Estimating the impact of enabling NHS information systems to share patients' medicines information digitally

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MAIN REPORT

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ABBREVIATIONS

A&E	Accident and Emergency
ADE	Adverse drug event
ADR	Adverse drug reaction
API	Application programming interface
BPMH	Best possible medication history
CCG	Clinical Commissioning Group
DHSC	Department of Health and Social Care
dm+d	dictionary of medicines and devices
EHR	Electronic health records
eMedsRec	Digitally-enabled medicines reconciliation
ePMA	Electronic Prescribing and Medicines Administration
EPS	Electronic Prescription Service
FAE	Finished admission episode
FCE	Finished consultant episode
FHIR	Fast Healthcare Interoperability Resources
IFT	Inter-facility transfer
ISN	Information standards notice
LYG	Life-years gained
MedsRec	Medicines reconciliation
NHS	National Health Service
NHSE	NHS England
pADE	Preventable adverse drug event
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
QALY	Quality-adjusted life-years
RR	Relative risk
SCR	Shared care record
WHO	World Health Organization

PLAIN ENGLISH SUMMARY

The challenge

Taking medicines for long-term conditions is something people do every day. When people are admitted to, or discharged from hospital, this process is usually called a care transfer or transition. it is very important that they, their families and people involved in their care, have the right information about their medicines. The information the NHS holds about a patient's medications and allergies is usually held in many separate sources, such as general practice and hospital electronic medication records. It is often fragmented and stored in different formats, using different vocabulary and then systems that do not connect with one another.

Sometimes mistakes are made when medicines information is transferred from one setting to another. Medicines may be missed off the list, extra ones added, or wrong doses written down. These mistakes are usually called 'medication discrepancies' or 'transition medication errors'. They are so common the World Health Organization has made it a priority for health service providers to find ways to reduce them. One effective way of doing this is 'medicines reconciliation', where a health care professional, usually a pharmacist, creates the most accurate list of medicines the patient is actually taking, also called a 'best possible medication history'. They do this by speaking to the patient, family, general practitioner (GP) and looking at the patient's medical records. Some errors may still be missed by medicines reconciliation, potentially causing harm to the patient. Resolving this harm and treating the patient costs the NHS money.

The solution

To address this, all medication messages used by different NHS IT systems needs to be standardised. Messages need to be interoperable, meaning many different IT systems can exchange and make use of data and information across system and organisational boundaries. If the same information about a patient's medicines could be accessed by all their healthcare providers, there could be important improvements to their care. The development of systems that can help electronic or digital medicines reconciliation has shown promise and reducing time taken to complete the process, and to further reduce unintended discrepancies, mostly centred around hospital admission and discharge. The NHS is introducing new digital information standards during 2023. This will make it easier for the correct information about medicines to be transferred between electronic records accessed by different healthcare providers.

What we did

To understand how the new digital information standards can improve patient safety, we asked these questions:

1. How many transition medication errors happen every year in England?
2. How do these errors affect patients (avoidable harm) and the NHS (avoidable cost)?
3. How will the errors, avoidable harm and cost be affected by the new digital information standards?

No-one routinely collects this information, so we used published research and talked to experts to help us.

What we found

We calculated that the total number of transition medication errors (when using standard medicines reconciliation without the new digital information standards) was around 1.8 million in England per year, with almost 370,000 patients being admitted, transferred, or discharged experiencing a transition medication error.

Over a year, around 31,000 people are estimated to experience harm from a transition medication error, with over half of these due to transition medication errors at hospital admission. The transition medication errors

may lead to over 36,000 additional days spent in hospital, costing the NHS around £17.4 million per year. Approximately 45 people may die from these transition medication errors.

We calculated that, with the introduction of the new digital information standards, the number of transition medication errors and the number of people affected would reduce by 40% from 1.8 million to 1.1 million and from almost 370,000 to around 220,000 per year, respectively. There would also be more than 12,000 fewer people experiencing harm, with approximately 14,000 fewer days spent in hospital per year. This would save around £6.6 million per year and prevent around 20 people dying from these transition medication errors per year.

What this means for patients

The new digital information standards are likely to help make health care safer for patients.

SCIENTIFIC SUMMARY

1 INTRODUCTION

Access to accurate medicines information is key to the management of patients, especially when they transfer from one care setting to another, such as on admission to or discharge from hospital. However, there are often discrepancies or deficiencies in medicines information provision leading to clinically important medicines being omitted or being prescribed and administered inappropriately ('medication errors'). Harm caused by medication is referred to as an adverse drug event (ADE]. ADEs can occur even when the medicine is prescribed appropriately, (e.g. due to overdose, adverse drug reactions (ADRs) or allergies), but in the presence of a medication error, any resultant harm can be considered an 'avoidable' or 'preventable adverse drug event' (pADE). Medication errors at transfer between care settings is a WHO priority area in their 3rd global patient safety challenge in 2017 focused on medication safety. Health systems have a range of processes in place to mitigate against medication errors, including medicines reconciliation, which have been shown to reduce transition medication errors. In 2022, NHS Digital estimates per year in England that 167 million hospital prescription items are transcribed, consuming 1.2million hours hospital staff time and 9000 weeks general practice (GP) clinical and administrative time. Across many sectors, there have been huge leaps in technology development to enable information systems to share their information digitally, often referred to as system interoperability. Making patient and medicines information systems interoperable across care transitions and across electronic systems within individual health care organisations could reduce time taken by healthcare staff to reconcile medication discrepancies, improve patient experience, facilitate quicker discharge, support better healthcare planning and reduce risk of avoidable harm to patients. A nationwide initiative by NHS England to introduce interoperability into all NHS health and social care settings is the national roll-out of information standard notification 'ISN DAPB4013: Medicine and Allergy/Intolerance Data Transfer'. There is a lack of evidence from systematic or other reviews supporting benefits of interoperability solutions to guide decisions on their implementation and use. This report estimates impact of ISN DAPB4013 on transition medication error rates, patient harm and associated NHS costs in England.

2 AIMS AND OBJECTIVES

The research study aimed to estimate the medication safety benefits that are expected to be evident following the implementation of information standard notification 'ISN DAPB4013: Medicine and Allergy/Intolerance Data Transfer' to patients and the NHS in England by answering the following questions:

1. What is the prevalence of medication errors at key transitions between care settings?
2. What is the estimated patient harm and NHS cost of transition medication errors?
3. How will improved information transfer affect transition medication errors, patient harm and NHS cost?

We focused on four transfer settings: Primary to secondary care; secondary to primary care; intra-hospital transition where there is transfer from one electronic prescribing system to another; inter-hospital transfer.

3 METHODS

This study used published evidence and stakeholder/expert input to estimate prevalence, patient harm and cost of transition medication errors, and the expected effect of the new information standards on these parameters using the following methods:

1. Rapid literature review to identify: a) transition medication error prevalence at interfaces between care locations in the UK; b) costs and health burden associated with transition medication errors in the UK; benefits and costs of interoperability systems designed to reduce transition medication errors.

2. Modelling to provide estimates of annual transition medication error prevalence and burden in the NHS in England before and after the implementation of the ISN DAPB4013.
3. Liaison and engagement with stakeholders was carried out to understand the composition, costs and expected benefits of the key components of ISN DAPB4013:
    - Fast Healthcare Interoperability Resources (FHIR)
    - Application programming interface (API) for exchanging electronic health records (EHR)
    - Dictionary of medicines and devices (dm+d) adoption
    - Enhanced electronic prescription service.

Key reviews served as the starting point for observational studies reporting prevalence and impact of medication error in the UK at transitions and studies of interoperability solutions to support medicines safety. Nine databases were searched for studies from 2000-June 2022 and five journals were hand-searched. Search strategies covered all specified information transfer transitions, preferentially included UK data, using data from other settings if necessary. Data extracted was combined in a narrative synthesis. We included all comparative study designs where the intervention was carried out at an information transfer transition, incorporated one or more elements included in ISN DAPB4013 and measured one of: medication errors, costs, or patient outcomes.

We used error rates reported in the studies above to estimate prevalence of transition medication errors in England per year. We found very little data indicating direct links between errors and patient harm. Therefore, we developed estimates of burden of transition medication errors using published work around adverse drug events (ADEs), where a retrospective judgement had been made that harm/burden was due to an ADE. The primary approach was to identify available UK-based case studies of estimates of burden on healthcare resources (inpatient admissions, inpatient length of stay, accident and emergency (A&E) visits and deaths) associated with transition medication errors and to extrapolate to estimate impact for England per annum.

We assumed the estimates of number of transition medication errors and burden from those transition medication errors for the 'current practice' scenario. We derived estimates of the anticipated effectiveness of ISN DAPB4013 implementation. We combined these data to allow derivation of indicative estimates of changes in patient harm, and costs from NHS England's perspective (£, cost year 2020/21). The population was people at risk of experiencing medication transition errors at defined transitions. The intervention was digitally-enabled interoperable medicines information transfer. The comparator was manual medicines information transfer. The outcomes assessed were transition medication errors, hospitalisations, adverse drug events, length of hospital stay, readmissions, deaths. It was assumed that, prior to ISN DAPB4013 introduction, all acute hospitals have electronic inpatient prescribing (therefore no discrepancies caused by manual chart re-writes are included in our estimates) and carry out standard (non-digitally-enabled) medicines reconciliation during an inpatient stay.

4 RESULTS: RAPID REVIEW

4.1 Transition medication error prevalence: From the 12 studies found reporting the prevalence of transition medication errors, it was not possible to pool estimates of prevalence due to study heterogeneity, so one UK study was used. No studies reported intra- or inter-hospital transfers, so the prevalence of transition medication errors during intra-hospital transfers was assumed to equal the prevalence of transition medication errors during drug chart rewrites. Prevalence of inter-hospital transition medication errors was assumed to be the same as at hospital admission.

4.2 Transition medication error harm and costs: Three studies relating to harm from transition medication errors in the context of the UK NHS were identified, specifically harm from transition medication errors relating to

discharge prescriptions, hospital admissions due to ADEs, and harm from ADEs that occur during hospitalisation.

4.3 Effect of interoperability: Five reviews of reviews, 31 reviews and 53 primary studies were retrieved to derive estimates of costs and benefits of ISN DAPB4013 implementation. One Spanish and one US study provided estimates of effectiveness for standard medicines reconciliation versus digitally-enabled medicines reconciliation on hospital admission and discharge, respectively. The impact of interoperability on transition medication errors during intra-hospital transfer, or inter-hospital transfer was not available. It was assumed that impact of interoperability on transition medication errors at both of these transitions would be the same as during a process of admission. This in turn assumed that standard medicines reconciliation was already in place at these transitions.

5 RESULTS: MODELLING

5.1 Transition medication error prevalence and burden

The total number of transition medication errors (in the presence of standard medicines reconciliation) was estimated to be 1,779,368 in England per year, with 369,195 patient episodes experiencing at least one transition medication error. The estimated burden of transition medication errors is characterised by number of people experiencing harm, excess bed days, cost to the NHS and deaths. Over a year, the total number of people estimated to experience harm from a transition medication error is 31,236, with the majority (52%) resulting from admission errors. The errors are estimated to result in 36,099 additional bed days of inpatient care, costing around £17.43 million per year. The total number of people estimated to die from these errors is 44 (Table 1).

