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REVIEW ARTICLE

Initiatives to Identify and Mitigate Medication Errors in England

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Abstract In response to the EU Directive on Pharmacovigilance, the National Health Service (NHS) in England and the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK have formed a partnership to work together to simplify and increase medication error reporting, improve data report quality, maximise learning and guide practice to minimise harm from medication errors by sharing incident data. This initiative will facilitate implementation of new requirements for medication error reporting and reduce the need for duplicate data entry by frontline staff. The initiative is also intended to provide new types of feedback from the National Reporting and Learning System run by the NHS England and from the Yellow Card Scheme run by the MHRA and to improve learning at the local level by clarifying medication safety roles and identifying key safety contacts to allow better communication between local and national levels. Finally, the partnership has established a new National Medication Safety Network to provide a forum for discussing potential and recognised safety issues, and for identifying trends and actions to improve the safe use of medicines. This article describes the initiative, the structure of which may act as a template for other countries.

Key Points

Changes to the definition of an adverse drug reaction and broadening of its scope has brought the National Health Service in England, UK and the Medicines and Healthcare Products Regulatory Authority together to issue a Patient Safety Alert

This has created a unique healthcare workforce with the aim of minimising risks from the use of medicines through increasing the number and quality of medication error reports, improving timeliness of reporting and better local and national communication

1 Introduction

A Patient Safety Alert (PSA) was issued to the National Health Service (NHS) in England on 20th March 2014 entitled, 'Improving Medication Error Incident Reporting and Learning'. This was a joint publication between the Medicines and Healthcare Products Regulatory Agency (MHRA) and NHS England [1]. The Stage Three Directive PSA requires organisations to act and confirm they have implemented the specific solutions or actions detailed therein to mitigate the risk of medication safety incidents, with the emphasis on medication errors. A checklist of actions was required to be signed off in a set timeframe. This article explains the background to this initiative

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including: the burden of harm from medication errors and how medication errors resulting in harm are now defined as adverse drug reactions (ADRs). It provides a summary of the actions recommended in the PSA and how success will be measured in the future.

Apart from the public health benefit of mitigating risk from medication errors, a number of drivers were key to reinforcing this joint partnership between the MHRA and NHS England. These included the World Health Organisation (WHO) Research Project, 'Monitoring Medicines funded by the European Union' [2] and the change in the definition of an ADR through the new pharmacovigilance legislation detailed within The EU Directive on Pharmacovigilance [3].

The joint partnership sought the following to address the under-reporting of medication incidents, to try and change the patient safety culture and perceptions of reporting such incidents to national authorities, to strengthen the governance and reduce burden of reporting for healthcare professionals and to encourage safer practice both locally and nationally.

2 The Burden of Medication Errors

Research evidence indicates the following medication error rates in the medicine use processes in England:

- prescribing error rate in hospital, 7 % of prescription items [4];
- prescribing errors rate in general practice, 5 % of prescriptions of which 0.18 % were severe errors [5];
- dispensing error rate in hospitals, 0.02–2.7 % of dispensed medicines [6];
- dispensing error rates in community pharmacies, 0.01–3.32 % dispensed medicines [6]; and,
- medicine administration errors in hospital, 3–8 % [7].

There is limited research to quantify actual harm arising from medication errors. A prospective study was conducted in two large hospitals in Merseyside to determine the current burden of ADRs in the NHS. The study found that of 18,820 patients aged over 16 years admitted to hospital over a 6-month period, there were 1,225 admissions judged to be related to an ADR, giving a prevalence of 6.5 %. Of these 1,225, the ADR was judged to have led directly to the admission in 80 % of cases. The majority (72 %) of ADR-related admissions were judged as avoidable, including medication errors. The median bed stay was 8 days, accounting for 4 % of the hospital bed capacity. The projected annual cost of such admissions to the NHS was £466 million [8].

The National Reporting and Learning System (NRLS) was established in 2003 to collect patient safety incidents (PSIs—that had harmed or had the potential to harm patients) involving NHS patients in England and Wales and disseminate learning from analysis of these incidents to minimise serious risks identified [9].

