrong medication or wrong dose given by a doctor, nurse, hospital or pharmacist in the past two years ranged from 3% in Australia to 7% in Norway (Figure 4.2). In Poland, 3% of hospitalised patients reported medication-related incidents. These data need to be interpreted with care: they may be underreported because patients may not know about all cases of medication error (OECD, 2019[190]). Countries should continue to adopt **patient-reported experiences of safety**, including those related to medication-related harm and errors.

### Figure 4.2. Patients reporting that they experienced a medication-related mistake, 2020 (or nearest year)




Note: Data for the general population are from the Commonwealth Fund 2020 International Health Policy Survey.
Source: OECD Pilot Data collection on Patient-Reported Experience of Safety, 2020-21.

While much recent focus on strengthening people-centred measures of health systems has been on expanding patient-reported outcome measures, this should be complemented by systems built to capture **patient-reported outcomes related to medication side effects** as part of assessments of health outcomes. Effective side-effect management can improve health outcomes by increasing medication adherence and reducing negative impacts of medication. A striking example comes from the area of cancer treatment where the use of patient reported-outcomes in monitoring chemotherapy in the US increased cancer survival by 5 months (Basch et al., 2017[191]). A similar study from France found that electronic use of patient-reported outcomes when following patients being treated for lung cancer increased life expectancy by 7.6 months compared to usual care—with authors concluding that one of the main reasons for the improvement being that medication-related harms were detected earlier (Denis et al., 2019[192]).

### *Supporting people-centred care systems and promoting shared-decision making*

Ensuring that patients can make informed decisions about their treatment and participate in their treatment process is a core tenet of people-centred health systems—and key to ensuring public trust. However, poor health literacy and the lack of shared decision-making structures can reduce patients' ability to participate in their care—and in turn, impact health outcomes. Poor health literacy has been associated with poorer overall health for older adults, including poorer medication adherence and a higher risk of mortality (Moreira, 2018[193]). Education on the risks and benefits of medications should be clearly and consistently communicated via policy interventions to **improve medication literacy**. There are opportunities to leverage communication systems and public outreach which have been strengthened due to outreach related to the COVID-19 pandemic. At the micro-level, prescribers should engage in **shared-decision making** discussions with patients. Patients should feel they have the necessary information to make an informed decision and that they have enough time to discuss treatment options with their prescriber.

## Capitalising on COVID-19 related improvements in access, including care in pharmacies and digital health

### *Building medication safety into digital advancements that have been made in the health sector*

Digitalisation of health services has been significantly expanded in response to the COVID-19 pandemic—in particular, the expansion of telemedicine and digitalisation of scheduling COVID-19 related services, such as testing and vaccination. A 2021 OECD survey found that sixteen of 24 countries reported having introduced new technologies to improve health data for the purposes of improving health data quality, coverage, and timeliness. Countries have made significant investments in systems for public health monitoring, assessments of resource use and availability, and data to monitor the status of non-COVID related health needs (OECD, 2022[194]).

Reduced person-to-person interactions led to the digitalisation of a number of health activities that were not typically conducted online previously —potentially leading to the creation of new tools (online medication review) and new datasets for informing policy making. Much of these data may be unstructured and will require coding using artificial intelligence or natural language processing to convert them to meaningful information. Telemedicine may contribute in several ways to providing care in the right place at the right time, for example, by improving the process and appropriateness of referrals. There should be careful oversight and regulation of digital services for health in order to maximise benefits and avoid harm, but used effectively, they have potential to improve medication safety by expanding improving access (Pecina and North, 2016[195]).

Electronic prescribing strategies and clinical decision support have been found to be effective in decreasing medication errors and medication-related harms and are associated with a reduction in prescribing of

potentially inappropriate medications (Roumeliotis et al., 2019[196]). E-prescribing systems allow prescribers to write prescriptions that can be retrieved by a pharmacy electronically, to assess a patient's medication regimen at the point of care, and can be used to identify non-adherence, reduce workload, improve stock management, simplify reimbursement, and enable the preparation of orders before patients arrive. In addition, ePrescriptions can facilitate transparency, by making doctors more accountable for what they prescribe (e.g. allowing the evaluation of adherence to clinical guidelines), and making pharmacies more accountable for what they dispense and in what timeframes. COVID-19 has further cemented adoption and use of electronic drug prescribing, which has great potential in improving medication safety outcomes as well (OECD, 2022[194]). In **Poland**, the COVID-19 crisis has coincided with the introduction of the nationwide e-prescription system—this includes systems for ordering and filling of prescriptions remotely. In **Austria**, new policies were put in place to allow patients to receive prescriptions without physical visits to the prescribing physician. In the **Czech Republic**, systems were put in place to operationalise electronic prescriptions (eRecept).

**Australia** accelerated the rollout of an electronic prescription system to support telehealth consultations and help protect health care providers and patients from COVID-19, by removing the need to present to a GP in person to obtain a prescription. As of August 2021, more than 15 million original and repeat electronic prescriptions had been issued. The benefits of electronic prescriptions are perceived at patient, health care provider and, more broadly, at a system level, and include:

- Reducing the administrative burden for health care providers and organisations (such as more effective management of repeat prescription requests);
- Supplementing delivery of telehealth services to ensure continuity of patient care;
- Providing an opportunity to protect community members and health care providers from exposure to infectious diseases (such as COVID-19); and
- Maintaining patient privacy and integrity of personal information.

ePrescribing systems generate valuable data for use in drug utilisation review, which can then be used to enhance prescriber feedback mechanisms, information to patients, or advise policy makers in real time as to trends in prescribing practices. Linkages with eHRs is the next frontier—where together the **data from ePrescribing and eHRs can be used to monitor outcomes** (including, but not limited to the occurrence of medication-related harms) **in almost real-time** to enhance safe medicines use and rational use of medications.

### *Expanding the roles of pharmacies and pharmacists*

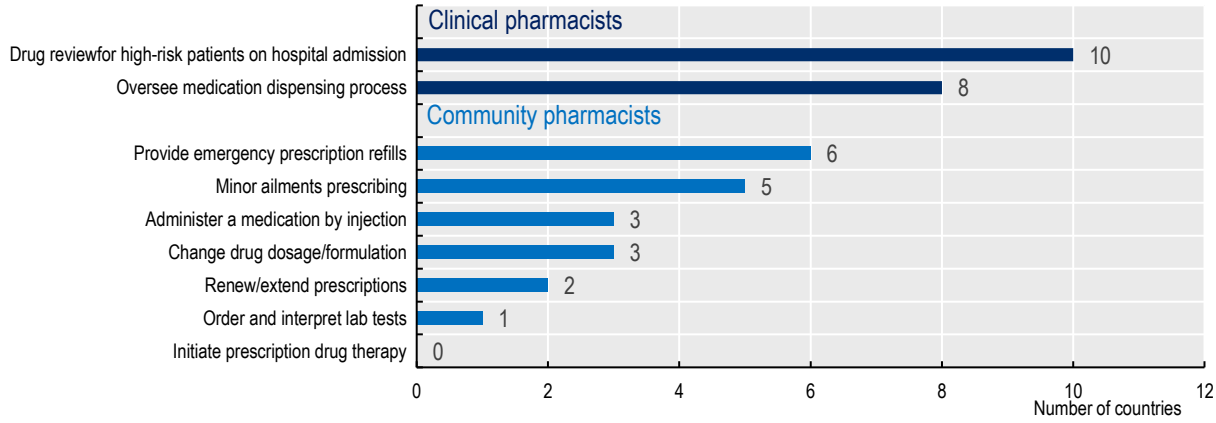
In many OECD countries, the scope of practice of community pharmacists has been expanded so that they can take on some of the tasks from doctors and nurses (OECD, 2020[197]; OECD, 2020[198]). There is widespread acknowledgement that **pharmacists are under-utilised** and their expanded role has the potential to support and improve safe, effective and efficient use of medications (Mossialos et al., 2015[199]). Pharmacists' involvement in helping to identify and reduce AMEs and promote medication adherence is well-accepted. Their tasks are expanding well beyond this and this expansion should be evaluated rigorously to assess its impact – both positive and negative – on patient outcomes, safety, professional development, human resources and reimbursement (Law et al., 2012[200]).

During the COVID-19 pandemic, several countries have made efforts to mobilise pharmacists and care assistants. In **Austria**, **Canada**, **Ireland**, **Portugal** and the **United States**, pharmacists have been allowed to extend prescriptions beyond previous limits and to prescribe certain medications, allowing physicians to focus on more important cases and minimise the number of medical consultations (OECD, 2020[201]; PGEU, 2020[202]). In **France**, community pharmacists were given an exceptional authorisation to renew prescriptions of drugs for chronic diseases. In Australia, Germany, Israel, Netherlands, Norway and

Switzerland, these changes are permanent and community pharmacists are able to provide emergency prescription refills (see Figure 4.3).