Table 1: Summary of annual transition medication error rates, harm and costs, by transition and total

Parameters	Admission	Intrahospital transfer	Interhospital transfer	Discharge	TOTAL
Number of transition medication errors	924,551	48,596	21,146	785,075	1,779,368
Number of patient episodes with ≥1 transition medication error	193,593	10,176	4,428	160,998	369,195
Number of patients with harm from transition medication error	16,379	861	375	13,621	31,235
Excess bed days due to harm	17,558	923	402	17,216	36,098
Cost of excess bed days (20/21 prices)	£6,531,557	£343,312	£149,385	£10,404,549	£17,428,802
Deaths due to harm	30	2	1	12	44

5.2 Impact of ISN implementation on error rates and burden

Figure 1 summarises transition medication error rates at hospital admission and discharge, and intra- and inter-hospital transfer in the absence of any medicines reconciliation, presence of standard medicines reconciliation and addition of interoperability standards to standard medicines reconciliation.

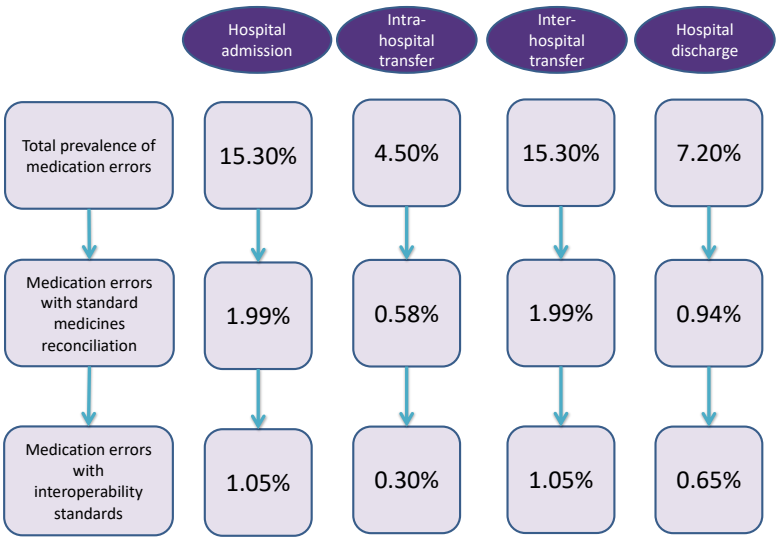

Figure 1 Prevalence of transition medication errors at key care-setting transfers in the absence of medicines reconciliation, with standard, and with digitally-enabled medicines reconciliation

Applying the estimated impact of ISN DAPB4013 implementation on the burden of medication errors at care transitions reduced the number of errors and number of patient episodes with an error by 40% from 1,779,368 to 1,065,541, and from 369,195 to 220,782, respectively. The ISN DAPB4013 implementation is estimated to result in 12,556 fewer people estimated to experience harm from a transition medication error, 14,275 fewer bed days of inpatient care, saving around £6.59 million per year and preventing 20 people dying from these errors. (See Table 2)

Table 2: Summary of impact of ISN implementation on annual transition medication error rates, harm and costs for each transition, and total

Reduction in parameters by ISN implementation	Admission	Intrahospital transfer	Interhospital transfer	Discharge	TOTAL
Number of transition medication errors	436,065	22,920	9,973	244,868	713,827
Number of patient episodes with ≥1 transition medication error	91,308	4,799	2,088	50,216	148,412
Number of patients with harm from transition medication error	7,725	406	177	4,248	12,556
Excess bed days due to harm	8,281	435	189	5,370	14,276
Cost of excess bed days	£3,080,613	£161,923	£70,457	£3,245,216	£6,558,210
Deaths due to harm	14	1	1	4	20

6 DISCUSSION

Medication transition errors persist despite standard medicines reconciliation, and the improved interoperability from planned ISN DAPB4013 implementation will substantially reduce transition medication error prevalence, and associated harm and cost.

We have assumed that hospitals in England have medicines reconciliation in place during a patient's admission, such that our 'before interoperability' baseline transition medication error rates are what would be seen with these systems in place. This reduces the baseline transition medication error rates substantially, which reduces

the scope of ISN DAPB4013 to further reduce transition medication errors, and thus provides what is probably a conservative estimate of effectiveness of ISN DAPB4013.

The suggested benefits of ISN DAPB4013 implementation from this report focus on patient safety and associated costs. The overall benefits of ISN DAPB4013 implementation incorporate other benefits, in terms of healthcare professional time saved, improved patient experience and quality of care, facilitating quicker discharge, enhanced capacity for cross organisational medicine optimisation, and supporting better healthcare planning.

7 RECOMMENDATIONS

Our key recommendations are:

- The ability of interoperability solutions to support more responsive and timely medicines reconciliation during admission or transfers requires service expansion and reconfiguration.
- We need UK data on the proportion of patients undergoing medicines reconciliation, how long after care transfer this occurs, and patient risk factors for transition medication errors allowing targeting of high-risk patients, such as polypharmacy.
- We need to measure transition medication error prevalence, including at inter- and intra- hospital transfer, both prior to, and after, ISN DAPB4013 implementation to assess the impact on transition medication errors, medicines reconciliation capacity, and health care professional confidence in decision-making.

We also recommend a more explicit role for patients, carers and families in these developments to improve medication safety in transitions of care**.**

MAIN REPORT

1 INTRODUCTION

1.1. BACKGROUND

Medicines are the most common intervention in healthcare, with an estimated 4.5 trillion doses taken worldwide in 2020 [1]. Medication errors lead to avoidable harm and costs. Our previous work estimated that 237 million medication errors occur at some point in the medication process in England annually, costing the NHS £98 million per year, consuming 181,626 bed-days, and contributing to 1708 deaths [2]. The World Health Organization's Third Global Patient Safety Challenge: Medication Without Harm aimed to reduce the global level of severe, avoidable harm related to medications by 50% between 2017 and 2022 [3]. Medication errors and the harm caused by them contributes to make big news in the media.[4] As part of this challenge, three key areas of concern were identified: medication safety in transitions of care, polypharmacy and high-risk situations. The resultant WHO report around medication safety in transitions of care highlighted the need to improve medication safety in transitions of care through leadership, medicines reconciliation capacity and capability, patient partnership, and improving information quality and availability [5].

Access to accurate medicines information is key to the management of patients, especially when they transfer from one care setting to another, such as an admission to and discharge from hospital. However, there are often unintended discrepancies and deficiencies in medicines information provision, leading to clinically important medicines being omitted or being given inappropriately [6]. Fragmented, inconsistent medication information transfer between settings can jeopardise patient safety by placing the patient at risk of taking incorrect medications and complicating the provider's role of assessing and treating patients, based on imperfect information [7]. Over 60% of patients may have at least one unintended medication discrepancy (a type of medication error) at hospital admission [8]. Over 40% of patients may experience post-discharge medication error(s), for whom a large proportion may be at risk of moderate harm [9]. Commonly erroneously duplicated medicines are often those with significant potential for harm if associated with a medication error, such as amlodipine, furosemide, bisoprolol, senna, insulin, metformin, alprazolam and morphine [10]. Some groups of patients are at particularly high risk of medication discrepancies, such as chronic kidney disease, where 62% of patients in an outpatient setting were reported to have a medication discrepancy [11]. One English study reported that intentional hospital medication changes were not actioned in primary care within seven days of discharge for 13% of patients and at least one change was actioned incorrectly for 6% of patients [12]. Up to one third of medication discrepancies at care transfer are probably clinically significant [13]. These transition medication errors can result in avoidable patient harm and healthcare costs [2]. It is likely that information transfer when patients are transferred between hospitals, or between prescribing systems within one hospital (such as from ICU to a ward[14]) is vulnerable to the same type of unintended medication discrepancies. Most hospitals in England use electronic prescribing systems for their inpatient wards, but some also have multiple systems within one hospital, or have both electronic and paper-based systems [15]. Furthermore, many hospitals have electronic prescribing systems that are not able to share medication information or prescription orders with the pharmacy dispensing system, requiring manual re-keying of medicines information. Error-free transfer of medicines information across these systems is a challenge.

Most health systems have a range of processes in place to mitigate against errors affecting the transfer of medicines information. Such processes may often involve some form of medicines reconciliation, which is

generally shown to be effective in reducing medication errors [6, 16, 17]. These services are time-consuming, costly and variably implemented. Across many sectors, there have been huge leaps in technology development to enable information systems to share their information digitally, often referred to as system interoperability. It is anticipated that enabling clinical systems in different care settings to share digital patient information across care transitions, including medication information or prescription orders, could reduce a lot of the time taken by healthcare staff to reconcile particularly unintentional medication discrepancies and improve patient experience, facilitate quicker discharge, support better healthcare planning and reduce the risk of avoidable harm to patients. Research suggests that adherence to discharge summary checking is better when records are interoperable [18]. As part of a nationwide initiative by NHS England to introduce interoperability into all NHS health and social care settings, this report focuses on the estimated effects of medicines interoperability solutions on medication error rates, patient harm and associated NHS costs.

1.2. DEFINING MEDICATION ERRORS, MEDICATION DISCREPANCIES, ADVERSE DRUG EVENTS AND MEDICATION RECONCILIATION

There is a lack of consensus about the definition of a medication error. A systematic review found 26 different terminologies employed for a medication error [8]. An inclusive definition of a medication error is provided by The United States National Coordinating Council for Medication Error Reporting and Prevention: 'Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures and systems including prescribing, order communication, product labelling packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use'[19]. This definition is broad and suggests that errors are preventable at the level of the individual and 'system' across different stages of the medication use pathway.

Unintentional medication discrepancies are a type of medication error, and are the mismatch, or inconsistency, of information between a patient's medications lists across health care settings. In this report, we use the term *transition medication error*, which are sometimes called unintentional medication discrepancies. Transition medication error categories vary across the literature, but have been summarised as: omitted medicines, extra medicines, duplicated medicines, wrong dose, wrong frequency, and acute medicines prescribed for chronic use [7]. A 'gold standard' medication list, or best possible medication history (BPMH), implies that the medication list is the most accurate reflection of what the patient actively is taking and any deviation from the 'gold standard' would be an error. However, it is not straightforward to determine the gold standard list for a patient, and thus any transition medication error.

Harm caused by medication is referred to as an adverse drug event (ADE) [7]. ADEs can occur even when the medicine is prescribed appropriately, (e.g. due to overdose, adverse drug reactions (ADRs) or allergies), but if there are questions about whether the prescription was appropriate, any resultant harm can be considered 'preventable' or 'avoidable'. In this report, we use the term 'avoidable adverse drug event' to refer to actual or potential harm caused by a medication error.

Medicines reconciliation is a widely practised process and can be defined as 'the process of identifying the most accurate list of a patient's current medicines including the name, dosage, frequency and route, and comparing them to the current list in use, recognising and documenting any discrepancies, thus resulting in a complete list of medications' [20]. This requires verification of a medicines history with the patient and/or carer, pharmacy, or other health-care provider(s) to generate a BPMH. Multiple methods of medicines reconciliation have been

tested and implemented using paper-based forms, collaborative approaches, and pharmacy-led services, most commonly employed at admission to or discharge from hospital. Reconciliation at hospital admission, for example, involves verification of the patient's drug history before admission, clarification that the history is accurate, and, finally, reconciliation of the previous primary care prescription and the initial prescription [21]. It can also uncover any over-the-counter medicines a patient is taking, that may not be recorded in any clinical IT system. A recent Cochrane review of 20 studies (18 of which described pharmacy-led medicines reconciliation) concluded that, compared with no medicines reconciliation, medicines reconciliation reduces the number of patients with at least one unintentional medication discrepancy, reporting a risk ratio (RR) of 0.53 (95% CI 0.42 to 0.67) [6]. More recently, the development of interoperable systems to facilitate electronic or digital medicines reconciliation has shown promise in reducing time taken to complete the process and to further reduce unintentional discrepancies, mostly centred around hospital admission and discharge [16, 17].