In a review of medication error incidents reported to the NRLS over 6 years between 2005 and 2010, there were 525,186 incidents reported. Of these, 86,821 (16 %) of medication incidents reported actual patient harm, with 822 (0.9 %) resulting in death or severe harm [10].

3 The Role of National Pharmacovigilance Centres in Medication Error Reporting and Learning

National pharmacovigilance centres have not traditionally had a formally recognised role in medication error reporting and learning. The traditional definition of an ADR has been one that associates noxious and unintended events with a licensed medicine and occurs with doses normally used in humans [11]. This definition has usually been interpreted as use in accordance with the marketing authorisation for individual medicinal products. Medication errors, for example where healthcare professionals have selected the wrong medicine, wrong dose or wrong route, have usually been considered out of scope of traditional pharmacovigilance activities. The need to broaden the scope of pharmacovigilance and evolve systems to better address a range of safety concerns including medication errors was identified in a WHO report in 2002 [12].

Pharmaceutical companies, specifically those that hold a marketing authorisation, are obligated to discuss medication errors, with or without suspected ADRs, within their periodic safety update reviews and risk management plans for their medicinal products; these are reviewed by national competent authorities such as the MHRA. Such reports are reviewed alongside all available safety information, including suspected ADR reports, during the continuous assessment of a medicine's safety profile to ensure the benefits of taking a particular medication continue to outweigh the potential risks.

Some research has been conducted in pharmacovigilance centres to determine whether medication error reports have been reported as ADRs through their spontaneous reporting systems. In 2006, the WHO, the Uppsala Monitoring Centre for Pharmacovigilance and the Moroccan National Pharmacovigilance Centre initiated a joint pilot project that reviewed the collection and analysis of information on ADRs related to medication errors [13–15]. The pilot project demonstrated that while some pharmacovigilance centres regularly collected and identified ADRs, which were due to medication errors, there were others that 'inadvertently' collected this information as typical suspected ADR reports. The project also

investigated the presence of other systems (usually operated by patient safety organisations) for collecting medication error reports, in selected countries, and if there was any collaboration between these systems and pharmacovigilance centres.

The UK's spontaneous pharmacovigilance reporting scheme; called the Yellow Card Scheme, encompasses the collection of voluntary reporting of suspected ADRs by patients (including carers and parents) and healthcare professionals. The Yellow Card Scheme is run by the MHRA and in 2013 received over 31,000 reports [16], of which only 3 % described suspected reactions occurring as a result of a medication error [17]. However, most spontaneous reporting schemes worldwide are associated with an unknown and variable level of under-reporting [18–23], as the absolute number of ADRs occurring is not known. ADR reporting rates may be influenced by the seriousness of reactions, their ease of recognition, extent of use of a particular drug and promotion and publicity about a drug [22, 24–28].

In the UK, it has been estimated that 10 % of serious ADRs and between 2 and 4 % of non-serious ADRs are reported [24] and that serious reactions are five times more likely to be reported than non-serious reactions [25]. The level of under-reporting of ADRs to different medicines is variable and dependent on a number of factors. Surveys of attitudes to reporting of ADRs suggest that lack of time, and uncertainty as to whether the reaction was caused by a drug, are among the most common factors in deterring reporting [23, 29, 30]. Although under-reporting is an inherent feature or spontaneous schemes, it is thought to occur less frequently with serious and unlabelled reactions (those that are not listed within the product information for patients and healthcare professionals). In the UK, although 52 % of health professionals cite the MHRA as the regulator, brand awareness levels are high with strong recognition of the Yellow Card Scheme among health professionals. Eighty-eight percent of pharmacists mention the Yellow Card Scheme as the place to report a suspected ADR and, similarly, 85 % of general practitioners mention the Yellow Card Scheme as a place to report suspected ADRs [31].

Patient safety organisations have developed over the last 20 years in response to the growing recognition that preventable harms occur too often in healthcare systems worldwide. Patient safety organisations can be state funded or independent. Their role usually involves advocacy, education and the operation of a reporting and learning system for all types of PSIs or specific types of PSIs, e.g., medication errors.