Many of the changes initiated at the onset of COVID-19 to increase the role of community pharmacists have carried over to 2022. The roles that pharmacists play can vary by country. In **Japan** and the Netherlands, pharmacists can change prescriptions to generic drugs. Additional guidance for pharmacists on changing prescriptions in the Netherlands is available via a 'responsible changing of medicines' policy[29]**.** In **Germany, Luxemburg**, and **Portugal**, pharmacists have been allowed to administer vaccines for COVID-19. In the **Netherlands** and **Portugal** pharmacists are able to renew or extend prescriptions for contraceptives. In certain areas in the **Netherlands** they may order laboratory tests.

## Figure 4.3. Countries reporting expanded roles for clinical and community pharmacists




Note: N=21 responding countries, Countries may be counted in multiple categories.
Source: OECD survey on the assessment of the adoption of systems and interventions to improve medication safety, 2022

In some cases, reforms to expand the role of pharmacists pre-date the COVID-19 pandemic. Since 2017 **Belgium** has had a policy of establishing "reference pharmacists" for patients living with chronic health conditions. The role of these pharmacists is to maintain patients' medication regimens and coordinate other health care providers[30]. In **Australia**, in response to the bushfire crisis in January 2020, the Government temporarily expanded the range of Pharmaceutical Benefits Scheme-subsidised medicines that could be supplied without a prescription under the Continued Dispensing Emergency measure—previously only permitted for certain oral contraceptives and lipid-lowering medicines (statins). The policy allows approved pharmacists to dispense an expanded list of products when cessation of therapy could lead to undesirable health outcomes, and the prescriber is not contactable or is unable to provide a valid PBS prescription. The pharmacist may provide one continued dispensing supply per eligible person within a 12-month period if the person has previously been prescribed the medicine, if the therapy is stable and the medicine is safe and appropriate for the person. Emergency arrangements were extended from 1 April 2020 to support the response to the COVID-19 pandemic, and have been further extended several times, most recently until 30 June 2022. In **Scotland (United Kingdom)** and **Estonia** pharmacists have been integrated into

[29] https://www.knmp.nl/media/1301
[30] https://www.inami.fgov.be/fr/professionnels/sante/pharmaciens/Pages/pharmacien-reference-accompagner-patients-chroniques.aspx

multidisciplinary care teams. Interventions to **leverage community and clinical pharmacists** can be maintained or expanded as a mechanism to improve medication safety outcomes.

## Conclusions

OECD countries have already made significant progress in implementing functional tools to monitor and assess medication safety. The next frontier is operationalising the data reforms to make systems safer in real-time. A number of countries can be looked to as leaders in the field, and their health information infrastructures can be viewed as a roadmap for improving medication safety.

In addition to improved monitoring, medication safety needs to be institutionalised through good governance practices and a culture of safety. Smart investments in digital tools and systems have the opportunity to improve the use of medications. But just as in other sectors, the process of adopting and implementing new processes and ways of working can also lead to safety lapses and need to be evaluated. Further analysis is needed to assess the potential harms and costs resulting from long term medication-related harms. **The innovations to improve medication safety in the health sector have great potential,** but require careful evaluation and calibration when implemented by countries to prevent the introduction of new safety risks.

# References


AAFP (2017), *Low Back Pain*, https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/back-pain.html (accessed on 14 April 2022). [42]

Aida, K. et al. (2021), "Potentially inappropriate medications at discharge among elderly patients at a single tertiary emergency medical institution in Japan: a retrospective cross-sectional observational study", *Acute medicine & surgery*, Vol. 8/1, https://doi.org/10.1002/AMS2.711. [82]

Alvim, M. et al. (2015), "Adverse events caused by potential drug-drug interactions in an intensive care unit of a teaching hospital", *Revista Brasileira de Terapia Intensiva*, Vol. 27/4, p. 353, https://doi.org/10.5935/0103-507X.20150060. [72]

AMCP (2019), *Drug Utilization Review*, https://www.amcp.org/about/managed-care-pharmacy-101/concepts-managed-care-pharmacy/drug-utilization-review (accessed on 11 March 2022). [35]

Arellano, C. et al. (2016), "Using two tools to identify Potentially Inappropriate Medications (PIM) in elderly patients in Southern Chile", *Archives of Gerontology and Geriatrics*, Vol. 67, pp. 139-144, https://doi.org/10.1016/J.ARCHGER.2016.08.001. [83]

Armitage, J. et al. (2019), "Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials", *The Lancet*, Vol. 393/10170, pp. 407-415, https://doi.org/10.1016/S0140-6736(18)31942-1. [40]

Auraaen, A., K. Saar and N. Klazinga (2020), "System governance towards improved patient safety: Key functions, approaches and pathways to implementation", *OECD Health Working Papers*, No. 120, OECD Publishing, Paris, https://doi.org/10.1787/2abdd834-en. [138]

Australian Government Department of Health (2020), *Quality Use of Medicines (QUM)*, https://www1.health.gov.au/internet/main/publishing.nsf/Content/nmp-quality.htm (accessed on 11 March 2022). [141]

Australian Government Department of Veterans' Affairs (2021), *Home - Veterans' MATES*, https://www.veteransmates.net.au/ (accessed on 31 March 2022). [120]

Ayalew, M., H. Tegegn and O. Abdela (2019), "Drug Related Hospital Admissions; A Systematic Review of the Recent Literatures", *Bulletin of Emergency & Trauma*, Vol. 7/4, p. 339, https://doi.org/10.29252/BEAT-070401. [15]

Barbazza, E. et al. (2021), "The experiences of 33 national COVID-19 dashboard teams during the first year of the pandemic in the WHO European Region: a qualitative study", *medRxiv*, p. 2021.11.23.21266747, https://doi.org/10.1101/2021.11.23.21266747. [181]

Basch, E. et al. (2017), "Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment", *JAMA*, Vol. 318/2, p. 197, https://doi.org/10.1001/jama.2017.7156. [191]

Bates, D. and H. Singh (2018), "Two Decades Since To Err Is Human: An Assessment Of Progress And Emerging Priorities In Patient Safety", *https://doi.org/10.1377/hlthaff.2018.0738*, Vol. 37/11, pp. 1736-1743, https://doi.org/10.1377/HLTHAFF.2018.0738. [9]

Batta, A., B. Kalra and R. Khirasaria (2020), "Trends in FDA drug approvals over last 2 decades: An observational study", *Journal of Family Medicine and Primary Care*, Vol. 9/1, p. 105, https://doi.org/10.4103/JFMPC.JFMPC_578_19. [3]

Becker, W. et al. (2017), "Barriers and facilitators to use of non-pharmacological treatments in chronic pain", *BMC Family Practice*, Vol. 18/1, https://doi.org/10.1186/S12875-017-0608-2. [43]

Belkhir, L. and A. Elmeligi (2019), "Carbon footprint of the global pharmaceutical industry and relative impact of its major players", *Journal of Cleaner Production*, Vol. 214, pp. 185-194, https://doi.org/10.1016/J.JCLEPRO.2018.11.204. [90]

Bernheim, R. (2016), *Public Engagement in Emergency Preparedness and Response: Ethical Perspectives in Public Health Practice - Oxford Medicine*, https://oxfordmedicine.com/view/10.1093/med/9780190270742.001.0001/med-9780190270742-chapter-5 (accessed on 25 July 2022). [186]

Bouvy, J., M. De Bruin and M. Koopmanschap (2015), "Epidemiology of Adverse Drug Reactions in Europe: A Review of Recent Observational Studies", *Drug Safety*, Vol. 38/5, pp. 437-453, https://doi.org/10.1007/S40264-015-0281-0/TABLES/6. [22]

Brownlee, S. et al. (2017), "Evidence for overuse of medical services around the world", *Lancet (London, England)*, Vol. 390/10090, pp. 156-168, https://doi.org/10.1016/S0140-6736(16)32585-5. [109]

Brummett, C. et al. (2017), "New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults", *JAMA Surgery*, Vol. 152/6, pp. e170504-e170504, https://doi.org/10.1001/JAMASURG.2017.0504. [117]

Canadian Deprescribing Network (2019), *Do I still need this medication? Is deprescribing for you?*, https://www.deprescribingnetwork.ca/ (accessed on 5 April 2019). [130]