1.3. ASSESSMENT OF BURDEN ON PATIENTS AND HEALTHCARE PROVIDERS

The safety aim of reducing unintentional medication discrepancies is to reduce patient harm. The evidence directly linking medication errors in general to patient harm and/or costs is sparse, with studies using varying methods and having variable quality.[22] This is also the case with evidence linking transition medication errors to harm. The most common approach has been to assess the impact of ADEs on healthcare resource use such as hospitalisations and readmissions, hospital length of stay and activity in primary care. A recent Cochrane review of 20 medicines reconciliation studies, concluded that, compared with no medicines reconciliation, probably due to diverse and/or flawed study design, there was no certainty of the effect on the secondary clinical outcomes of ADEs, preventable adverse drug events (pADEs) and healthcare utilisation [6]. Due to methodological and measurement complexity, ethical considerations and the need for impractically large sample sizes and long follow-up times, studies tend to report error rates but not actual impact (patient harm or cost) arising from them. The key ethical issue is that once an error has been detected at any point in the medication use process in a research study, it cannot be left uncorrected to reach the patient. This is because it would be unethical to follow an uncorrected error through the medication use process to see if it causes harm. The medicines reconciliation literature tends to examine transition medication error rates, but a usually unknown proportion will reach the patient meaning the value of transition medication error rates is limited as a measure of harm. Nonetheless, measuring transition medication error rates has intrinsic value in that they identify which and when transition medication errors occur most commonly, allowing better targeting and testing of interventions.

1.4. ASSESSMENT OF SEVERITY AND CAUSALITY

In our study, we want to estimate the harm caused by transition medication errors. To deal with the evidence gap between the transition medication error and the harm caused, we need to refer to studies that have estimated what the harm would have been if the transition medication error had reached the patient. Many studies have used the concept of ranking errors by some subjective judgment of severity, using a range of rating scales. For example, the tool developed by Dean and Barber divides errors into 'minor', 'moderate', or 'severe'.[23] [23]Limitations of this approach lie with the intrinsic subjectivity of the method,[24] and the fact that many studies develop their own severity assessment system, limiting the comparability of results from different studies. By 2013, there had been 40 medication error harm severity rating scales reported in the literature [25].

Whether the harm, or ADE, has been caused by a transition medication error is not always clear. If harm does occur, the transition medication error may be only one of many factors leading to a poor outcome. For older,

more frail patients it can be difficult to attribute poor outcomes, such as readmission, directly to the ADE. These patients have higher resource use, including polypharmacy, and are already at greater risk of harm as a result. Furthermore, not all ADEs are avoidable as ADEs can occur when the medicine is use correctly. In studies looking at ADEs retrospectively, causality is usually assessed retrospectively by a group of clinicians. For example, in a study of hospital admissions associated with medication errors by Hallas et al (1990) [26], 20% were judged to be coincidental (i.e. reason for admission coincidental to medication error), 63% were judged as possibly avoidable and 9% were judged as definitely avoidable. There is variability in how this causality is assigned between studies, making comparison difficult. Many ADE studies tend to judge large numbers of ADEs as possibly avoidable,[26] [27, 28] which are likely to include many cases where hindsight bias might suggest the prescribing decision was wrong, when it had been based on careful balancing of benefits versus harms taking into account evidence-based guidelines and patient preferences. In previous work we have made the conservative assumption is that only definitely avoidable ADEs approximate the harm from medication errors[2], which produces more conservative estimates of avoidable harm, than if possibly and definitely avoidable ADEs are included, as in the work by the National Patient Safety Agency (NPSA) [29, 30].

1.5. IMPLEMENTATION OF ISN DAPB4013

The information the National Health Service in England (NHS) holds about medications and allergies is often fragmented, stored in different formats, using different vocabulary, and in systems that do not connect with one another. Some systems, such as all the main primary care systems, are not owned by the NHS, which makes implementing improvement, even locally, more difficult. Together, this makes that information difficult to share within and between health providers. NHS Digital estimates per year in England there are 167 million hospital transcriptions, consuming 1.2 million hours hospital staff time and 9000 weeks general practice (GP) clinical and administrative time [31]. Insufficient access to information puts a significant stress on both patients and health care professionals, and in turn causes additional workload and risky workarounds [32]. From 2015, NHS providers have had access to the Summary Care Record (SCR) which is an electronic record of key aspects of patient information, created from GP medical records, but without the function of digital ttransfer of data [33]. An English study of the use of a SCR by pharmacy teams to support the medicines reconciliation process after hospital admission, by making the information more accessible, demonstrated that an average of 29 minutes was saved per patient when establishing a drugs history, as well fewer faxes and phone calls to GP practices [34]. Another small pilot study of SCR use in an English private hospital suggested that 9.2 minutes were saved, and the mean number of medication discrepancies detected was increased from 1.7 to 2.13 per patient[35]. It is known that a lack of interoperability between care settings leads to medication errors, such as drugs missed, drugs added, wrong dose, frequency, or allergy information missed. To address this, all medication messages used by different NHS IT systems need to be standardised. Messages need to be interoperable, meaning different IT systems can exchange and make use of data and information across system and organisational boundaries. The NHS Long Term Plan includes clear aims to improve interoperability in the NHS as part of a digital transformation agenda [36]. This has been operationalised as key components of ISN DAPB4013 which is being introduced into the NHS in England in 2023:

- Fast Healthcare Interoperability Resources (FHIR),
- application programming interface (API) for exchanging electronic health records (EHR),
- dictionary of medicines and devices (dm+d) adoption (dm+d is the standard that allows medicines to be accurately identified),
- SNOMED CT (structured clinical vocabulary for use in an electronic health record, from procedures and symptoms through to clinical measurements, diagnoses and medications) adoption,

- enhanced electronic prescription service (EPS). The established EPS enables electronic prescriptions to be sent directly to named dispensing sites such as pharmacies, and is present in community prescribing and urgent care. The Enhanced EPS aims to extend this functionality to secondary care, whilst also upgrading the EPS platform to allow further improvements in future).[37]

The aim of ISN DAPB4013 is to contribute to the NHS's wider aim 'to create fully interoperable, computable medication and prescription information across the NHS enabling seamless transfer of care and ultimately a patient centred consolidated medication record'[38]. (A consolidated medication record enables access to accurate patient medication information at the point of care from across health care providers using shared information recording standards[39] (Source: https://digital.nhs.uk/services/digital-and-interoperable-medicines). Each NHS site has to use:

- FHIR-based APIs (from NHS Digital's API catalogue, filtered by FHIR) to join up care for patients;
- NHS number (NHS Digital) and NHS data registers and comply with NHS clinical information standards;
- ICD-10 (the World Health Organization's International Classification of Diseases, version 10);
- structured clinical vocabulary SNOMED CT (on NHS Digital's website);
- data sets are published in an open machine-readable format, under an Open Government Licence, unless they contain personally identifiable information, sensitive information, or where publishing the data would infringe the intellectual property rights of someone outside the NHS or government;
- comply with the GS1 barcodes standard as set out in Scan4Safety.[40]

1.6. IMPACT OF INTEROPERABILITY ON TRANSITION MEDICATION ERRORS AND ASSOCIATED HARM

There is little evidence evaluating transition medication errors, and even less around the impact of interoperability solutions, although there is an increasing evidence-base suggesting a positive effect [16, 17]. In a qualitative UK study exploring views of clinical staff toward prescribing and discharge communications before and after introducing a hospital electronic prescribing and administration system, post-implementation staff agreed that the system increased patient safety especially around the quality of discharge medication communication [41]. Research suggests that adherence to discharge summary checking is better when records are interoperable [18]. It is anticipated that making information systems across care transitions interoperable could reduce the time taken by healthcare staff to reconcile medication discrepancies and improve patient experience, facilitate quicker discharge, support better healthcare planning and reduce risk of avoidable harm. However, these developments are usually highly disruptive whilst being introduced, requiring significant diversion of staff time, and financial investment, as well as clear leadership and planning. In an already overburdened health service, this can hinder implementation. However, health care systems care about the safety of their patients, so evidence around impact on patient safety may encourage wider implementation of interoperability solutions. This is the case with the implementation of NHS England's information standard ISN DAPB4013: Medicine and Allergy/Intolerance Data Transfer.

2. AIMS AND OBJECTIVES

This research study aimed to estimate the benefits that are expected to be evident following the implementation of information standard 'ISN DAPB4013: Medicine and Allergy/Intolerance Data Transfer' to patients and the NHS in England. The aim is to estimate potential costs and benefits of the programme in terms of fewer

transition medication errors, reduced harm and reduced burden to the NHS in England by answering the following questions:

1. What is the prevalence of medication errors at key transitions between care settings or movement of medicines information between systems?
2. What is the patient harm and NHS cost of these transition medication errors?
3. How will improved information transfer impact on transition medication errors, patient harm and NHS cost?

3. METHODS

3.1. OVERVIEW

This study used available evidence and stakeholder/expert input to estimate the prevalence, patient harm and cost of medication errors at key transitions, and the expected effect of adopting and using the new information standards on these parameters. There are three interlinked elements of work:

1. A rapid review to identify: a) literature on the prevalence of transition medication errors at interfaces between care locations in the UK (Review 1); b) literature on the costs and health burden associated with these transition medication errors in the UK (Review 2); c) published estimates of benefits and costs of interoperable systems designed to reduce transition medication errors at interfaces between care locations (Review 3).
2. Modelling to provide estimates of transition medication error prevalence and error burden for medication errors at interfaces between care locations in the NHS in England informed by the literature obtained (and drawing on other evidence as appropriate).
3. Modelling to provide estimates of impact of the implementation of ISN DAPB4013 on transition medication errors, patient harm and NHS cost.

Throughout the project, we consulted with stakeholders from Digital and Interoperable Medicines Programme NHS England and NHS Improvement, hospital/IT/safety pharmacists and IT professionals working in this field in the NHS, and IT suppliers: FDB (First Databank UK Ltd), Better UK & Ireland, Dosium and Omnicell. More details of individuals who contributed their expertise are provided in the Acknowledgements.

3.1.1. Transitions under investigation

There are multiple transitions that can involve information transfer. In this study we focus on the following information transfer settings: Primary care to secondary care; secondary care to primary care; intra-hospital transition (**where there is transfer from one electronic prescribing system to another*); inter-hospital transition.

Transitions excluded were: Ambulance Trusts; when patients change GP practice (GP2GP); private hospitals (separate governance structures); devolved nations (focus on England only); hospital prescribing to dispensing; outpatient/emergency care to community pharmacy. Maternity and paediatric care data have not been excluded from our estimates.

Hospital prescribing to dispensing was excluded as a transition as there were no data available focusing on the effect of interoperability in hospital prescribing to dispensing systems. Hospital inpatient dispensing is delivered in multiple ways in England, a 10-year old survey reporting bedside medication lockers (92%), patients' own drugs (89%) and 'one-stop dispensing' medication labelled with administration instructions for use at discharge as well as during the inpatient stay (85%)[42]. Two-thirds of hospitals used drug trolleys; 50% used patient-

specific inpatient supplies on most wards. None of the hospitals completing the survey reported use of unit-dose dispensing; 7% used an electronic drug cabinet in some ward areas. It is likely that the picture has changed since this survey. However, lack of data available around proportion of inpatient prescribing medication orders made to pharmacy departments compared with use of patient's-own drugs, one-stop dispensing, ward stock dispensing and closed-loop dispensing prevented estimation of realistic rates of prescribing orders to hospital pharmacies for dispensing.