This research into the role of national pharmacovigilance centres and medication errors was taken forward in the Monitoring Medicines Project funded by the Seventh Framework Programme of the Research Directorate of the European Commission in 2009 [2]. The overall objective of the study was to optimise drug safety monitoring to enhance patient safety and achieve better health outcomes. The outputs were intended to strengthen what is known about medicines, sharing that knowledge, and putting that knowledge to use, to reduce patient deaths and adverse effects due to medicines. There were a number of project work packages including two concerned with organising an international training course and producing guidance on medication error reporting and learning for national pharmacovigilance centres.

Partner organisations involved with the work on medication error reporting and learning were the WHO, the Uppsala Monitoring Centre, the Moroccan National Pharmacovigilance Centre and the National Patient Safety Agency, England and Wales (now disbanded), supported by the Institute for Safe Medication Practices, Canada. Training on medication error reporting and learning for representatives from 10 national pharmacovigilance centres took place in March 2011 in the National Poisons and Pharmacovigilance Centre in Rabat, Morocco. Representatives from national pharmacovigilance centres from the following countries attended the training: Brazil, Ghana, Iran, Kenya, Morocco, the Netherlands, New Zealand, Spain, Switzerland, Tunisia and Thailand.

Materials and feedback from the training course were used to develop WHO guidance on medication error reporting and learning systems for pharmacovigilance centres to support the overall objectives of the project [32].

Key findings of the Monitoring Medicines Project were:

- national pharmacovigilance reporting systems, although primarily set up to collect and investigate suspected ADRs, have many data fields that are necessary for capturing information concerning medication errors and other data fields can be easily added to databases and reporting forms;
- depending on the stage of development of the safety culture on a national basis with healthcare regulators and providers, national pharmacovigilance centres in the future may wish to advertise that they will formally operate a medication error reporting and learning system in addition to their traditional services; or they may wish to continue to operate their spontaneous ADR reporting systems for the analysis and identification of any associated medication errors;
- seminars and training courses and other initiatives should be organised to improve reporting of medication errors by healthcare professionals. National pharmacovigilance centres will need to develop new methods, or strengthen existing systems and expertise to identify ADRs associated with medication errors, root cause

analysis, and understanding of human factors, healthcare delivery and product design, to be able to identify new risks to patient safety and additional safeguards to minimise the risk of harm arising from medication errors; and,
- effective communication between staff at national pharmacovigilance centres, patient safety organisations, healthcare professionals and patients is paramount for collective learning to prevent medication errors and to promote patient safety.

4 New Requirements for Medication Error Reporting in the EU Directive on Pharmacovigilance

Under the new EU Directive 2010/84/EU1, which came into force in July 2012, the term 'adverse drug reaction' is defined as 'a response to a medicinal product that is noxious and unintended, resulting not only from the authorised use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorisation, including the misuse, off-label use and abuse of the medicinal product' [3].

The directive states that EU Member States should operate a pharmacovigilance system to collect information that is useful for the monitoring of medicines. This includes information on suspected ADRs arising from use of a medicine within the terms of the marketing authorisation, as well as from use outside these terms. This includes overdose, misuse, abuse and medication errors, as well as suspected adverse reactions associated with occupational exposure.

Member States should ensure that reports of suspected ADRs arising from an error associated with the use of a medicine that are brought to their attention are made available to the EudraVigilance (EU Drug Regulating Authorities [Eudra] Vigilance) pharmacovigilance database and to any authorities, bodies, organisations or institutions responsible for patient safety within that Member State. This (Eudra) is the data processing network and management system for the reporting and evaluation of suspected adverse reactions during the development of new drugs and for following the marketing authorisation of medicinal products in the European Economic Area. Patients and healthcare professionals will be able to report these suspected ADRs directly using standard web-based forms through their national reporting portals.