Canadian Patient Safety Institute (2018), *Medication Without Harm – Canada's contribution to a global effort to reduce medication errors*, https://www.patientsafetyinstitute.ca/en/NewsAlerts/News/pages/medication-without-harm-2018-09-14.aspx (accessed on 31 January 2022). [93]

Cano, F. and S. Rozenfeld (2009), "Adverse drug events in hospitals: a systematic review", *Cadernos de saude publica*, Vol. 25 Suppl 3/SUPPL. 3, https://doi.org/10.1590/S0102-311X2009001500003. [21]

Carmona-Huerta, J. et al. (2019), "Polypharmacy in a hospitalized psychiatric population: Risk estimation and damage quantification", *BMC Psychiatry*, Vol. 19/1, pp. 1-10, https://doi.org/10.1186/S12888-019-2056-0/FIGURES/3. [49]

Carrasco-Garrido, P. et al. (2010), "Trends of adverse drug reactions related-hospitalizations in Spain (2001-2006)", *BMC Health Services Research*, Vol. 10/1, pp. 1-7, https://doi.org/10.1186/1472-6963-10-287/TABLES/5. [97]

Cascade, E., A. Kalali and S. Kennedy (2009), "Real-World Data on SSRI Antidepressant Side Effects", *Psychiatry (Edgmont)*, Vol. 6/2, p. 16, http:///pmc/articles/PMC2719451/ (accessed on 31 January 2022). [59]

Chandra, A. et al. (2021), "The Health Costs of Cost-Sharing", https://doi.org/10.3386/W28439. [89]

Chou, R. et al. (2015), "The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop", *Annals of internal medicine*, Vol. 162/4, pp. 276-286, https://doi.org/10.7326/M14-2559. [116]

Coleman, E. et al. (2005), "Posthospital Medication Discrepancies: Prevalence and Contributing Factors", *Archives of Internal Medicine*, Vol. 165/16, pp. 1842-1847, https://doi.org/10.1001/ARCHINTE.165.16.1842. [25]

Colla, C. et al. (2017), "Interventions Aimed at Reducing Use of Low-Value Health Services: A Systematic Review", *Medical care research and review : MCRR*, Vol. 74/5, pp. 507-550, https://doi.org/10.1177/1077558716656970. [137]

Cook, D. et al. (2022), "Cost-effectiveness and Economic Benefit of Continuous Professional Development for Drug Prescribing: A Systematic Review", *JAMA Network Open*, Vol. 5/1, pp. e2144973-e2144973, https://doi.org/10.1001/JAMANETWORKOPEN.2021.44973. [161]

CQC (2022), *Adult inpatient survey 2020 | Care Quality Commission*, https://www.cqc.org.uk/publications/surveys/adult-inpatient-survey-2020 (accessed on 31 January 2022). [66]

Cresswell, K. et al. (2017), "Safety risks associated with the lack of integration and interfacing of hospital health information technologies: a qualitative study of hospital electronic prescribing systems in England", *BMJ Quality & Safety*, Vol. 26/7, pp. 530-541, https://doi.org/10.1136/BMJQS-2015-004925. [173]

Davies, E. et al. (2009), "Adverse Drug Reactions in Hospital In-Patients: A Prospective Analysis of 3695 Patient-Episodes", *PLOS ONE*, Vol. 4/2, p. e4439, https://doi.org/10.1371/JOURNAL.PONE.0004439. [205]

de Bienassis, K. et al. (2022), *Health data and governance developments in relation to COVID-19 : How OECD countries are adjusting health data systems for the new normal*, OECD Health Working Paper, https://www.oecd-ilibrary.org/social-issues-migration-health/health-data-and-governance-developments-in-relation-to-covid-19_aec7c409-en (accessed on 22 May 2022). [176]

de Bienassis, K. and N. Klazinga (2022), *Developing international benchmarks of patient safety culture in hospital care : Findings of the OECD patient safety culture pilot data collection and considerations for future work*, OECD Health Working Papers, https://www.oecd-ilibrary.org/social-issues-migration-health/developing-international-benchmarks-of-patient-safety-culture-in-hospital-care_95ae65a3-en (accessed on 25 February 2022). [167]

de Figueiredo, A. et al. (2020), "Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study", *The Lancet*, Vol. 396/10255, pp. 898-908, https://doi.org/10.1016/S0140-6736(20)31558-0/ATTACHMENT/853684EA-3E2B-4ACB-A386-FEAEA7A055F5/MMC2.XLSX. [179]

Denis, F. et al. (2019), "Two-Year Survival Comparing Web-Based Symptom Monitoring vs Routine Surveillance Following Treatment for Lung Cancer", *JAMA*, Vol. 321/3, pp. 306-307, https://doi.org/10.1001/JAMA.2018.18085. [192]

Dick, L., J. Moodie and A. Greiner (2022), "Are we ready? Operationalising risk communication and community engagement programming for public health emergencies", *BMJ Global Health*, Vol. 7/3, p. e008486, https://doi.org/10.1136/BMJGH-2022-008486. [188]

Drenth-van Maanen, A., I. Wilting and P. Jansen (2020), "Prescribing medicines to older people—How to consider the impact of ageing on human organ and body functions", *British Journal of Clinical Pharmacology*, Vol. 86/10, pp. 1921-1930, https://doi.org/10.1111/BCP.14094. [48]

Dubois, D. et al. (2018), "Changes in Prescribing Symptomatic and Preventive Medications in the Last Year of Life in Older Nursing Home Residents", https://doi.org/10.3389/fphar.2017.00990. [129]

Dubrall, D. et al. (2021), "Descriptive analysis of adverse drug reaction reports in children and adolescents from Germany: frequently reported reactions and suspected drugs", *BMC Pharmacology and Toxicology*, Vol. 22/1, pp. 1-16, https://doi.org/10.1186/S40360-021-00520-Y/TABLES/8. [52]

Duong, Q. et al. (2022), "Antibiotic exposure and adverse long-term health outcomes in children: a systematic review and meta-analysis", *Journal of Infection*, https://doi.org/10.1016/J.JINF.2022.01.005. [77]

Eickhoff, C. et al. (2012), "Nature and frequency of drug-related problems in self-medication (over-the-counter drugs) in daily community pharmacy practice in Germany", *Pharmacoepidemiology and Drug Safety*, Vol. 21/3, pp. 254-260, https://doi.org/10.1002/PDS.2241. [7]

El Morabet, N. et al. (2018), "Prevalence and Preventability of Drug-Related Hospital Readmissions: A Systematic Review", *Journal of the American Geriatrics Society*, Vol. 66/3, pp. 602-608, https://doi.org/10.1111/JGS.15244. [24]

Elliott, M. et al. (2021), "Characteristics and Reporting of Number Needed to Treat, Number Needed to Harm, and Absolute Risk Reduction in Controlled Clinical Trials, 2001-2019", *JAMA Internal Medicine*, Vol. 181/2, pp. 282-284, https://doi.org/10.1001/JAMAINTERNMED.2020.4799. [39]

Elliott, R. et al. (2021), "Economic analysis of the prevalence and clinical and economic burden of medication error in England", *BMJ Quality and Safety*, Vol. 30/2, pp. 96-105, https://doi.org/10.1136/BMJQS-2019-010206. [98]

Elshaug, A. et al. (2017), "Levers for addressing medical underuse and overuse: achieving high-value health care", *Lancet (London, England)*, Vol. 390/10090, pp. 191-202, https://doi.org/10.1016/S0140-6736(16)32586-7. [107]

Elson, R., H. Cook and A. Blenkinsopp (2017), "Patients' knowledge of new medicines after discharge from hospital: What are the effects of hospital-based discharge counseling and community-based medicines use reviews (MURs)?", *Research in Social and Administrative Pharmacy*, Vol. 13/3, pp. 628-633, https://doi.org/10.1016/J.SAPHARM.2016.05.001. [27]

EMA (2019), "Report on pharmacovigilance tasks from EU Member States and the European Medicines Agency (EMA), 2015-2018 Report on pharmacovigilance tasks from EU Member States and the European Medicines Agency", http://www.ema.europa.eu (accessed on 13 July 2022). [152]

EMA (n.d.), *Medication errors*, https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/medication-errors (accessed on 13 July 2022). [153]

EMA (n.d.), *Pharmacovigilance: Overview*, https://www.ema.europa.eu/en/human-regulatory/overview/pharmacovigilance-overview (accessed on 13 July 2022). [151]

Emslie-Smith, A. et al. (2001), "Contraindications to metformin therapy in patients with Type 2 diabetes--a population-based study of adherence to prescribing guidelines", *Diabetic medicine : a journal of the British Diabetic Association*, Vol. 18/6, pp. 483-488, https://doi.org/10.1046/J.1464-5491.2001.00509.X. [69]