3.1.2. Outcomes

The outcomes used in this study are medication errors that occur at information transfer, and are also defined as unintentional medication discrepancies, referred to in this report as *transition medication errors*. Intentional medication changes during the medication reconciliation process are not included in this definition. Discrepancy categories include omissions, extra medicines, duplicated medicines, wrong dose, wrong frequency, and acute medicines prescribed for chronic use [7].

Impact on patient harm is measured using hospitalisations, ADEs, length of hospital stay, readmissions and deaths. A hospital readmission is a second admission to the hospital within a certain period of time. In literature, different time periods are used between the hospital discharge and readmission, ranging from 30 days to three years. However, a period of 30 days is most common.

The cost perspective taken was that of NHS England, whereby annual costs were estimated by attaching publicly available unit costs to hospital admissions, using 2020/21 as the cost year.

3.1.3. Impact of interoperability solutions

Most hospitals in England have some form of medicines reconciliation in place during a patient's admission, which is generally shown to be effective in reducing transition medication errors [6, 16, 17]. Therefore we assume in our study that prior to ISN introduction, transition medication error rates are what would be expected in the presence of standard medicines reconciliation.

It was assumed that, prior to ISN introduction, all hospitals in England:

- Have electronic prescribing for standard inpatient wards (therefore no discrepancies caused by manual chart re-writes are included in our estimates);
- Did not have 100% interoperability between standard inpatient ward electronic prescribing systems and other electronic prescribing systems (such as ED, ICU, theatres) 'intra-hospital transfer';
- Did not have 100% interoperability between different hospital electronic prescribing systems 'inter-hospital transfer';
- Carry out standard (non-interoperable, non-digitally-enabled, pharmacist-led) medicines reconciliation during an inpatient stay.

The evaluation is summarised in the following PICO framework:

Population:	People at risk of experiencing transition medication errors at defined interfaces
Intervention:	Digitally-enabled interoperable medicines information transfer
Control:	Manual medicines information transfer (which can include use of systems that provide access to digital information, but requires manual transfer to another medicines information system (such as the shared care record)

Outcomes:	Transition medication errors, hospitalisations, adverse drug events, length of hospital stay, readmissions, deaths

3.2. RAPID REVIEW

A systematic search for studies was undertaken from February to July 2022 via: contact with experts in the field; searching of electronic databases and the grey literature; checking of bibliographies and citation searching of retrieved papers. We used a comprehensive pearl-growing and iterative approach to deal with the complexity of finding published work in this area, a challenge common to this type of public health topic [43]. We started with key reviews [44] [45], the WHO report[5] and other publications with which the team were familiar to allow development of an initial search strategy, along with extracting reviews from reviews of reviews. Databases searched were: Medline, Embase, DARE, Cochrane, PsycInfo, CENTRAL, Cinahl, Web of Science from 2000-June 2022. We carried out citation searches and chain searches of all sources found. Non-indexed journals publishing in this area were hand-searched (in June 2022): Journal of Medicines Optimisation (JOMO), International Journal of Pharmacy Practice, Research in Social and Administrative Pharmacy, International Journal of Clinical Pharmacy, and European Journal of Hospital Pharmacy. Conference abstracts were excluded. The review included full text journal publications only and studies reported in English. Quality assessment of included studies was undertaken[46], summary tables and narrative syntheses were produced. Authors were not routinely contacted.

3.2.1. Review 1: to provide estimates of error prevalence

A rapid review of the literature was completed to identify studies that reported the prevalence of transition medication errors in England. The search strategy comprised terms for epidemiologic outcomes, care transitions, and medication errors. Prevalence was defined as the total number of items prescribed that have an error divided by the total number of items prescribed (ie. the proportion of items prescribed that have a medication error). Observational (prospective or retrospective) studies that aimed to estimate the prevalence of medication errors were included. Reporting systems under-report errors (one study found that an error reporting system reported only 2.3% of those found by retrospective case note review[47]) so are not useful for deriving error incidence/prevalence. Studies of interventions designed to reduce the rate of transition medication errors were included if the baseline (pre-intervention) or control group error rates were reported. Studies were read in full by two authors (SPG; RNK) to determine whether they met the inclusion criteria for Review 1. Appendix 1a reports the electronic database search strategy for Review 1. A PRISMA diagram of included studies is reported in Appendix 2a.

3.2.2. Review 2: to provide estimates of error harm and associated costs

A rapid review was carried out to identify published estimates of harm from all types of medication errors, not just transition medication errors. The primary aim of the search was to identify papers relating to the UK NHS or Irish healthcare systems. This search was not restricted to harm from transition medication errors only, to maximise the likelihood of identifying relevant papers. The search strategy was derived from a recent systematic review related to patient harm associated with ADEs [48] which used terms to identify ADEs and harm outcomes. Database searches were supplemented by citation and chain-searching five key publications in the field [2, 27, 45, 49, 50]. (see Appendix 1b and Appendix 2b for the search strategy and PRISMA diagram, respectively).

3.2.3. Review 3: to provide estimates of costs and benefits of ISN implementation

A rapid review was carried out to identify published estimates of benefits of interoperability systems designed to reduce transition medication errors at interfaces between care locations and transcription. Key recent reviews were the starting point for studies of interoperability solutions to support medicines safety at care location transitions in the UK setting [51] [6] [52-54]. We included all comparative study designs where the intervention was carried out at a care location transition, incorporated one or more elements included in ISN DAPB4013 and measured one of: transition medication error rates, costs, patient outcomes. This broad inclusion criterion was a pragmatic decision to identify a range of studies that were relevant to ISN DAPB4013. Study types included UK-based primary comparative studies, reviews (systematic, rapid, narrative, meta-analyses) and reviews of reviews. (see Appendix 1c and Appendix 2c for the search strategy and PRISMA diagram, respectively).

3.3. MODELLING

3.3.1. Estimates of error prevalence

We used transition medication error rates reported in the studies identified during the reviews to estimate the prevalence of transition medication errors in England as a whole. Extrapolation methods were determined by data availability.

3.3.2. Methods to estimate medication errors undetected by medicines reconciliation

The added value of interoperability solutions, relative to current practice, is to reduce the number of transition medication errors that remain undetected by standard medicines reconciliation at care transitions. However, the prevalence of these undetected transition medication errors was not reported in the literature. Instead, the literature on medication errors at care transitions often reports transition medication errors detected during routine activities in standard care, for example, the number of errors detected by standard medicines reconciliation at admission or discharge. Therefore, the number of transition medication errors detected by medicines reconciliation were subtracted from the estimated total number of transition medication errors at four care transitions: admission, intra-hospital ePMA transfers, inter-hospital transfers, and discharge. In the absence of relevant data around the total number of transition medication errors at these care transitions, these were estimated by applying the treatment effect for medicines reconciliation versus no medicines reconciliation to the observed prevalence of transition medication errors detected by medicines reconciliation from Review 1[1]. A Cochrane review of randomised controlled trials reported a relative risk reduction in items prescribed with a transition medication error of 0.13 following medicines reconciliation versus no medicines reconciliation [6].

3.3.3. Methods to estimate the total number of transition medication errors per year

The following section describes, for each specified care transition, how the prevalence estimates were scaled to population-level estimates for England.

[1] $error^{UD} = \left(\frac{error^{MR}}{(1-RR)}\right) - error^{MR}$ where $error^{UD}$ is the total number of transition medication errors undetected by medicines reconciliation, $error^{MR}$ is the total number of transition medication errors detected by medicines reconciliation, and RR is the relative risk reduction of transition medication errors after medicines reconciliation compared with no medicines reconciliation.

Admission to hospital: The number of transition medication errors at admission was estimated by multiplying the prevalence of transition medication errors (Review 1) by the total number of items prescribed per year at hospital admission in England (46,521,652 items). The total number of items prescribed per year at admission was calculated by multiplying the mean number of items prescribed per inpatient (n=4.78 items) [55] with the total number of finished elective and emergency admission episodes in England (9,741,243 episodes) [56]. The total number of finished elective and emergency admission episodes was calculated by subtracting the number of day case finished consultant episodes (7,386,255 episodes) from the total number of finished admission episodes (17,127,498 episodes) reported by NHS Digital between 2018-19 [56]. Data from this year were chosen to exclude effects of the COVID-19 pandemic on hospital admissions.

Intra-hospital transfer: In the absence of directly measured data, the proportion of inpatients who experience an intra-hospital ePMA transfer was estimated by proxy from the proportion of patients who transfer between wards. A freedom of information request for 42 hospital Trusts found that the proportion of inpatients who transfer between wards ranged between 9% and 88% of inpatients [57]. Boncea *et al* (2022) [58] report a case-control study of intra-hospital transfers and hospital-acquired infections in elderly patients. An intra-hospital transfer was defined as moving between a ward or unit resulting in a change of ward ID. In the control cohort (ie. patients without hospital-acquired infection), 71.7% of patients had at least one intra-hospital transfer during their inpatient stay. Given the elderly nature of the estimation sample (median age: 79 years), this proportion of patients who transferred between wards is likely to be an overestimate for the average inpatient population. Therefore, we assumed conservatively that 17.9% of inpatient stays resulted in a ward transfer (ie. one-quarter of 71.7%). Whilst this estimate falls within the observed range (9% to 88% of inpatients), there is considerable uncertainty in its true value. To incorporate this uncertainty, the value of this estimate was varied in a Scenario Analysis (see Section 3.3.9). This proportion was multiplied by the total number of finished elective and emergency admission episodes (9,741,243 episodes) [56] to estimate the total number of inpatient ePMA transfers per year (1,746,118 transfers). The total number of items prescribed at intra-hospital transitions (8,339,006 items) was calculated by multiplying the number of ePMA transfers with the average number of items prescribed as above (n=4.78 items) [55]. The number of transition medication errors during intra-hospital ePMA transfers was calculated by multiplying the number of items prescribed at intra-hospital transitions by the prevalence of transition medication errors during intra-hospital transfer identified by Review 1.

Inter-hospital transfer: The number of medication errors during movement to a new hospital was calculated by multiplying the number of items prescribed at inter-hospital transfers (1,064,006 items) by the prevalence of transition medication errors when transferring between hospitals identified by Review 1. In the absence of directly collected data, the number of items prescribed during inter-hospital transfers was calculated by multiplying the annual inter-hospital transfers (222,794 transfers) by the average number of items prescribed as above (n=4.78 items) [55]. The annual number of inter-hospital transfers was estimated from the most recent total number of inter-facility transfer incidents (category 1 to 4) reported in the Ambulance System Indicators for England over a 12-month period (2021-22) [59]. This was the first complete dataset available that was not collected during the main COVID-19 pandemic period.

Discharge from hospital admission: The number of transition medication errors at discharge was estimated by multiplying the prevalence of transition medication errors from Review 1 by the total number of items prescribed per year at discharge in England (83,518,624 items). The total number of items prescribed per year at discharge was calculated by multiplying the mean number of items per discharge prescription in Lloyd *et al*. (n=4.9 items) [60] with the total number of finished admission episodes (FAE) (17,127,498 episodes) reported by NHS Digital between 2018-19 [56].