The European Medicines Agency organised a workshop on medication errors in February 2013 to raise awareness of the new requirements with stakeholders involved with the reporting, evaluation and prevention of medication errors [33]. Discussions took place to: clarify what constitutes a medication error and the new legal requirements for reporting cases at the EU level; get a better understanding of how medication errors are managed at the national level; share best practice for the prevention of medication errors; and make proposals to streamline efforts and resources between national competent authorities, pharmacovigilance centres and patient safety organisations and improve cooperation at the national and international level.

The workshop resulted in six key recommendations to: (1) harmonise and further develop terminologies and definitions of medication errors at EU and international levels; (2) establish collaborative relationships between national patient safety authorities, national regulators and the European Commission; (3) develop new methods to identify medication errors from a patient safety and pharmacovigilance perspective through data pooling and analysis; (4) promote the systematic assessment and prevention of the risk of medication errors during the life cycle of a medicine, including prior to granting a marketing authorisation through the EU risk-management planning process; (5) actively engage and build capacity with patient and consumer groups and healthcare professionals to improve safe medication practices; and (6) support research into safe medication practices [34].

Following the workshop, the Heads of Medicines Agencies agreed on 28th November 2013 that by September 2015 [34] there would be: (1) creation of a medication error coding group; (2) further development of codes and search criteria for medication errors; (3) development of a good practice guidance on coding and reporting medication errors; (4) development of a good practice guide on risk minimisation and prevention of medication errors; (5) an awareness campaign on reporting requirements; and (6) creation of a communication toolbox in the context of healthcare delivery.

5 Initiatives to Improve Medication Error Reporting and Learning in England

In England, there are two national reporting systems for medication incidents. The MHRA operates its pharmacovigilance system for collecting and analysing ADRs known as the Yellow Card Scheme [35]. Established 50 years ago, the Yellow Card Scheme is recognised as one of the first spontaneous reporting systems for ADRs in the world and has been considered a model for spontaneous systems. It has a proven track record as an early warning system and the value of the Yellow Card Scheme has been demonstrated many times as an important contribution to public health [36].

If a new side effect to a medicine is identified, information is carefully considered in the context of the overall side-effect profile for the medicine, and how the side-effect

profile compares with other medicines used to treat the same condition. If it is deemed necessary, further action is taken, which can include regulatory action to ensure that the medicinal product is used in a way that minimises risk and maximises benefits to the patient, such as adding a new side effect to the product information for the authorised products. The MHRA regularly circulates communications to healthcare professionals and patients via its electronic monthly bulletin called the 'Drug Safety Update' [37]. Rarely, if the risks are considered to outweigh the benefits of a particular product, then regulatory action can be taken to revoke its licence and or remove it from the UK market. All reports are assessed by the MHRA regardless of severity or seriousness, meaning that all reports of medication errors are assessed. Only a small percentage of Yellow Card reports to the MHRA involve suspected ADRs associated with medication errors; 841 reports (3 %) from a total of 26,073 suspected ADR reports received in 2012 [17]. These reports are identified empirically and shared with the NRLS.

Medication error incidents are reported directly to the NRLS [38]. In 2012, 142,403 medication error reports were reported to the NRLS [39]. This reporting system and national database are intended for PSIs defined as 'any unintended or unexpected incident, which could have or did lead to harm for one or more patients receiving NHS care' [40]. The strength of the NRLS is in its potential to inform 'why' errors occur and what system changes were implemented to improve safety.

Medication incidents are any PSIs where there has been an error in the process of prescribing, preparing, dispensing, administering, monitoring or providing advice on medicines. These PSIs can be divided into two categories; errors of commission or errors of omission. The former include, for example, mis-selection of the wrong medicine or wrong dose. Errors of omission include, for example, omitted dose or a failure to monitor, such as international normalised ratio for anticoagulant therapy.

Analysis of NRLS reports in the national database has allowed new risks to be identified and communicated formally through the use of PSA, Rapid Response Reports and Signals by the former National Patient Safety Agency [41]. The NHS England now carries out this work [42].