European Medicines Agency (2021), *Public data from Article 57 database*, https://www.ema.europa.eu/en/human-regulatory/post-authorisation/data-medicines-iso-idmp-standards/public-data-article-57-database (accessed on 3 January 2022). [5]

European Union (2019), *SIMPATHY project*, http://www.simpathy.eu/ (accessed on 5 April 2019). [132]

FDA (2020), *Fact Sheet: FDA at a Glance*, https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance (accessed on 3 January 2022). [4]

FDA (2019), "FDA Sentinel Initiative", https://www.fda.gov/safety/fdas-sentinel-initiative. [148]

Fernández, E. et al. (2020), "Potential cost savings by prevention of adverse drug events with a novel medication review program", *Journal of the American Pharmacists Association*, Vol. 60/3, pp. 462-469.e4, https://doi.org/10.1016/J.JAPH.2019.12.004. [103]

Fick, D. et al. (2019), "Polypharmacy: Evaluating Risks and Deprescribing", *American Family Physician*, Vol. 100/1, pp. 32-38, https://doi.org/10.1111/JGS.15767. [207]

Flory, J. et al. (2018), "Identifying prevalence and risk factors for metformin non-persistence: a retrospective cohort study using an electronic health record", *BMJ Open*, Vol. 8/7, p. e021505, https://doi.org/10.1136/BMJOPEN-2018-021505. [60]

FPS (2022), *Sécurité des patients | FPS Public Health*, https://www.health.belgium.be/en/node/27848 (accessed on 11 March 2022). [140]

Fralick, M. et al. (2020), "Estimating the Use of Potentially Inappropriate Medications Among Older Adults in the United States", *Journal of the American Geriatrics Society*, Vol. 68/12, pp. 2927-2930, https://doi.org/10.1111/JGS.16779. [105]

Freeman, P. et al. (2019), "Utilization of prescription drug monitoring programs for prescribing and dispensing decisions: Results from a multi-site qualitative study", *Research in Social and Administrative Pharmacy*, Vol. 15/6, pp. 754-760, https://doi.org/10.1016/J.SAPHARM.2018.09.007. [166]

Garcia, R. and S. Joseph (2006), *Five ways you can reduce inappropriate prescribing in the elderly: A systematic review*, https://mdedge-files-live.s3.us-east-2.amazonaws.com/files/s3fs-public/Document/September-2017/5504JFP_AppliedEvidence2.pdf (accessed on 25 March 2019). [133]

German Medical Association (2022), *Arzneimitteltherapiesicherheit (AMTS)*, https://www.akdae.de/AMTS/ (accessed on 11 March 2022). [143]

Glasziou, P. et al. (2017), "Evidence for underuse of effective medical services around the world", *Lancet (London, England)*, Vol. 390/10090, pp. 169-177, https://doi.org/10.1016/S0140-6736(16)30946-1. [110]

Greiver, M. et al. (2019), "Improving care for elderly patients living with polypharmacy: protocol for a pragmatic cluster randomized trial in community-based primary care practices in Canada", *Implementation Science*, Vol. 14/1, https://doi.org/10.1186/s13012-019-0904-4. [131]

Gurwitz, J. et al. (2005), "The incidence of adverse drug events in two large academic long-term care facilities", *The American journal of medicine*, Vol. 118/3, pp. 251-258, https://doi.org/10.1016/J.AMJMED.2004.09.018. [14]

Guthrie, B. et al. (2015), "The rising tide of polypharmacy and drug-drug interactions: Population database analysis 1995-2010", *BMC Medicine*, Vol. 13/1, pp. 1-10, https://doi.org/10.1186/S12916-015-0322-7/TABLES/4. [68]

Håkansson Lindqvist, M., M. Gustafsson and G. Gallego (2019), "Exploring physicians, nurses and ward-based pharmacists working relationships in a Swedish inpatient setting: a mixed methods study", *International Journal of Clinical Pharmacy*, Vol. 41/3, p. 728, https://doi.org/10.1007/S11096-019-00812-8. [165]

Heneghan, C. and K. Mahtani (2019), "Absolute effects of statins in the elderly", *BMJ Evidence-Based Medicine*, Vol. 24/5, pp. 200-202, https://doi.org/10.1136/BMJEBM-2019-111189. [41]

Hepler, C. and L. Strand (1990), "Opportunities and responsibilities in pharmaceutical care", *American Journal of Hospital Pharmacy*, Vol. 47/3, pp. 533-543, https://doi.org/10.1093/AJHP/47.3.533. [108]

Huang, Y., J. Moon and J. Segal (2014), "A Comparison of Active Adverse Event Surveillance Systems Worldwide", *Drug Safety*, Vol. 37/8, p. 581, https://doi.org/10.1007/S40264-014-0194-3. [146]

IHI (2018), *IHI Global Trigger Tool for Measuring Adverse Events | IHI - Institute for Healthcare Improvement*, http://www.ihi.org/resources/Pages/Tools/IHIGlobalTriggerToolforMeasuringAEs.aspx (accessed on 16 March 2022). [172]

IMS (2015), "Global Medicines Use in 2020", http://www.theimsinstitute.org (accessed on 3 January 2022). [1]

IMS Institute (2012), *Advancing the responsible use of Medicines: Applying Levers for Change*. [74]

Insani, W. et al. (2021), "Prevalence of adverse drug reactions in the primary care setting: A systematic review and meta-analysis", *PLOS ONE*, Vol. 16/5, p. e0252161, https://doi.org/10.1371/JOURNAL.PONE.0252161. [13]

IOM (2007), "Preventing Medication Errors", https://doi.org/10.17226/11623. [31]

IQVIA (2021), *Global Medicine Spending and Usage Trends: Outlook to 2025*, https://www.iqvia.com/insights/the-iqvia-institute/reports/global-medicine-spending-and-usage-trends-outlook-to-2025 (accessed on 21 December 2021). [2]

Ishiguro, C. et al. (2016), "The MIHARI project: establishing a new framework for pharmacoepidemiological drug safety assessments by the Pharmaceuticals and Medical Devices Agency of Japan", *Pharmacoepidemiology and Drug Safety*, Vol. 25/7, pp. 854-859, https://doi.org/10.1002/PDS.4032. [144]

ISMP (2018), *High-Alert Medications in Acute Care Settings | Institute For Safe Medication Practices*, https://www.ismp.org/recommendations/high-alert-medications-acute-list (accessed on 16 March 2022). [171]

Ivanković, D. et al. (2021), "Features Constituting Actionable COVID-19 Dashboards: Descriptive Assessment and Expert Appraisal of 158 Public Web-Based COVID-19 Dashboards", *J Med Internet Res 2021;23(2):e25682 https://www.jmir.org/2021/2/e25682*, Vol. 23/2, p. e25682, https://doi.org/10.2196/25682. [182]

Jeffries, M. et al. (2017), "Understanding the implementation and adoption of a technological intervention to improve medication safety in primary care: A realist evaluation", *BMC Health Services Research*, Vol. 17/1, pp. 1-11, https://doi.org/10.1186/S12913-017-2131-5/TABLES/5. [11]

Jolivot, P. et al. (2014), "A systematic review of adult admissions to ICUs related to adverse drug events", *Critical Care*, Vol. 18/6, pp. 1-17, https://doi.org/10.1186/S13054-014-0643-5/FIGURES/5. [53]

Kalisch Ellett, L. et al. (2018), "Reducing hypnotic use in insomnia management among Australian veterans: Results from repeated national interventions", *BMC Health Services Research*, Vol. 18/1, pp. 1-10, https://doi.org/10.1186/S12913-018-3443-9/TABLES/3. [119]

Kalisch, L. et al. (2011), "The prescribing cascade", *Australian Prescriber*, Vol. 34/6, pp. 162-166, https://doi.org/10.18773/AUSTPRESCR.2011.084. [28]

Kantar (2021), *International public opinion: Research on the vaccination campaign against COVID 19*, https://www.kantar.com/inspiration/society/study-finds-vaccine-hesitant-public-in-france-and-us (accessed on 31 March 2022). [180]

Katsuno, H. et al. (2021), "Evaluation of the Direct Costs of Managing Adverse Drug Events in all Ages and of Avoidable Adverse Drug Events in Older Adults in Japan", *Frontiers in Pharmacology*, Vol. 12, p. 3182, https://doi.org/10.3389/FPHAR.2021.761607/BIBTEX. [95]