3.3.4. Estimates of transition medication error burden

Some medication errors do not lead to harm, others can lead to serious harms and death [61]. Ideally, the data needed to assess impact of medication errors occurring are sufficient to encompass all effects of the error and patient outcomes (intermediate measures such as primary and secondary health care utilisation, fatal and non-fatal serious harm outcomes (such as GI bleed, stroke, death rates), health status, life-years gained (LYG)/lost, quality-adjusted life-years (QALYs)). The costs associated with harm can be viewed from a healthcare provider perspective, as we have done in this study, or more broadly from a societal perspective. However, the evidence directly linking medication errors to patient harm and/or costs is sparse. Therefore, it has been necessary to utilise existing sources of data to allow the estimation of burden in terms of patient harm and cost to the NHS. It was necessary to rely on retrospective judgements that the harm presented was: (1) due to an ADE; and (2) that it was avoidable. The primary approach used was to identify available UK-based case studies of estimates of burden from ADEs and extrapolate to estimate the impact for England per annum. Data from non-UK case studies were used to supplement this evidence where UK studies were not available. For our base-case, we considered the number of hospitalisations (readmissions) and deaths associated with discharge to primary care with an error, and increased length of hospitalisations and deaths associated with admission, intra- and interhospital transfer errors. The key assumption is that definitely avoidable ADEs approximate the harm from medication errors; hence these studies were considered acceptable.

3.3.5. Methods for estimating the potential of reported transition medication errors to cause harm

The proportion of inpatient episodes where a definitely avoidable ADE occurs (i.e. inpatients who have harm from a medication error) was derived from Davies *et al* (2009) [49] to be 0.9%. The total number of FAEs used in the estimation of the number of transition medication errors was multiplied by 0.9% to estimate the number of patients with harm from a transition medication error. Davies *et al* (2009) also reported that 17.9% of ADEs related to drugs that were initiated prior to hospitalisation (i.e. drugs that they would have been taking at admission). This was applied to the number of patients with harm from a transition medication error to estimate the number of patients with harm from a transition medication error at the point of admission. The number of people with harm from an admission medication error was divided by the number of people with an admission medication error to generate the proportion of people who had a transition medication error who experience harm. This proportion was used throughout the modelling to estimate the number of patients experiencing harm based on the number of transition medication errors that occurred at the different transitions.

3.3.6. Methods for developing estimates of burden of medication errors

For transition medication errors that occurred during a process of admission (i.e. inpatient admission, intra-hospital transfer, inter-hospital transfer), the associated harm and burden were derived from the study of inpatient ADEs in a UK hospital by Davies *et al* (2009) [49]. In that study, of the people who had an ADE, 26.8% of people had an extended hospital admission, with a mean additional length of stay of 4 days. The excess bed day cost in the NHS (as a weighted mean of the cost for elective and non-elective admissions) was multiplied by 4 days for 26.8% patients with a transition medication error on admission. The excess bed day cost was most recently reported in the NHS schedule of reference costs in 2017/18 [62]. This value was inflated to a 2020/21 price year using the NHSCII pay and prices index [63]. Davies *et al* (2009) also reported that of the people who have an ADE, 0.18% of them die as a result. The number of people estimated to have a transition medication error during an admission process was multiplied by 0.18% to estimate the number of deaths.

For transition medication errors that occurred at the point of discharge following an inpatient stay, or in relation to an outpatient or accident and emergency (A&E) attendance, the associated harm and burden were derived from a prospective cohort study across five NHS hospitals by Parekh *et al* (2018) [50]. This study reported that of the people with medication-related harm following hospital discharge, 21.1% were re-admitted to hospital. We used this value of 21.1% as a proxy for the harm caused by perpetuation of transition medication errors into primary care. This value of 21.1% was multiplied by the estimated number of people with a transition medication error at discharge, outpatients, or A&E attendance to estimate the number of people (re)admitted. The cost of these (re)admissions was estimated based on the mean cost of non-elective hospital admissions in the NHS in 2020/21 [64]. Osanlou *et al* (2022) published a recent observational study of adults admitted to an English hospital where an ADE was the reason for admission [65]. This study reported that the median duration of admissions due to ADEs was 6 days, which we used to estimate the number of bed days associated with these errors. Osanlou *et al* (2022) also reported that 0.42% of people admitted to hospital due to an ADE died as a result. This percentage (0.42%) was multiplied by our estimate of the number of people who were (re)admitted to hospital due to an error to estimate the number of people who died.

3.3.7. Estimates of costs and benefits of ISN implementation

Liaison and engagement with stakeholders (initially Department of Health and Social Care (DHSC), National Health Service England (NHSE), NHS Digital, hospital IT, computing, interoperability and safety pharmacists, chief pharmacists, ePMA suppliers) was carried out to understand the composition, costs and expected benefits of the key components of ISN DAPB4013 (Fast Healthcare Interoperability Resources (FHIR), application programming interface (API) for exchanging electronic health records (EHR), dm+d adoption and enhanced electronic prescription service).

We assumed the estimates of the number of transition medication errors and the burden from those errors derived in Review 2 was the 'current practice' scenario. We derived estimates (base-case and plausible alternative scenarios) of the anticipated effectiveness of ISN implementation from Review 3. We combined these data to allow derivation of indicative estimates of costs and benefits.

3.3.8. Base-case

For transition medication errors that occurred during a process of admission (i.e. inpatient admission, intra-hospital transfer, inter-hospital transfer), the impact of interoperability on the rate of transition medication errors was derived from Zoni *et al* (2012) [66]. Based on the proportion of medications prescribed with an unintended discrepancy before and after the implementation of medicines interoperability, the RR of an error was 0.53 post-intervention. See Section 4.3 for more detail.

For transition medication errors following discharge from an inpatient admission, the impact of interoperability was derived from Smith *et al* (2016) [67]. The RR of a transition medication error was 0.69 in the post-implementation period compared to the pre-implementation period. See Section 4.3 for more detail.

The impact of interoperability on the rate of transition medication errors during a process of intra-hospital transfer, or inter-hospital transfer was not available. Therefore, we assumed that this would equate to impact of interoperability on the rate of transition medication errors during a process of hospital admission.

3.3.9. Scenario analysis

Where more than one plausible model parameter was identified, the 'best guess' was used in the base case model and the alternative used in a scenario analysis. In the base case analysis, transition medication error rates were derived from the paper by Ashcroft *et al* (2015) [55] for all transitions. An alternative transition medication error rate at discharge was also identified in the literature searches in the paper by Lloyd *et al* (2021) [60]. Using the same approach described above, an undetected transition medication error rate of 3.29% was derived from the detected transition medication error rate of 22.0% reported in the paper. Also in relation to transition medication errors at discharge, the number of items prescribed at discharge form the paper by Lloyd *et al* (2021) was used in the base case model (4.9). An alternative paper by Onatade *et al* (2017) reported a mean of 8.4 items per discharge prescription [68]. In the base case model, duration of a prolongation of an inpatient stay due to a transition medication error was taken from Davies *et al* (2009) (4 days) [49]. As an alternative, Osanlou *et al* (2022) reported a median of 6 days in hospital due to a transition medication error [65]. The impact of assuming an alternative length of stay of 6 days was explored for errors at points of admission (i.e. admission, intra-hospital transfer, inter-hospital transfer).In the base-case analysis we derived the proportion of transition medication errors that lead to harm from our estimate of the prevalence of transition medication errors at admission and our estimate of the prevalence of harm from transition medication errors at admission (8.5%) as there were no UK-based publications reporting both transition medication errors and harm from transition medication errors. A large robust Canadian study reported the proportion of medication errors leading to harm (10.2%) [69]. In relation to the impact of implementing **ISN** DAPB4013 on the prevalence of transition medication errors, in the base case model we used transition-specific data identified from separate papers. As a scenario analysis we used a single pooled relative risk (RR) of a transition medication error in the post-implementation period (compared to pre-implementation) from a meta-analysis of interventions across different transitions by Mekonnen *et al* (2016) (RR 0.55; 95% CI 0.51 to 0.58) [16].

4. RESULTS

4.1. REVIEW 1: TO PROVIDE ESTIMATES OF ERROR PREVALENCE

The search identified twelve studies that estimated the prevalence of transition medication errors at care transitions in England [55, 68, 70-79]. Appendix 3 reports the complete data extraction table for these twelve studies. The majority of included studies (n=10/12, 83%) reported transition medication errors at discharge from hospital. Eight studies (66%) reported transition medication errors at admission to hospital. Five studies (42%) reported transition medication errors at both hospital admission and discharge transitions. Seven studies (58%) reported evidence from a single hospital only. The remaining studies generated evidence from between three and twenty hospitals in England.

No studies reported evidence of transition medication errors at two transitions of care: intra-hospital transfers and inter-hospital transfers. Therefore, in the absence of this evidence, the following assumptions regarding the prevalence of transition medication errors were made. First, the prevalence of transition medication errors during intra-hospital transfers was assumed to equal the prevalence of transition medication errors during drug chart rewrites. Second, the prevalence of transition medication errors during inter-hospital transfers was assumed to be the same as the prevalence of transition medication errors at hospital admission.

It was not possible to pool estimates of prevalence due to heterogeneity in the designs of each study. Therefore, a decision was made to select the most relevant and representative study for current clinical practice in England. The criteria to inform this decision comprised patient sample size, the number of included hospitals, and the

range of medical specialities covered by the study. Ashcroft *et al* (2015) [55] was selected as the most relevant study to estimate the prevalence of transition medication errors at admission and discharge in England. This study was selected for three reasons: (i) it included the largest number of patients; (i) it was the largest multi-centre study, and (iii) the estimation sample comprised all prescriptions across all ward specialities. The prevalence of transition medication errors at admission (13.3% of items prescribed) and discharge (6.3% of items prescribed) were identified by medicines reconciliation as per standard care. The incidence of transition medication errors during drug chart rewrites (3.9% of items prescribed) were identified as part of routine hospital pharmacy services.

4.2. REVIEW 2: TO PROVIDE ESTIMATES OF TRANSITION MEDICATION ERROR BURDEN

The search identified one review [80] and four primary studies [60] [50, 81, 82]. Further searching of reviews, reference lists and hand searching retrieved another 16 potential source studies (see Appendix 4 for details). Table A4.2 summarises the studies retained for use in the modelling. Studies relating to harm from medication errors in the context of the UK NHS were identified, specifically harm from medication errors relating to discharge prescriptions [50, 60], hospital admissions due to ADEs [50, 65], and harm from ADEs that occur during hospitalisation [49].

4.3. REVIEW 3: TO PROVIDE ESTIMATES OF COSTS AND BENEFITS OF ISN IMPLEMENTATION

The search retrieved 16 reviews (including 3 reviews of reviews[83-85] and 13 reviews[86-88] [16, 17, 89-96]) and 6 primary studies[21, 97-101]. One review was subsequently excluded as it was not about IT-enhanced medicines information interoperability.[89] We added two further reviews of reviews,[102, 103], two Cochrane reviews [6, 104], and 17 extra recent or potentially relevant reviews we had found separately and through handsearching [14, 51, 52, 54, 105-118]. The reviews of reviews and reviews were used as a source of other reviews, primary studies or combined results (meta-analysis) for the effect of an 'IT' component. The five reviews of reviews, and 31 reviews are summarised in Appendix 5.

In our initial review we identified six UK-based primary studies[21, 97-101]. These studies did not provide sufficient effectiveness data to populate the transitions under investigation in this study. Due to very few UK studies being available, we made the decision to include studies from other settings. Further searching of reviews, reference lists and handsearching retrieved another 47 primary studies (see Appendix 6 for details). Appendix 6 also summarises studies excluded and reasons for exclusion. We retained studies for use in the modelling to allow estimation of the impact of interoperability in the presence of standard medicines reconciliation. We found no suitable studies that reported the effectiveness of interoperability between electronic prescribing and dispensing systems in secondary care, so had to exclude this information transfer setting.