The NHS England and the MHRA formed a collaborative partnership to work together to simplify and increase reporting, improve data report quality, and maximise learning and guide practice to minimise harm from medication errors through the sharing of their incident data. The initiative facilitates the new requirements for medication errors in the EU Directive and reduces the need for duplicate data entry by frontline healthcare professionals. The initiative is also intended to provide new types of feedback from both organisations, including the NRLS and Yellow Card Scheme, improve learning at the local level, clarify medication safety roles and identify key safety contacts to allow better communication between local and national levels. Together, a new National Medication Safety Network has been established as a novel forum for discussing potential and recognised safety issues, and for identifying trends and actions to improve the safe use of medicines in England for medicines.

New feedback includes direct communication with individual Medication Safety Officers (MSOs) from the NHS England and the MHRA to request more information and improvements in data quality systems when insufficient information is submitted in a serious incident reported to the NRLS. In addition, monthly meetings for the medication safety network provide a method of informal communication to review recent reports and discuss reporting quality and local and national actions to address identified issues.

A PSA describing this new initiative was published in March 2014 [1]. A similar initiative has been taken to improve the reporting and learning of medical device incidents [43].

Prior to issuing the PSA, discussions with the MHRA and the NHS England's stakeholders were conducted and both the alert and its supporting documentation was subjected to open consultation to improve the practicalities detailed therein.

The flow of medication incident report information and national analysis of this information are shown in Figs. 1 and 2.

The PSA requires the NHS to act with clear recommendations for all large healthcare provider organisations (defined below[1]) in England to take the following actions:

- identify a board level director (medical or nursing supported by the chief pharmacist) or in community pharmacy and home healthcare, the superintendent pharmacist, to have the responsibility to oversee medication error incident reporting and learning;
- identify a Medication Safety Officer (MSO) and email their contact details to the Central Alerting System team. This person will be a member of a new National Medication Safety Network, support local medication error reporting and learning, and act as the main contact for the NHS England and the MHRA; and,
- identify an existing or new multi-professional group to regularly review medication error incident reports, improve reporting and learning, and take local action to improve medication safety [1].

[1] Large healthcare provider organisations in England comprise all NHS trusts, large independent healthcare and medicine homecare companies and community pharmacy companies with 50 or more community pharmacies registered with the General Pharmaceutical Council.