Khan, R. and K. Socha-Dietrich (2018), *Investing in medication adherence improves health outcomes and health system efficiency : Adherence to medicines for diabetes, hypertension, and hyperlipidaemia*, OECD Health Working Papers, https://www.oecd-ilibrary.org/social-issues-migration-health/investing-in-medication-adherence-improves-health-outcomes-and-health-system-efficiency_8178962c-en (accessed on 3 January 2022). [73]

Koppel, R. et al. (2008), "Workarounds to Barcode Medication Administration Systems: Their Occurrences, Causes, and Threats to Patient Safety", *Journal of the American Medical Informatics Association : JAMIA*, Vol. 15/4, p. 408, https://doi.org/10.1197/JAMIA.M2616. [10]

Laatikainen, O. et al. (2017), "The prevalence of medication-related adverse events in inpatients—a systematic review and meta-analysis", *European Journal of Clinical Pharmacology*, Vol. 73/12, pp. 1539-1549, https://doi.org/10.1007/S00228-017-2330-3/FIGURES/4. [17]

Laatikainen, O., S. Sneck and M. Turpeinen (2022), "Medication-related adverse events in health care—what have we learned? A narrative overview of the current knowledge", *European Journal of Clinical Pharmacology*, Vol. 78/2, p. 159, https://doi.org/10.1007/S00228-021-03213-X. [30]

Lancaster, K., T. Rhodes and M. Rosengarten (2020), "Making evidence and policy in public health emergencies: lessons from COVID-19 for adaptive evidence-making and intervention", *Evidence & Policy*, Vol. 16/3, pp. 477-490, https://doi.org/10.1332/174426420X15913559981103. [187]

Law, M. et al. (2012), "Independent Pharmacist Prescribing in Canada:", *http://dx.doi.org/10.3821/1913-701X-145.1.17*, Vol. 145/1, pp. 17-23, https://doi.org/10.3821/1913-701X-145.1.17. [200]

Lee, H. (2019), "The Effects after Implementing a Drug Utilization Review System on Contraindicated Drug use: A Systematic Review", *Korean J Clin Pharm*, Vol. 29/1, pp. 9-17, https://doi.org/10.24304/kjcp.2019.29.1.9. [157]

Leendertse, A. et al. (2011), "Preventable hospital admissions related to medication (HARM): Cost analysis of the HARM study", *Value in Health*, Vol. 14/1, pp. 34-40, https://doi.org/10.1016/J.JVAL.2010.10.024. [96]

Létinier, L. et al. (2019), "Risk of drug-drug interactions in out-hospital drug dispensings in France: Results from the DRUG-drug interaction prevalence study", *Frontiers in Pharmacology*, Vol. 10/MAR, p. 265, https://doi.org/10.3389/FPHAR.2019.00265/BIBTEX. [70]

Liew, T. et al. (2020), "The prevalence and impact of potentially inappropriate prescribing among older persons in primary care settings: multilevel meta-analysis", *Age and Ageing*, Vol. 49/4, pp. 570-579, https://doi.org/10.1093/AGEING/AFAA057. [81]

Lim, R. et al. (2022), "The Extent of Medication-Related Hospital Admissions in Australia: A Review from 1988 to 2021", *Drug Safety*, Vol. 45/3, pp. 249-257, https://doi.org/10.1007/S40264-021-01144-1/TABLES/5. [92]

Lopes, L. et al. (2022), "Data sources for drug utilization research in Latin American countries-A cross-national study: DASDUR-LATAM study", *Pharmacoepidemiology and drug safety*, Vol. 31/3, pp. 343-352, https://doi.org/10.1002/PDS.5404. [155]

Mair, A. et al. (2017), "Polypharmacy Management by 2030: a patient safety challenge", *The SIMPATHY Consortium*. [102]

Malet-Larrea, A. et al. (2016), "The impact of a medication review with follow-up service on hospital admissions in aged polypharmacy patients.", *British journal of clinical pharmacology*, Vol. 82/3, pp. 831-8, https://doi.org/10.1111/bcp.13012. [135]

Márquez, P. et al. (2017), "Potentially Inappropriate Antihypertensive Prescriptions to Elderly Patients: Results of a Prospective, Observational Study", *Drugs and Aging*, Vol. 34/6, pp. 453-466, https://doi.org/10.1007/S40266-017-0452-Z/TABLES/9. [125]

Masnoon, N. et al. (2017), "What is polypharmacy? A systematic review of definitions", *BMC Geriatrics*, Vol. 17/1, https://doi.org/10.1186/s12877-017-0621-2. [47]

Masnoon, N. et al. (2017), "What is polypharmacy? A systematic review of definitions", *BMC Geriatrics*, Vol. 17/1, pp. 1-10, https://doi.org/10.1186/S12877-017-0621-2/TABLES/1. [38]

Mazzotti, E. et al. (2012), "Treatment-related side effects and quality of life in cancer patients", *Supportive Care in Cancer*, Vol. 20/10, pp. 2553-2557, https://doi.org/10.1007/S00520-011-1354-Y/TABLES/1. [58]

McCarthy, L., J. Visentin and P. Rochon (2019), "Assessing the Scope and Appropriateness of Prescribing Cascades", *Journal of the American Geriatrics Society*, Vol. 67/5, pp. 1023-1026, https://doi.org/10.1111/JGS.15800. [29]

McIntosh, J. et al. (2017), "Polypharmacy and Integrated Care: Identifying synergies in implementation", *International Journal of Integrated Care*, Vol. 17/5, p. 77, https://doi.org/10.5334/IJIC.3382. [139]

Migliazza, K. et al. (2021), "Potentially inappropriate medications and medication combinations before, during and after hospitalizations: an analysis of pathways and determinants in the Swiss healthcare setting", *BMC health services research*, Vol. 21/1, https://doi.org/10.1186/S12913-021-06550-W. [37]

Ministerio de Salud (n.d.), *Regulatory framework*, https://www.ministeriodesalud.go.cr/index.php/marco-normativo (accessed on 18 March 2022). [149]

Moreira, L. (2018), *HEALTH LITERACY FOR PEOPLE-CENTRED CARE Where do OECD countries stand?*, http://www.oecd.org/els/health-systems/health-working-papers.htm (accessed on 25 July 2019). [193]

Morin, L. et al. (2018), "The epidemiology of polypharmacy in older adults: register-based prospective cohort study", *Clinical Epidemiology*, Vol. Volume 10, pp. 289-298, https://doi.org/10.2147/clep.s153458. [44]

Morin, L. et al. (2017), "Choosing Wisely? Measuring the Burden of Medications in Older Adults near the End of Life: Nationwide, Longitudinal Cohort Study", *The American journal of medicine*, Vol. 130/8, pp. 927-936.e9, https://doi.org/10.1016/J.AMJMED.2017.02.028. [128]

Mortelmans, L., E. Goossens and T. Dilles (2022), "Beliefs about medication after hospital discharge in geriatric patients with polypharmacy", *Geriatric Nursing*, Vol. 43, pp. 280-287, https://doi.org/10.1016/J.GERINURSE.2021.12.007. [65]

Mossialos, E. et al. (2015), "From "retailers" to health care providers: Transforming the role of community pharmacists in chronic disease management", *Health Policy*, Vol. 119/5, pp. 628-639, https://doi.org/10.1016/J.HEALTHPOL.2015.02.007. [199]

MSH (2012), *MDS-3: Managing Access to Medicines and Health Technologies - Management Sciences for Health*, https://msh.org/resources/mds-3-managing-access-to-medicines-and-health-technologies/ (accessed on 15 March 2022). [111]

Mulley, A., C. Trimble and G. Elwyn (2012), "Stop the silent misdiagnosis: patients' preferences matter", *BMJ*, Vol. 345/7883, https://doi.org/10.1136/BMJ.E6572. [112]

Naniche, D. et al. (2021), "Beyond the jab: A need for global coordination of pharmacovigilance for COVID-19 vaccine deployment", *eClinicalMedicine*, Vol. 36, https://doi.org/10.1016/J.ECLINM.2021.100925. [177]

NHS (2021), *2021/22 priorities and operational planning guidance: Implementation guidance*, https://www.england.nhs.uk/wp-content/uploads/2021/03/B0468-implementation-guidance-21-22-priorities-and-operational-planning-guidance.pdf (accessed on 12 July 2021). [183]

NIH (2021), *The dangers of polypharmacy and the case for deprescribing in older adults | National Institute on Aging*, https://www.nia.nih.gov/news/dangers-polypharmacy-and-case-deprescribing-older-adults (accessed on 31 March 2022). [114]

Nobili, A. et al. (2011), "Polypharmacy, length of hospital stay, and in-hospital mortality among elderly patients in internal medicine wards. The REPOSI study", *European journal of clinical pharmacology*, Vol. 67/5, pp. 507-519, https://doi.org/10.1007/S00228-010-0977-0. [20]