Two systematic reviews explicitly examined the added impact of interoperability on transition medication errors in the presence of standard medicines reconciliation [16, 17]. Both reviews reported results according to specific outcomes: proportion of patients with at least one discrepancy; mean number of discrepancies per patient; proportion of medication orders with discrepancies. The older review by Mekonnen *et al* (2016) includes 10 studies, none of which are from the UK, and it is not clear that all these studies examine standard medicines reconciliation versus digitally-enabled medicines reconciliation. The meta-analysis reports a risk ratio of 0.37 (95% CI: 0.08-1.70) for effect on proportion of patients with medication discrepancies. This risk ratio is heavily

biased by inclusion of Agrawal *et al* (2009) [119] which should not have been included because the comparator was a two-week pilot of the electronic medicines reconciliation intervention. This gives an overestimate of effect size due to the large sample size of one arm of the Agrawal study. The meta-analysis also reports a risk ratio of 0.55 (95% CI: 0.51-0.58) for effect on incidence of medication discrepancies. The more recent Killin systematic review (2021) included six studies, none of which are from the UK, and only includes two of the studies included by Mekonnen *et al* (2016) and then three subsequent studies all focusing on discharge [17]. The lack of overlap of primary papers in these two reviews demonstrates how complex it appears to be to define or critically appraise standard medicines reconciliation versus digitally-enabled medicines reconciliation, and to find studies given heterogeneous coding approaches. In addition to the concerns about some of the studies included in the Mekonnen meta-analysis, they only present one risk ratio for all medicines reconciliation, irrespective of whether it occurs at admission or discharge, so we would have to assume digitally-enabled medicines reconciliation will have the same effect across these transitions. Instead, we decided to select then combine discrete studies for effect size of standard medicines reconciliation versus digitally-enabled medicines reconciliation for the four transitions under investigation.

Only a minority of studies retrieved examined standard medicines reconciliation versus digitally-enabled medicines reconciliation on hospital admission. The impact of interoperability on the rate of transition medication errors during a process of admission was derived from a Spanish study by Zoni *et al* (2012) [66] in the absence of a suitable UK-based study. This before and after study was included in the Mekonnen meta-analyses and assessed to have a low risk of bias [16]. It compared standard paper-based medicines reconciliation in patients on three or more medicines and with a hospital stay of 24hrs or more (n=162), carried out by nurses who had been trained by pharmacists, with the same intervention enhanced by the addition of an IT application designed to access medicines details prior to admission. Although slightly different from how standard medicines reconciliation would be delivered in England, we considered this study presented the most sensible estimate of the effect of digitally-enabled medicines reconciliation at hospital admission. The primary outcome of unintended discrepancies (transition medication errors) decreased from 3.5% to 1.8% after the intervention ($p = 0.03$), reporting a risk ratio of 0.53 (95% CI: 0.30-0.92) for effect on incidence of transition medication errors. The proportion of patients with at least one transition medication error was 23.7% in the first phase and 14.6% in the second phase (p value 0.20), reporting a risk ratio of 0.62 (95% CI: 0.32-1.18) for effect on proportion of patients with transition medication errors. Omission was the most common transition medication error.

The impact of interoperability on the rate of transition medication errors during a process of discharge was derived from a before and after US study by Smith *et al* (2016) [67]. The intervention was a mandatory electronic medication record-based discharge medication reconciliation procedure, with reports given to patients and sent to primary care physicians compared with a non-mandatory paper-based discharge medication reconciliation procedure, in hospitalised medical patients (n=835) with two or more comorbidities and five or more chronic medicines at a single centre. This before and after study was included in the Killin systematic review and assessed to have a low risk of bias [17]. Although slightly different from how standard medicines reconciliation would be delivered in England, we considered this study presented the most sensible estimate of the effect of digitally-enabled medicines reconciliation at hospital discharge. The primary outcome was discharge medication errors which were lower post-intervention (adjusted OR 0.57, 95% CI 0.44–0.74, $p<0.001$). There was no change in 30-day rehospitalisation, emergency department visit, and primary care provider follow-up visit rates.

The impact of interoperability on the rate of transition medication errors during a process of intra-hospital transfer, or inter-hospital transfer was not available. Therefore, it was assumed that impact of interoperability on the rate of medication errors at both of these transitions would be the same as during a process of admission. This in turn assumed that standard medicines reconciliation was already in place at these transitions.

4.4. MODELLING

All of the estimates in the following sections are reported to the nearest whole number.

4.4.1. Estimates of transition medication error prevalence

Table 1 reports the estimated prevalence of transition medication errors undetected by medicines reconciliation at admission, admission to hospital, discharge from hospital, intra-hospital transfers and between inter-hospital transfers was estimated to be 1.99%, 0.58%, 1.99% and 0.94% of items prescribed, respectively. These values were derived from Ashcroft et al (2015) [55].

Table 1. Estimated prevalence of transition medication errors undetected by standard medicines reconciliation

Transition	Estimated prevalence of transition medication errors*	Source
Admission	1.99%	Ashcroft *et al*. (2015) [55]
Intra-hospital transfer	0.58%	Ashcroft *et al*. (2015) [55]
Inter-hospital transfer	1.99%	Ashcroft *et al*. (2015) [55]
Discharge	0.94%	Ashcroft *et al*. (2015) [55]

**Prevalence was defined as the total number of items prescribed or dispensed with an undetected medication error divided by the total number of items prescribed. The prevalence of undetected transition medication errors was calculated from the source paper following the approach described in section 3.3.2.. The prevalence of transition medication errors at inter-hospital transfer was equivalent to the prevalence of transition medication errors at admission.*

Figure 1 summarises transition medication error rates at hospital admission and discharge, and intra- and inter-hospital transfer in the absence of any medicines reconciliation, presence of standard medicines reconciliation and addition of interoperability standards to standard medicines reconciliation.

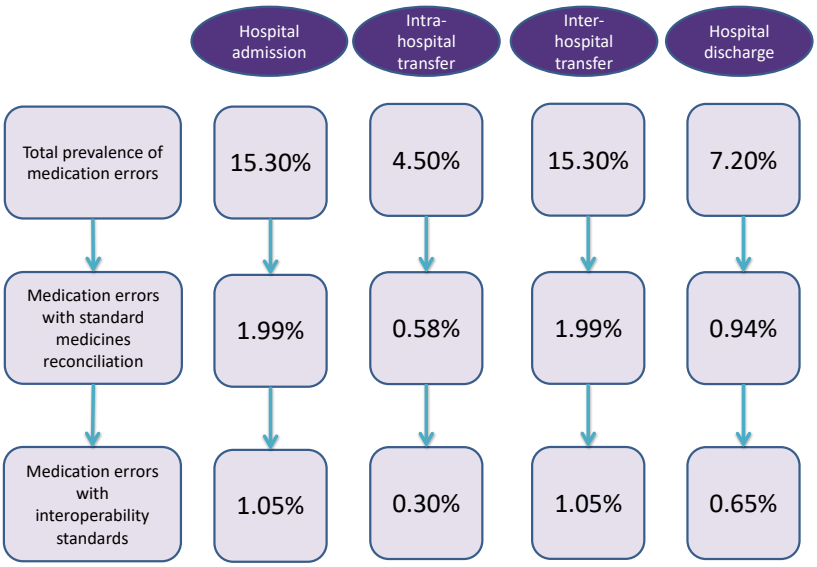

Figure 1: Prevalence of transition medication errors at key care-setting transfers for different levels of medicines reconciliation.

The estimated annual number of transition medication errors and number of patient episodes experiencing at least one transition medication error are summarised by transition in Table 2. The total annual number of transition medication errors (in the presence of standard medicines reconciliation) was estimated to affect 1,779,368 items prescribed per year. The relative contribution of each care transition was: admission to hospital (52% of all transition medication errors); discharge from hospital (44% of all transition medication errors); intra-hospital transfers (3% of all transition medication errors); and inter-hospital transfers (1% of all transition medication errors).

Table 2. Estimated annual number of transition medication errors and number of patient episodes experiencing at least one transition medication error (in the presence of standard medicines reconciliation)

	Admission	**Intra-hospital transfer**	**Inter-hospital transfer**	**Discharge**	**TOTAL**
BASE CASE MODEL*					
Number of transition medication errors	924,551	48,596	21,146	785,075	1,779,368
Number of patient episodes with at least one transition medication error	193,593	10,176	4,428	160,998	369,195
Sensitivity analysis: transition medication error rate at discharge derived from Lloyd *et al* (2021) (3.29%) [60]					
Number of transition medication errors	924,551	48,596	21,146	2,745,555	3,739,848
Number of patient episodes with at least one transition medication error	193,593	10,176	4,428	563,042	771,239
Sensitivity analysis: number of items per discharge prescription from Onatade *et al* (2017) (8.4) [68]					
Number of transition medication errors	924,551	48,596	21,146	1,352,387	2,346,680

Number of patient episodes with at least one transition medication error	193,593	10,176	4,428	160,998	369,195

**Base case model: transition medication error rate at discharge 0.94% [55]; number of items per discharge prescription 4.9 [60]*

As part of a sensitivity analysis, assuming a higher prevalence of transition medication errors at discharge (3.29% of items prescribed [60]) increased the total number of transition medication errors (3,739,848 transition medication errors) relative to the base case analysis. Similarly, assuming a higher mean number of items prescribed at discharge (8.4 items per patient [68]) increased the total number of transition medication errors (2,346,680 transition medication errors) relative to the base case analysis.

4.4.2. Estimates of transition medication error burden

The estimated burden of transition medication errors is summarised by transition in Table 3. Over a year, the total number of patient episodes estimated to experience harm from a transition medication error is 31,236, with the majority (52%) resulting from transition medication errors during admission . The transition medication errors are estimated to result in 36,099 additional bed days of inpatient care, costing around £17.43 million per year. The total number of people estimated to die from these transition medication errors is 45. The number of excess inpatient bed days could be as many as 45,539 if an alternative estimate of the duration of error-related admissions and re-admissions is used, with an estimated cost of around £20.94m. If a less conservative estimate of the proportion of transition medication errors that result in harm is used, then the number of people expected to experience harm increases to 37,659. The number of excess bed days of inpatient care for these patients is 43,521, costing £21.01 million. The number of people dying from transition medication errors increases to 54 per year.

Table 3. Estimated burden of transition medication errors

	Admission	Intra-hospital transfer	Inter-hospital transfer	Discharge	TOTAL
BASE CASE MODEL*					
Number of patients with harm from transition medication error	16,379	861	375	13,621	31,236
Excess bed days due to harm	17,558	923	402	17,216	36,099
Cost of excess bed days	£6,531,557	£343,312	£149,385	£10,404,549	£17,428,803
Deaths due to harm	30	2	1	12	45
Sensitivity analysis: length of stay due to medication error from Osanlou *et al* (2022) (6 days)[65]					
Excess bed days due to harm	26,337	1,384	602	17,216	45,539
Cost of excess bed days	£9,797,336	£514,968	£224,077	£10,404,549	£20,940,930
Sensitivity analysis: proportion of medication errors leading to harm derived from Tamblyn *et al* (2019) (10.2%)[69]					
Number of patients with harm from transition medication error	19,747	1,038	452	16,422	37,659
Excess bed days due to harm	21,168	1,113	484	20,756	43,521
Cost of excess bed days	£7,874,591	£413,904	£180,101	£12,543,956	£21,012,552
Deaths due to harm	36	2	1	15	54

**Base case model: length of stay due to error 4 days [49]; proportion of errors leading to harm 8.5% [49]*

4.4.3. Estimates of costs and benefits of ISN DAPB4013 implementation

The estimated impact of ISN DAPB4013 implementation on the number of transition medication errors is summarised by transition point in Table 4. The total number of transition medication errors is estimated to be 713,826 lower after ISN DAPB4013 is implemented, with 148,411 fewer patients experiencing at least one transition medication error. As expected, when the before ISN DAPB4013 transition medication error rate or the number of items per prescription are assumed to be higher, the benefit of implementing ISN DAPB4013 is greater.