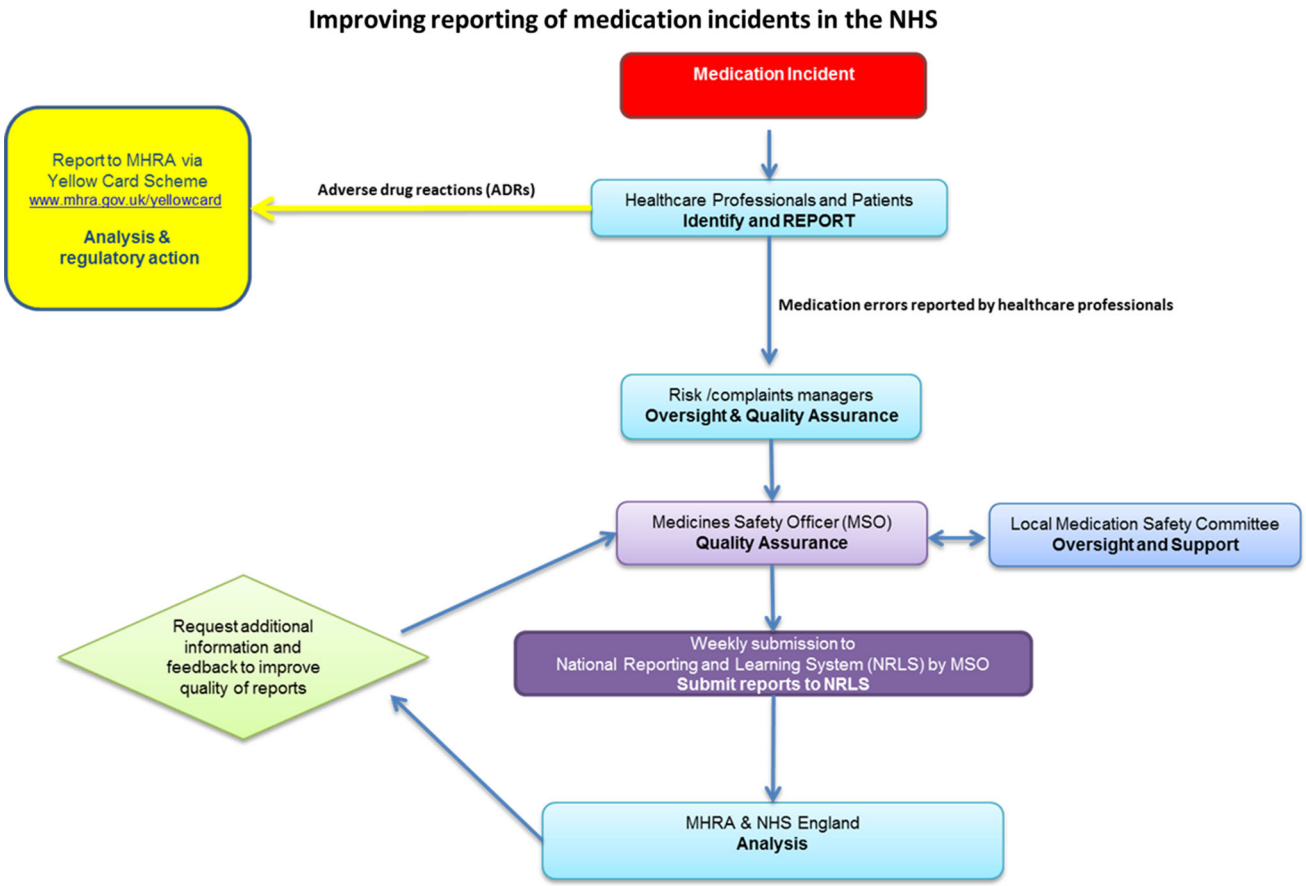

Fig. 1 The flow of medication incident report information in a healthcare provider organisation, e.g., NHS hospital trust or community pharmacy retail company. *MHRA* Medicines and Healthcare Products Regulatory Agency, *NHS* National Health Service, *NRLS* National Reporting and Learning System

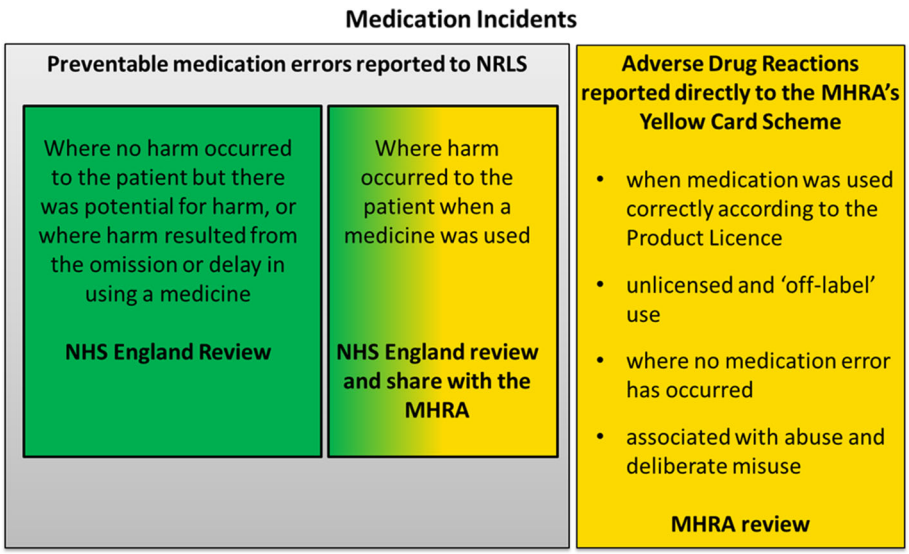

Fig. 2 Analysis of medication incident reports at the national level. *MHRA* Medicines and Healthcare Products Regulatory Agency, *NHS* National Health Service, *NRLS* National Reporting and Learning System

By the 9th January 2015, 354 MSOs had registered from health and independent sectors with the MHRA and the NHS England. One MSO is nominated for each organisation. While the number of organisations is in constant flux, this is estimated to represent 80 % of those that might nominate. Notably, Clinical Commissioning Groups were invited but are yet to fully engage. The new National Medication Safety Network was established with the objectives to improve reporting and learning of medication incidents by educating and training MSO in patient safety science and disseminate relevant research and information concerning new risks and best practice.