Nuffield Trust (2021), *Are patients told about medication side effects?*, https://www.nuffieldtrust.org.uk/resource/are-patients-told-about-medication-side-effects (accessed on 31 January 2022). [67]

Oderkirk, J. (2017), "Readiness of electronic health record systems to contribute to national health information and research"*, OECD Health Working Papers*, No. 99, OECD Publishing, Paris, https://doi.org/10.1787/9e296bf3-en. [174]

OECD (2022), "Antimicrobial Resistance in the EU/EEA A One Health Response". [121]

OECD (2022), *Health data and governance developments in relation to COVID-19*, https://doi.org/10.1787/aec7c409-en. [194]

OECD (2021), *Enhancing public trust in COVID-19 vaccination: The role of governments*, OECD Policy Responses to Coronavirus (COVID-19), https://www.oecd.org/coronavirus/policy-responses/enhancing-public-trust-in-covid-19-vaccination-the-role-of-governments-eae0ec5a/ (accessed on 7 July 2021). [178]

OECD (2021), *Health at a Glance 2021*, OECD Publishing, Paris, https://doi.org/10.1787/19991312. [6]

OECD (2021), *Health for the People, by the people*, OECD Publishing, Paris, https://doi.org/10.1787/2074319x. [185]

OECD (2020), *Beyond containment: Health systems responses to COVID-19 in the OECD*, http://www.oecd.org/coronavirus/policy-responses/beyond-containment-health-systems-responses-to-covid-19-in-the-oecd-6ab740c0/ (accessed on 29 June 2020). [201]

OECD (2020), *Realising the Potential of Primary Health Care*, https://www.oecd.org/health/realising-the-potential-of-primary-health-care-a92adee4-en.htm (accessed on 24 March 2022). [197]

OECD (2020), *Strengthening the frontline: How primary health care helps health systems adapt during the COVID 19 pandemic*, https://www.oecd-ilibrary.org/social-issues-migration-health/strengthening-the-frontline-how-primary-health-care-helps-health-systems-adapt-during-the-covid-19-pandemic_9a5ae6da-en (accessed on 1 April 2021). [198]

OECD (2019), *Addressing Problematic Opioid Use in OECD Countries*, OECD Health Policy Studies, OECD Publishing, Paris, https://doi.org/10.1787/a18286f0-en. [115]

OECD (2019), *Health in the 21st Century: Putting Data to Work for Stronger Health Systems*, OECD Health Policy Studies, OECD Publishing, Paris, https://doi.org/10.1787/e3b23f8e-en. [12]

OECD (2019), *Patient-reported Safety Indicators: Question Set and Data Collection Guidance*. [168]

OECD (2019), *Patient-Reported Safety Indicators: Question Set and Data Collection Guidance*, OECD, Paris, https://www.oecd.org/health/health-systems/Patient-reported-incident-measures-December-2019.pdf. [190]

OECD (2019), *Pharmaceutical Residues in Freshwater: Hazards and Policy Responses*, OECD Studies on Water, OECD Publishing, Paris, https://doi.org/10.1787/c936f42d-en. [91]

OECD (2019), "Using Routinely Collected Data to Inform Pharmaceutical Policies: Analytical Report for OECD and EU countries", OECD, Paris, https://www.oecd.org/health/health-systems/Using-Routinely-Collected-Data-to-Inform-Pharmaceutical-Policies-Analytical-Report-2019. [147]

Paul, K. and M. Doogue (2016), "Long-term prescribing of new oral anticoagulants", *Australian Prescriber*, Vol. 39/6, pp. 200-204, https://doi.org/10.18773/AUSTPRESCR.2016.068. [78]

Payne, R. et al. (2014), "Prevalence of polypharmacy in a Scottish primary care population", *European Journal of Clinical Pharmacology*, Vol. 70/5, pp. 575-581, https://doi.org/10.1007/S00228-013-1639-9/TABLES/2. [113]

Pecina, J. and F. North (2016), "Early e-consultation face-to-face conversions", *Journal of Telemedicine and Telecare*, Vol. 22/5, pp. 269-276, https://doi.org/10.1177/1357633X15602634. [195]

Pérez, T. et al. (2018), "Prevalence of potentially inappropriate prescribing in older people in primary care and its association with hospital admission: longitudinal study", *BMJ*, Vol. 363, p. 4524, https://doi.org/10.1136/BMJ.K4524. [85]

PGEU (2020), "Position Paper on the Role of Community Pharmacists in COVID-19-Lessons Learned from the Pandemic". [202]

Piau, A. et al. (2012), "[Definition and issue of medications underuse in frail elderly patients]", *Geriatrie et psychologie neuropsychiatrie du vieillissement*, Vol. 10/2, pp. 129-135, https://doi.org/10.1684/PNV.2012.0346. [122]

Picker, D. et al. (2015), "The number of discharge medications predicts thirty-day hospital readmission: A cohort study", *BMC Health Services Research*, Vol. 15/1, pp. 1-8, https://doi.org/10.1186/S12913-015-0950-9/TABLES/3. [26]

PMDA (2021), "Pharmaceuticals and Medical Devices Safety Information", https://www.pmda.go.jp/english/index.html (accessed on 18 March 2022). [159]

Poldervaart, J. et al. (2017), "In-hospital prescription changes and documentation in the medical records of the primary care provider: Results from a medical record review study", *BMC Health Services Research*, Vol. 17/1, pp. 1-10, https://doi.org/10.1186/S12913-017-2738-6/TABLES/6. [163]

Pratt, N. et al. (2015), "Commitment questions targeting patients promotes uptake of under-used health services: Findings from a national quality improvement program in Australia", *Social Science & Medicine*, Vol. 145, pp. 1-6, https://doi.org/10.1016/J.SOCSCIMED.2015.09.019. [123]

Pronovost, P. et al. (2016), "Fifteen years after To Err is Human: a success story to learn from", *BMJ Quality & Safety*, Vol. 25/6, pp. 396-399, https://doi.org/10.1136/BMJQS-2015-004720. [8]

Radecka, A. et al. (2018), "Enhancing Pharmacovigilance Capabilities in the EU Regulatory Network: The SCOPE Joint Action", *Drug Safety*, Vol. 41/12, pp. 1285-1302, https://doi.org/10.1007/S40264-018-0708-5/FIGURES/4. [154]

Rashidian, A. et al. (2015), "Pharmaceutical policies: effects of financial incentives for prescribers", *The Cochrane database of systematic reviews*, Vol. 2015/8, https://doi.org/10.1002/14651858.CD006731.PUB2. [136]

Redmond, P. et al. (2018), "Impact of medication reconciliation for improving transitions of care", *The Cochrane database of systematic reviews*, Vol. 8/8, https://doi.org/10.1002/14651858.CD010791.PUB2. [164]

Renaudin, P. et al. (2021), "Clinical, economic, and organizational impact of the clinical pharmacist in an orthopedic and trauma surgery department", *Journal of Patient Safety*, Vol. 17/8, pp. E1507-E1513, https://doi.org/10.1097/PTS.0000000000000539. [100]

Rice, J. et al. (2017), "Long-term Systemic Corticosteroid Exposure: A Systematic Literature Review", *Clinical Therapeutics*, Vol. 39/11, pp. 2216-2229, https://doi.org/10.1016/J.CLINTHERA.2017.09.011. [76]

Rieder, M. (2019), "Adverse Drug Reactions in Children: Pediatric Pharmacy and Drug Safety", *The Journal of Pediatric Pharmacology and Therapeutics : JPPT*, Vol. 24/1, p. 4, https://doi.org/10.5863/1551-6776-24.1.4. [51]

Robb, G. et al. (2017), *Medication-related patient harm in New Zealand hospitals*, https://journal.nzma.org.nz/journal-articles/medication-related-patient-harm-in-new-zealand-hospitals (accessed on 23 February 2022). [55]

Roberti, G. et al. (2020), "Steroid-induced glaucoma: Epidemiology, pathophysiology, and clinical management", *Survey of Ophthalmology*, Vol. 65/4, pp. 458-472, https://doi.org/10.1016/J.SURVOPHTHAL.2020.01.002. [80]

Rotar, A., M. Van Den Berg and N. Klazinga (2020), "An expert-based mapping of healthcare system strategies to support rational drug prescribing in primary care across 13 European countries", *Health research policy and systems*, Vol. 18/1, https://doi.org/10.1186/S12961-020-00605-W. [126]

Rottenkolber, D., J. Hasford and J. Stausberg (2012), "Costs of Adverse Drug Events in German Hospitals-A Microcosting Study", *JVAL*, Vol. 15, pp. 868-875, https://doi.org/10.1016/j.jval.2012.05.007. [203]