Table 4. Estimated impact of ISN implementation on prevalence of medication errors at care transitions

	Admission	Intra-hospital transfer	Inter-hospital transfer	Discharge	TOTAL
Number of transition medication errors					
BASE CASE MODEL					
Before ISN DAPB4013	924,551	48,596	21,146	785,075	1,779,368
After ISN DAPB4013	488,486	25,676	11,172	540,207	1,065,541
Difference	-436,065	-22,920	-9,973	-244,868	-713,826

	Admission	Intra-hospital transfer	Inter-hospital transfer	Discharge	TOTAL
Sensitivity analysis: transition medication error rate at discharge derived from Lloyd *et al* (2021) (3.29%) [60]					
Before ISN DAPB4013	924,551	48,596	21,146	2,745,555	3,739,848
After ISN DAPB4013	488,486	25,676	11,172	1,889,206	2,414,540
Difference	-436,065	-22,920	-9,973	-856,348	-1,325,306
Sensitivity analysis: number of items per discharge prescription from Onatade *et al* (2017) (8.4) [68]					
Before ISN DAPB4013	924,551	48,596	21,146	1,352,387	2,346,680
After ISN DAPB4013	488,486	25,676	11,172	930,573	1,455,907
Difference	-436,065	-22,920	-9,973	-421,814	-890,772
Number of patients with at least one transition medication error					
BASE CASE MODEL					
Before ISN DAPB4013	193,593	10,176	4,428	160,998	369,195
After ISN DAPB4013	102,285	5,376	2,339	110,782	220,782
Difference	-91,308	-4,799	-2,088	-50,216	-148,411
Sensitivity analysis: transition medication error rate at discharge derived from Lloyd *et al* (2017) (3.29%) [60]					
Before ISN DAPB4013	193,593	10,176	4,428	563,042	771,239
After ISN DAPB4013	102,285	5,376	2,339	387,427	497,427
Difference	-91,308	-4,799	-2,088	-175,615	-273,810

**Base case model: transition medication error rate at discharge 0.94% [55]; number of items per discharge prescription 4.9 [60]*

The estimated annual impact of ISN DAPB4013 implementation on the burden of transition medication errors is summarised by transition point in Table 5. Implementation of ISN DAPB4013 is estimated to reduce the number of people experiencing harm from a transition medication error by 12,556, saving 14,275 of NHS bed days, £6,558,209 in associated costs, and 20 lives. Increasing the assumed length of stay for an error-related admission/readmission increases the burden of transition medication errors, with a higher cost-saving of £8,214,707 if an admission length of 6 days is assumed (compared with 4 days in the base-case model).

Table 5. Estimated annual impact of ISN DAPB4013 implementation on burden of transition medication errors at care transitions

	Admission	Intra-hospital transfer	Inter-hospital transfer	Discharge	TOTAL
Number of patients with at harm from a transition medication error					
BASE CASE MODEL					
Before ISN DAPB4013	16,379	861	375	13,621	31,236

	Admission	Intra-hospital transfer	Inter-hospital transfer	Discharge	TOTAL
After ISN DAPB4013	8,654	455	198	9,373	18,680
Difference	-7,725	-406	-177	-4,248	-12,556
Sensitivity analysis: proportion of transition medication errors leading to harm derived from Tamblyn *et al* (2019) (10.2%) [69]					
Before ISN DAPB4013	19,747	1,038	452	16,422	37,659
After ISN DAPB4013	10,433	548	239	11,300	22,520
Difference	-9,313	-490	-213	-5,122	-15,138
Excess bed days due to transition medication errors					
BASE CASE MODEL					
Before ISN DAPB4013	17,558	923	402	17,216	36,099
After ISN DAPB4013	9,277	488	212	11,846	21,823
Difference	-8,281	-435	-189	-5,370	-14,275
Sensitivity analysis: length of stay due to error from Osanlou *et al* (2022) (6 days)[65]					
Before ISN DAPB4013	26,337	1,384	602	17,216	45,539
After ISN DAPB4013	13,915	731	318	11,846	26,810
Difference	-12,422	-653	-284	-5,370	-18,729
NHS cost of excess bed days due to transition medication errors					
BASE CASE MODEL					
Before ISN DAPB4013	£6,531,557	£343,312	£149,385	£10,404,549	£17,428,803
After ISN DAPB4013	£3,450,944	£181,389	£78,927	£7,159,332	£10,870,592
Difference	-£3,080,613	-£161,923	-£70,457	-£3,245,216	-£6,558,209
Sensitivity analysis: length of stay due to transition medication error from Osanlou (6 days) *et al* (2022) [65]					
Before ISN DAPB4013	£9,797,336	£514,968	£224,077	£10,404,549	20,940,930
After ISN DAPB4013	£5,176,416	£272,083	£118,391	£7,159,332	12,726,222
Difference	-£4,620,920	-£242,885	-£105,686	-£3,245,216	-8,214,707
Deaths due to transition medication errors					
BASE CASE MODEL					
Before ISN DAPB4013	30	2	1	12	45
After ISN DAPB4013	16	1	0	8	25
Difference	-14	-1	-1	-4	-20
Sensitivity analysis: proportion of transition medication errors leading to harm derived from Tamblyn *et al* (2019) (10.2%)[69]					

	Admission	Intra-hospital transfer	Inter-hospital transfer	Discharge	TOTAL
Before ISN DAPB4013	36	2	1	15	54
After ISN DAPB4013	19	1	0	10	30
Difference	-17	-1	-1	-5	-24

**Base case model: length of stay due to transition medication error 4 days [49]; proportion of transition medication errors leading to harm 8.5% [49]*

Table 6 summarises the estimated impact on implementing ISN DAPB4013 based on the RR of the impact of interoperability reported in a meta-analysis by Mekonnen *et al* (2016) [16], applied to all transitions. The RR from the meta-analysis (0.37) was smaller than all of the transition-specific RRs used in the base case analysis (0.53-0.71). A smaller RR means that a larger impact of interoperability on reducing the number of transition medication errors is assumed.

Table 6. Estimated annual impact of ISN DAPB4013 on prevalence and burden of transition medication errors at care transitions (Numbers reported are the difference between before and after implementation of ISN DAPB4013)

Reduction in:	Admission	Intra-hospital transfer	Inter-hospital transfer	Discharge	TOTAL
BASE CASE MODEL*					
Number of transition medication errors	436,065	22,920	9,973	244,868	713,826
Number of patient episodes with at least one transition medication error	91,308	4,799	2,088	50,216	148,411
Number of patient episodes with harm from transition medication error	7,725	406	177	4,248	12,556
Excess bed days due to harm	8,281	435	189	5,370	14,275
Cost of excess bed days	£3,080,613	£161,923	£70,457	£3,245,216	£6,558,209
Deaths due to harm	14	1	1	4	20
Sensitivity analysis: RR of transition medication error from Mekonnen *et al* (2016) (0.55) [16]					
Number of transition medication errors	416,048	21,868	9,516	353,284	800,716
Number of patient episodes with at least one transition medication error	87,117	4,579	1,992	72,449	166,138
Number of patient episodes with harm from transition medication error	7,370	387	169	6,129	14,056
Excess bed days due to harm	7,901	415	181	7,747	16,244
Cost of excess bed days	£2,939,201	£154,490	£67,223	£4,682,047	£7,842,961
Deaths due to harm	14	1	0	5	20

**Base case model RRs: admission (0.53) [66], intra- and inter-hospital transfers (0.53) [66] discharge (0.69) [67]*

5. DISCUSSION

5.1. KEY FINDINGS

The total number of transition medication errors (in the presence of standard medicines reconciliation) was estimated to be 1,779,368 in England per year, with 369,195 patients experiencing at least one transition medication error. The relative contribution of each care transition was: admission to hospital (924,551 transition medication errors, 52% of all errors); discharge from hospital (785,075 transition medication errors, 44% of all transition medication errors); intra-hospital transfers (48,596 transition medication errors, 3% of all transition medication errors); and inter-hospital transfers (21,146 transition medication errors, 1% of all transition medication errors).

The estimated burden of transition medication errors is characterised by number of people experiencing harm, excess bed days, costs to the NHS and deaths. Over a year, the total number of patient episodes estimated to experience harm from a transition medication error is 31,236, with the majority (52%) resulting from admission transition medication errors. The transition medication errors are estimated to result in 36,099 additional bed days of inpatient care, costing around £17.43 million per year. The total number of people estimated to die from these transition medication errors is 45 per year.

Applying the estimated impact of widespread ISN DAPB4013 implementation on the burden of transition medication errors reduced the number of transition medication errors and the number of patient episodes with a transition medication error from 1,779,368 to 1,065,541 (a 40% reduction), and from 369,195 to 220,782, respectively. The ISN DAPB4013 implementation is estimated to result in 12,556 fewer patient episodes experiencing harm from a transition medication error, 14,275 fewer bed days of inpatient care, saving around £6.59 million per year and preventing an estimated 20 people dying from these transition medication errors.

To investigate the impact of uncertainty in the input parameter values, a series of sensitivity analyses were performed to explore the corresponding impact on the key outcomes. If the transition medication error rate at discharge is assumed to be higher than the base case value of 0.94%, at 3.29% as suggested by Lloyd *et al* (2021) [60], this increases the number of transition medication errors prevented from 713,826 to 3,739,848, and the number of patient episodes prevented from having a transition medication error increases from 220,782 to 273,810. If the proportion of transition medication errors leading to harm is assumed to be higher than the base case value of 8.5%, at 10.2% as suggested by Tamblyn *et al* (2019) [69], this increases the number of patient episodes estimated to experience harm from a transition medication error from 12,556 to 15,138 and the number of deaths avoided increases from 20 to 24. If the length of stay due to a transition medication error is assumed to be higher than the base case value of four days, at 6 days as suggested by Osanlou *et al* (2022) [65] the number of bed days avoided increases from 14,275 to 18,729, and the costs saved increases from £6,558,209 to £8,214,707. If ISN DAPB4013 implementation is assumed to be slightly more effective, using the risk ratio of 0.55 from Mekonnen *et al* (2016) [16] across all transitions instead of the base case model risk ratio for admission (0.53) [66], intra- and inter-hospital transfers (0.53) [66] discharge (0.69) [67], The ISN DAPB4013 implementation is slightly more effective, with 166,138 fewer patient episodes having an error, 14,056 fewer people estimated to experience harm from a transition medication error, 16,244 fewer bed days of inpatient care, saving around £7.84 million per year and preventing 20 people dying from these errors per year.