Functionality of the network was tested through a series of pilot meetings with early identified MSOs before the first meeting to continuously improve its structure and content, which was fed back through participant polls. MSOs are invited to attend online monthly internet meetings, email discussion groups and online information forums each month to discuss topics identified at the local and national level. These include the identification of new risks and best practice to minimise these risks, implementing patient safety guidance, and improving incident reporting quality and learning.

Although in its infancy, the expected benefits of the new initiative will be measured by:

- an increase in the number of reports of medication incidents by organisation and healthcare sectors to both the NRLS and the Yellow Card Scheme. System-related errors are primarily reported through the former and pure ADRs unrelated to system failure through the latter. Incidents where a system error leads to an ADR that could have been avoided are automatically redirected from the NLRS to the MHRA;
- an improvement in the timeliness of report submissions to the NRLS. Patient safety incidents associated with severe harm or death should be reported within 48 h. Others ideally within a month of occurrence. National action is dependent on prompt reporting;
- improvement of the quality of reports, e.g., essential NRLS data fields completed;
- improvement of the accuracy of use of NRLS codes;
- improvement in the description of incidents; sufficient for learning;
- an increase in the number of new safety issues detected;
- more information on local actions taken to minimise harm from identified risks; and,
- improvements to safer practice.

The national medication safety network, NHS England and the MHRA intend to work with all stakeholders including pharmaceutical and medical devices industries, to develop actions to minimise identified medication error risks. This work will continue to include design for safety methods to improve the design of labelling, packaging and ergonomics, and build on previous guidance on these topics [44, 45].

6 Discussion and Conclusions

Identifying harms from medicines, alerting healthcare professionals, patients and other stakeholders of these harms, and taking appropriate action to manage and minimise these harms are important activities in healthcare. A change in the EU Directive on Pharmacovigilance to broaden the role of national pharmacovigilance centres to all harms arising from medicine use (including medication errors) is welcomed despite additional resource implications to the system. A more collaborative approach between national and local organisations, in the way described herein, should enable greater awareness and more effective risk minimisation activities in practice.

A more formal and systematic approach to vigilance activities by healthcare provider organisations and patient safety organisations will also be beneficial. Good Manufacturing Practice developed by medicine regulators and industry has been widely adopted by healthcare provider organisations that manufacture and prepare medicines to improve quality and safety [46]. The introduction of Good Vigilance Practice developed by medicines regulators and industry to cover ADR (and now including medication error) reporting activities in healthcare provider organisations will also improve quality and safety [47].

It is our view that an improved system of accountability and learning at both an organisational and individual level with regard to medication incident reporting, through further collaboration with healthcare professional regulators such as the Care Quality Commission, is vital to improving patient safety. This should incorporate training on recognising, managing, active reporting and prevention of medication incidents at all levels—undergraduate, postgraduate education curricula, continued professional development learning and healthcare professional revalidation and appraisal processes.

The MHRA and the NHS England are working with the UK Devolved Administrations (Scotland, Northern Ireland and Wales) to share learnings of this initiative and promote similar initiatives in the UK. They are also working with local risk management system suppliers to harmonise data collection from healthcare organisations to capture all relevant information required for national safety assessment and pharmacovigilance purposes.

The initiatives described herein, including new methods to simplify and increase reporting, improve data report quality, sharing reported data, improve learning at local level, clarifying medication safety roles and identifying key safety contacts to allow better communication between

local and national levels, are, in our view, the first steps in this process and may act as a template for other countries.

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