Roughead, E., S. Semple and E. Rosenfeld (2016), "The extent of medication errors and adverse drug reactions throughout the patient journey in acute care in Australia", *International Journal of Evidence-Based Healthcare*, Vol. 14/3, pp. 113-122, https://doi.org/10.1097/XEB.0000000000000075. [18]

Roumeliotis, N. et al. (2019), "Effect of Electronic Prescribing Strategies on Medication Error and Harm in Hospital: a Systematic Review and Meta-analysis", *Journal of General Internal Medicine*, Vol. 34/10, pp. 2210-2223, https://doi.org/10.1007/S11606-019-05236-8/FIGURES/3. [196]

Sağlık Hizmetleri Genel Müdürlüğü (2020), "Sağlıkta Kalite Standartları HASTANE", http://www.pozitifmatbaa.com (accessed on 11 March 2022). [145]

Sakiris, M. et al. (2021), "Prevalence of adverse drug events and adverse drug reactions in hospital among older patients with dementia: A systematic review", *British journal of clinical pharmacology*, Vol. 87/2, pp. 375-385, https://doi.org/10.1111/BCP.14417. [50]

Salah, H. et al. (2021), "Causes of hospitalization in the USA between 2005 and 2018", *European Heart Journal Open*, Vol. 1/1, https://doi.org/10.1093/EHJOPEN/OEAB001. [16]

Salas, M. et al. (2020), "Challenges facing drug utilization research in the Latin American region", *Pharmacoepidemiology and drug safety*, Vol. 29/11, pp. 1353-1363, https://doi.org/10.1002/PDS.4989. [156]

SCIJ (2015), *Regulation of Good Pharmacovigilance Practices No. 39417-s*, http://www.pgrweb.go.cr/scij/Busqueda/Normativa/Normas/nrm_texto_completo.aspx?param1=NRTC&nValor1=1&nValor2=80995&nValor3=103117&strTipM=TC (accessed on 18 March 2022). [142]

Scott, I. and S. Jayathissa (2010), *Quality of drug prescribing in older patients: Is there a problem and can we improve it?*, https://doi.org/10.1111/j.1445-5994.2009.02040.x. [45]

Seynaeve, S. et al. (2011), "Adverse Drug Events in Intensive Care Units: A Cross-Sectional Study of Prevalence and Risk Factors", *American Journal of Critical Care*, Vol. 20/6, pp. e131-e140, https://doi.org/10.4037/AJCC2011818. [54]

Shehab, N. et al. (2016), "US emergency department visits for outpatient adverse drug events, 2013-2014", *JAMA - Journal of the American Medical Association*, Vol. 316/20, pp. 2115-2125, https://doi.org/10.1001/jama.2016.16201. [64]

Skovlund, C. et al. (2016), "Association of Hormonal Contraception With Depression", *JAMA Psychiatry*, Vol. 73/11, pp. 1154-1162, https://doi.org/10.1001/JAMAPSYCHIATRY.2016.2387. [79]

Slawomirski, L., A. Auraaen and N. Klazinga (2017), *THE ECONOMICS OF PATIENT SAFETY Strengthening a value-based approach to reducing patient harm at national level*. [208]

Slight, S. et al. (2018), "The national cost of adverse drug events resulting from inappropriate medication-related alert overrides in the United States", *Journal of the American Medical Informatics Association*, Vol. 25/9, pp. 1183-1188, https://doi.org/10.1093/JAMIA/OCY066. [99]

Stark, R., J. John and R. Leidl (2011), "Health care use and costs of adverse drug events emerging from outpatient treatment in Germany: a modelling approach", *BMC health services research*, Vol. 11, https://doi.org/10.1186/1472-6963-11-9. [94]

Stewart, D. et al. (2017), "A modified Delphi study to determine the level of consensus across the European Union on the structures, processes and desired outcomes of the management of polypharmacy in older people", *PloS one*, Vol. 12/11, https://doi.org/10.1371/JOURNAL.PONE.0188348. [160]

Suleman, F. and E. Movik (2019), "Pharmaceutical policies: effects of educational or regulatory policies targeting prescribers", *The Cochrane database of systematic reviews*, Vol. 2019/11, https://doi.org/10.1002/14651858.CD013478. [127]

Taber, D. et al. (2021), "Significant hospitalization cost savings to the payer with a pharmacist-led mobile health intervention to improve medication safety in kidney transplant recipients", *American Journal of Transplantation*, Vol. 21/10, pp. 3428-3435, https://doi.org/10.1111/AJT.16737. [104]

Tamma, P. et al. (2017), "Association of Adverse Events With Antibiotic Use in Hospitalized Patients", *JAMA Internal Medicine*, Vol. 177/9, pp. 1308-1315, https://doi.org/10.1001/JAMAINTERNMED.2017.1938. [62]

Tandon, R. et al. (2020), "The impact on functioning of second-generation antipsychotic medication side effects for patients with schizophrenia: A worldwide, cross-sectional, web-based survey", *Annals of General Psychiatry*, Vol. 19/1, pp. 1-11, https://doi.org/10.1186/S12991-020-00292-5/TABLES/4. [63]

Tedla, Y. and L. Bautista (2016), "Drug Side Effect Symptoms and Adherence to Antihypertensive Medication", *American Journal of Hypertension*, Vol. 29/6, pp. 772-779, https://doi.org/10.1093/AJH/HPV185. [61]

Thorell, K. et al. (2019), "Importance of potentially inappropriate medications, number of chronic conditions and medications for the risk of hospitalisation in elderly in Sweden: a case–control study", *BMJ Open*, Vol. 9/9, p. e029477, https://doi.org/10.1136/BMJOPEN-2019-029477. [36]

Tran, T. et al. (2019), "The Prevalence and Nature of Medication Errors and Adverse Events Related to Preadmission Medications When Patients Are Admitted to an Orthopedic Inpatient Unit: An Observational Study", *The Annals of pharmacotherapy*, Vol. 53/3, pp. 252-260, https://doi.org/10.1177/1060028018802472. [19]

Truitt, E. et al. (2016), "Effect of the Implementation of Barcode Technology and an Electronic Medication Administration Record on Adverse Drug Events", *Hospital Pharmacy*, Vol. 51/6, p. 474, https://doi.org/10.1310/HPJ5106-474. [169]

Trygstad, T. et al. (2009), "Analysis of the North Carolina Long-Term Care Polypharmacy Initiative: A multiple-cohort approach using propensity-score matching for both evaluation and targeting", *Clinical Therapeutics*, Vol. 31/9, pp. 2018-2037, https://doi.org/10.1016/j.clinthera.2009.09.006. [134]

UNODC (2018), *World Drug Report 2018*, https://www.unodc.org/wdr2018/ (accessed on 16 March 2022). [118]

Uppsala Reports (2020), *COFEPRIS boosts ability to receive and analyse adverse drug reaction reports*, https://www.uppsalareports.org/articles/cofepris-boosts-ability-to-receive-and-analyse-adverse-drug-reaction-reports/ (accessed on 18 March 2022). [150]

US HHS (2014), "National Action Plan for Adverse Drug Event Prevention". [32]

van der Bles, A. et al. (2020), "The effects of communicating uncertainty on public trust in facts and numbers", *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 117/14, pp. 7672-7683, https://doi.org/10.1073/PNAS.1913678117/SUPPL_FILE/PNAS.1913678117.SAPP.PDF. [184]

Varga, S. et al. (2017), "Hospitalization rates during potentially inappropriate medication use in a large population-based cohort of older adults", *British Journal of Clinical Pharmacology*, Vol. 83/11, pp. 2572-2580, https://doi.org/10.1111/BCP.13365. [84]

Vargas, E. et al. (2003), "Effect of adverse drug reactions on length of stay in surgical intensive care units", *Critical care medicine*, Vol. 31/3, pp. 694-698, https://doi.org/10.1097/01.CCM.0000049947.80131.ED. [204]

Viktil, K. et al. (2007), "Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems", *British Journal of Clinical Pharmacology*, Vol. 63/2, pp. 187-195, https://doi.org/10.1111/j.1365-2125.2006.02744.x. [46]

Vimalananda, V. et al. (2018), "Patient, PCP, and specialist perspectives on specialty care coordination in an integrated health care system", *The Journal of ambulatory care management*, Vol. 41/1, p. 15, https://doi.org/10.1097/JAC.0000000000000219. [162]

Vitorino, M., P. Aguiar and P. Sousa (2020), "In-hospital adverse drug events: analysis of trend in Portuguese public hospitals", *Cadernos de Saúde Pública*, Vol. 36/3, p. e00056519, https://doi.org/10.1590/0102-311X00056519. [56]

Warth, J. et al. (2019), "Cost-related medication nonadherence among over-indebted individuals enrolled in statutory health insurance in Germany: A cross-sectional population study", *BMC Health Services Research*, Vol. 19/1, pp. 1-10, https://doi.org/10.1186/S12913-019-4710-0/TABLES/2. [88]

Wauters, M. et al. (2016), "Too many, too few, or too unsafe? Impact of inappropriate prescribing on mortality, and hospitalization in a cohort of community-dwelling oldest old", *British Journal of Clinical Pharmacology*, Vol. 82/5, pp. 1382-1392, https://doi.org/10.1111/BCP.13055. [124]

Weigmann, K. (2016), "Consumer reporting of adverse drug reactions: Systems that allow patients to report side effects of the drugs they are taking have yielded valuable information for improving drugs safety and health care", *EMBO Reports*, Vol. 17/7, p. 949, https://doi.org/10.15252/EMBR.201642616. [189]

Weir, D. et al. (2020), "Failure to follow medication changes made at hospital discharge is associated with adverse events in 30 days", *Health Services Research*, Vol. 55/4, pp. 512-523, https://doi.org/10.1111/1475-6773.13292. [75]

Wester, K. et al. (2008), "Incidence of fatal adverse drug reactions: a population based study", *British Journal of Clinical Pharmacology*, Vol. 65/4, p. 573, https://doi.org/10.1111/J.1365-2125.2007.03064.X. [57]

WHO (2019), "Medication Safety in High-risk Situations", http://apps.who.int/bookorders. (accessed on 4 January 2022). [33]

WHO (2017), *Medication Without Harm*, https://www.who.int/initiatives/medication-without-harm (accessed on 31 January 2022). [175]

WHO (2014), *Reporting and learning systems for medication errors: the role of pharmacovigilance centres*, https://www.who.int/publications/i/item/9789241507943 (accessed on 3 January 2022). [206]

WHO (2012), *The pursuit of responsible use of medicines: sharing and learning from country experiences*, https://apps.who.int/iris/handle/10665/75828 (accessed on 15 March 2022). [106]

WHO (2003), "Adherence to Long-Term Therapies: Evidence for action". [34]

WHO Barcelona Office (2019), “Can people afford to pay for health care? New evidence on financial protection in Europe”. [86]

Wilkes, S. et al. (2021), “A cost-benefit analysis of hospital-wide medication reviews: a period prevalence study”, Vol. 1, p. 3, https://doi.org/10.1007/s11096-021-01323-1. [101]

Wolfe, D. et al. (2018), “Incidence, causes, and consequences of preventable adverse drug reactions occurring in inpatients: A systematic review of systematic reviews”, *PLOS ONE*, Vol. 13/10, p. e0205426, https://doi.org/10.1371/JOURNAL.PONE.0205426. [23]

Yamaguchi, M. et al. (2019), “Establishment of the MID-NET ® medical information database network as a reliable and valuable database for drug safety assessments in Japan”, *Pharmacoepidemiology and drug safety*, Vol. 28/10, pp. 1395-1404, https://doi.org/10.1002/PDS.4879. [158]

Zheng, W. et al. (2021), “The impact of introducing automated dispensing cabinets, barcode medication administration, and closed-loop electronic medication management systems on work processes and safety of controlled medications in hospitals: A systematic review”, *Research in Social and Administrative Pharmacy*, Vol. 17/5, pp. 832-841, https://doi.org/10.1016/J.SAPHARM.2020.08.001. [170]

Zheng, W. et al. (2018), “Drug-drug interactions and their harmful effects in hospitalised patients: a systematic review and meta-analysis”, *European journal of clinical pharmacology*, Vol. 74/1, pp. 15-27, https://doi.org/10.1007/S00228-017-2357-5. [71]

Zivin, K. et al. (2010), “Factors influencing cost-related nonadherence to medication in older adults: a conceptually based approach.”, *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*, Vol. 13/4, pp. 338-45, https://doi.org/10.1111/j.1524-4733.2009.00679.x. [87]

# Annex A. National Contact Points for Snapshot Survey

| Country | Coordinator | Position | Organization |
|---|---|---|---|
| Australia | James Tammaro | Departmental Officer, International Strategies Branch | Australian Government Department of Health |
| Belgium | Annemie Vlayen | Coordinator Quality and Patient Safety | Federal Public Service of Health, Food Chain Safety and Environment |
| Costa Rica | Francisco Oviedo | Medical Officer | Ministry of Health / Department of Health Services |
| Canada | Lawrence Cheung | Director, Pharmaceutical Policy Division | Health Canada - Santé Canada |
| Czech Republic | Lukas Bouz | Ministerial counsellor for pricing and reimbursement of medicines | Ministry of Health of the Czech Republic |
| Estonia | Jane Idavain | Junior Researcher | National Institute for Health Development |
| Germany | 1.Anne Dwenger<br>2.Herbert Sommer and others | Chief of Unit (1), Desk Officer (2) | Federal ministry of Health |
| Israel | Dana Arad | Head of the patient safety division | Ministry of health |
| Italy | Agnese Cangini | Health economist | AIFA |
| Japan | Murakami Chika | Chief | Ministry of Health, Labour and Welfare |
| Republic of Korea | Soo-Hee Hwang<br>Sunim Park<br>Dea Hyung Yang<br>Jin Sun Park | Associate Research Fellow<br>Deputy Director<br>Deputy Director<br>Senior Researcher | Health Insurance Review & Assessment Service<br>Ministry of Food and Drug Safety<br>Ministry of Health and Welfare<br>Ministry of Health and Welfare |
| Latvia | Inese Kaupere | Director of the Department of Pharmacy | Ministry of Health of Latvia |
| Luxembourg | Olivier Moes | Pharmacist inspector | Directorate of Health, Division of Pharmacy and Medicines |
| Mexico | Nilson Agustin Contreras Carreto<br>Irma Aguilar Delfín | Encargado del Despacho de la Dirección General de Calidad y Educación en Salud<br>Technical Subdirector of Health Supplies Evaluation | Secretaría de Salud<br>General Health Council (Consejo de Salubridad General) |
| The Netherlands | Ronald Gijsen | Health care researcher / epidemiologist | National Institute for Public Health and the Environment (RIVM) |
| Norway | Kirsti Bjerke Sæthre | Senior adviser | Norwegian Directorate of Health |
| Portugal | Cláudia Furtado/ Márcia Silva | Head of department | INFARMED |
| Slovenia | Dr. Vesna Zupančič | Secretary | Ministry of Health of the Republic of Slovenia |
| Switzerland | Christoph Küng | Head of Drug Safety Division | Swissmedic |
| Türkiye | Elif Telis | Second Secretary | OECD Permanent Delegation |
| United States | Debo Odegbile | Senior Global Health Officer | Department of Health and Human Services |

# Annex B. Assumptions used in modelling the economic burden of unsafe medication practices in OECD countries

Burden of hospitalizations caused by adverse medication reactions:

- **3.5 % of all hospital stays are caused by an adverse medication reactions**
  - Median based on 2015 systematic review of 22 studies (Bouvy, De Bruin and Koopmanschap, 2015[22])

Burden of extended care due to adverse medication reactions in hospitalised patients:

- **0.59 preventable medication-related adverse events occur per 100 patients**
  - Pooled incidence estimate based on a systematic review of systematic reviews including 13 systematic reviews encompassing 37 unique primary studies (Wolfe et al., 2018[23])
- There was no consensus figure for the impact of medication-related adverse events on length of stay. Based on the existing literature we conservatively estimate that **each hospital-acquired preventable medication-related adverse event results in an additional length of stay of approximately 3 days**.
  - Increase of LOS by 2.9 days for patients experiencing ADRs in German Hospitals (Rottenkolber, Hasford and Stausberg, 2012[203])
  - Increase of LOS by 1.7 to 4.6 days for patients experiencing ADRs cited by the US National Action Plan for Adverse Drug Event Prevention (US HHS, 2014[32]).
  - Increase of LOS by 3.39 days (95% confidence interval, 1.47-5.31) for surgery patients experiencing ADRs (Vargas et al., 2003[204])
  - Median increase of LOS by 4 days (Q1–Q3, 2–7 days) in the US (Davies et al., 2009[205]).

Burden of preventable medication-related readmissions:

- **21% of hospital readmissions are medication-related, 69% of these are preventable**.
  - Median rates based on systematic review of 19 studies in 9 countries (El Morabet et al., 2018[24]).

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