5.2. STRENGTHS AND LIMITATIONS

The limitations in this study stem largely from lack of data. The estimates presented here are likely to be indicative rather than definitive, due to the lack of data to inform the modelling. We have had to exclude many transitions (such as nursing homes, mental health settings, and HIV clinics) and make a wide range of assumptions, as detailed in the methods. The impact of excluding care transitions from the analysis will underestimate the benefit of interoperability solutions in the NHS. Where assumptions have been made, we have used conservative estimates. Routine data are not generally collected in this area, so estimation of transition medication errors, burden and impact of ISN implementation needed to be estimated from published studies. Sourcing appropriate studies was challenging, partly due to variability in how studies in this area can be coded in bibliographic databases, and partly due to research in this area being published in non-indexed journals, not published at all, or not being done. This has also meant that we have not been able to carry out patient-group specific analyses. To handle uncertainties in the underlying data, we have reported a base-case estimate (based on more conservative values) and sensitivity analyses (to investigate the impact of varying these values).

Key assumptions had to be made in the estimation of numbers of transition medication errors at each transition. There was a lack of relevant data around transition medication errors at hospital admission and discharge, leading to the need to estimate total transition medication errors from studies examining medication errors detected during medicines reconciliation. We found no evidence around intra- and inter-hospital transfers, or medication errors associated with these transfers, leading to indicative estimates of numbers of both. Using ward transfers as a proxy for ePMA transfers is likely to overestimate the total number of ePMA transfers. Using ambulance service data on inter-facility transfers as a proxy for interhospital transfers may have underestimated the total number of interhospital transfers if some transfers were made by other forms of transport. We also made a number of assumptions to extrapolate the transition medication error rates obtained from these studies to the NHS in England. We have not differentiated between inter-hospital transfers within a single Trust or movement to a different Trust. We did not identify any data that would enable differential transition medication error rates to be estimated for these different types of transfer. The results may underestimate the benefits accrued in primary care. The impact of transition medication errors post-discharge will often be managed in primary care leading to increased GP workload. Therefore, reduced transition medication errors from secondary care to primary care will potentially free up GP time. Future research should be performed to quantify the magnitude of this impact on primary care provider resources.

There are four key limitations on the estimates of burden of transition medication errors: (1) the assumption that avoidable ADEs correspond to medication errors, (2) generalisability of the source studies to the NHS, (3) lack of primary data to inform estimates, and (4) assumptions about the valuation of healthcare resource use associated with transition medication errors. The studies relate only to ADEs in primary care leading to hospital admissions, and ADEs in secondary care leading to longer hospital stays. There are no national datasets of these parameters to allow assessment of burden. For this reason, we have extrapolated from these observational studies of one or two hospital trusts, and therefore assume that these data are representative of the national picture.

Given the paucity of data directly linking transition medication errors to outcomes and costs, we cannot make conclusions about the harm associated with transition medication errors directly. Therefore, we based our estimates on UK observational data of healthcare resources used to treat ADEs, as reported in the source studies. The source studies used published criteria to identify what proportion of all ADEs observed were avoidable. Notwithstanding the limitations of this approach, as described above, we have assumed that the occurrence of avoidable ADEs and their associated burden and cost, can be used to approximate the burden and cost of harm from transition medication errors. The final assumption is the unit costs attached to the burden reported in the

studies, primarily costs associated with unplanned hospitalisations and extended inpatient stays. We have used publicly available databases of prices which is necessarily an approximation of real costs incurred.

We required estimates of effectiveness at each of the transitions under investigation. This is because transition medication errors at admission, or intra/inter-hospital transfer are likely to have an impact on that hospitalisation episode (parameterised in this study as increase in length of stay and deaths), whereas transition medication errors at discharge are likely to have an impact on harm post-discharge, which was parameterised in this study as hospital readmissions, associated increase in bed-days and deaths. This approach may have underestimated the number of readmissions if there is a time lag between medication errors at admission or intra/inter-hospital transfer and harm caused by these medication errors after discharge. Also, we have no information on impact on primary care and community pharmacy services. Most studies examine adding interoperability solutions at hospital discharge, or at some undefined time during admission. In addition, there are significant inconsistencies in the operational definition and application of the medication reconciliation process in reviewed studies.[120] We were unable to find many UK-based studies around effectiveness of adding interoperability solutions to existing standard medicines reconciliation practices, so we have had to use studies from other settings. We selected studies with low risk of bias, with interventions relevant to a UK setting and clear unambiguous reporting of relevant primary outcomes [66, 67]. We found no studies examining effectiveness of intra/inter-hospital transfer, so were required to either exclude these transitions or to assume that effectiveness estimates from studies on transition errors at admission could be used, and we decided on the latter. In terms of the opportunity for transition medication errors in the transmission of prescription information when someone moves to a new ward or hospital, this may be additive (i.e. discharge prescription from initial ward/hospital followed by recording of prescriptions on new admission), so our estimate may be conservative.

Zoni *et al* (2012) [66] reported number of proportion of medications prescribed with an unintended discrepancy before and after the implementation of an interoperable intervention at hospital admission. This study was based in a hospital in Spain and only included people who were prescribed 3 or more drugs prior to admission therefore may not be fully representative of the general population in England. For transition medication errors following discharge from an inpatient admission, the impact of interoperability was derived from a study by Smith *et al* (2016) [67]. The paper reports the number of items prescribed with a transition medication error before and after the implementation of an interoperable intervention. Like the study by Zoni *et al* (2012), this study also only included more complex patients, this time those who were prescribed five or more medications prior to admission. The Smith analysis was based in a hospital in the US which may also limit generalisability to the population in England. We tested the impact of using these estimates through a sensitivity analysis with a meta-analysis carried out in this area that was not considered robust enough for the base-case analysis [16]. It should be noted that the confidence intervals around effectiveness point estimates for Zoni *et al* (2012), [66] (individual study estimate of effect) and Mekonnen *et al* (2016) [16] (meta-analysis estimate of effect) are very wide, reflecting the high degree of uncertainty around effectiveness in this area. This uncertainty in the published evidence includes the possibility of no added effect compared with standard medicines reconciliation practices. Further investigation into the effectiveness of applying interoperability standards compared with standard medicines reconciliation without interoperability in the NHS context would be valuable.

We were not able to control for the effect of the use of the SCR as part of the medicines reconciliation process. The SCR can be seen and used by authorised staff in other areas of the health and care system involved in the patient's direct care, but the information still needs to be manually transferred from one digital system to another. However, evidence suggests its use reduces time taken to carry out medicines reconciliation [34] and support improved detection of medication discrepancies[35].

Over half of the effect of medicines reconciliation on reducing potential transition medication errors occurs on admission to hospital, but most research available focuses on the number of transition medication errors at discharge, or at some undefined time between admission and discharge. This may be due to the greater ease with which discharge transition medication errors can be identified. Some studies combine reconciliation at admission and discharge, so identifying effects separately at admission (ie impact on that hospital stay) and discharge (ie impact on readmission, ED visits) had to be carefully identified. One example of this is Liu *et al* (2019), a Taiwanese study that measured potentially inappropriate medicines before and after electronic medicines reconciliation was introduced, both at admission and discharge [121]. Pre-intervention, potentially inappropriate medicines were reduced from 173 on admission to 88 (49%) at discharge. Post-intervention, potentially inappropriate medicines were reduced from 480 on admission to 156 (67.5%) at discharge. This study (or service) design does not allow assessment of the time from admission that the medicines reconciliation is caried out, and it is likely that swift medicines reconciliation close to admission can prevent transition medication errors that could cause harm during the admission. Performing medicines reconciliation earlier in the admissions process is a key operational factor in harms reduction. Liu *et al* (2012), also demonstrates that the comparator can have an important impact on effect size of the electronic medicines reconciliation intervention, as whilst digitally-enhanced medicines reconciliation improved transition medication errors more ($p<0.001$), there was still a substantial improvement with standard medicines reconciliation.

The real picture in English hospitals is also very much more complex than this. It is anticipated that all English hospitals will have ePMA in place for inpatients by the end of 2023, which will allow a degree of linkage with hospital pharmacy dispensing systems, other hospitals and primary care. The extent to which different Trusts have any, separate or integration of this standard inpatient ePMA with ePMA for ED, ICU, theatres and other specific specialist services is less clear, and is likely to be different across different Trusts. Provision of standard medicines reconciliation is variable across English hospitals, so the baseline transition medication error rates in individual trusts may be higher or lower than the single measure used in our work.

5.3. COMPARISON WITH PUBLISHED ESTIMATES OF MEDICATION ERROR PREVALENCE AND BURDEN

We are not aware of another published estimate of numbers and burden of transition medication errors. We have restricted our primary estimate to definitely avoidable ADEs, which is likely to have had a significant effect on our estimates. In 2007, the NPSA estimated NHS costs of preventable medication errors to be £774 million, at 2005/6 prices (£954 million at 2015/16 prices) [29, 30]. They used a hospital admissions rate due to definitely or probably preventable ADEs. In our subsequent work, we used a hospital admissions rate due to definitely preventable ADEs only which gave estimated NHS costs of preventable medication errors to be £98 million, at 2015/16 prices [2] .This suggests that a broader definition of avoidability could increase our estimates up to ten-fold. However, if this broader definition of avoidability is used, then it should be noted that widespread adoption of ISN DAPB4013 would only prevent a subset of these transition medication errors.

5.4. RECOMMENDATIONS

Our key recommendations are:

- The ability of interoperability solutions to support more responsive and timely medicines reconciliation during admission or transfers requires service expansion and reconfiguration.

- We need UK data on the proportion of patients undergoing medicines reconciliation, how long after care transfer this occurs, and patient risk factors for transition medication errors allowing targeting of high-risk patients, such as polypharmacy.
- We need to measure transition medication error prevalence, including at inter- and intra- hospital transfer, both prior to, and after, ISN DAPB4013 implementation to assess the impact on transition medication errors, medicines reconciliation capacity, and health care professional confidence in decision-making.

We also recommend a more explicit role for patients, carers and families in these developments to improve medication safety in transitions of care**.**

The WHO highlighted the need to improve medication safety in transitions of care through not just improving information quality and availability, but also through leadership, structures, medicines reconciliation capacity and capability, and patient partnership [5]. Medicines reconciliation services are time-consuming and costly. It is likely that, given limited capacity, that medicines reconciliation is provided variably between acute hospital settings, and also variably within the time-span of an admission. Patients who are subject to longer lengths of stay may be more likely to be captured by a medicines reconciliation service. A patient who is admitted as an emergency to A&E overnight, transferred to a ward the next day, and discharged that evening is much less likely to be captured by a medicines reconciliation service. It is not clear to what extent medicines reconciliation occurs reliably at admission, less than 24 hours after admission, during an intra or interhospital transfer, or just at some point prior to discharge. Access to correct medicines history at admission of an acutely ill patient could have a significant impact on quality of care and health outcomes, because interoperability solutions do not operate in a vacuum, and require a health care professional to be already undertaking medicines reconciliation so that they can realise the added benefit of that interoperability solution. The existence of ISN DAPB4013 alone is not sufficient to deliver benefits to patients. Rather, the widespread adoption and active use of ISN DAPB4013 across the NHS will be pivotal to realising the benefits of interoperability. A recent report by the King's Fund describes the steps needed to help interoperability improve patient care[122]. Fundamental to this is the need for positive working relationships between staff and care leaders, and an enabling environment which aligns capacity for change, skills development for the NHS workforce, and information governance. It is likely that the introduction of interoperability solutions, through making medicines reconciliation quicker and higher quality, will also allow more medicines reconciliation episodes to be done overall. This further impact on the reduction of transition medication errors has not been taken account of in our estimates, and the results should be interpreted in that context. The ability of interoperability solutions to support more responsive and timely medicines reconciliation during admission or transfers requires service expansion and reconfiguration. Development and resourcing of hybrid digital/clinical roles to inform technology solution design and implementation is required to realise these benefits.

A more explicit role for patients, carers and families is essential to improve medication safety in transitions of care. The WHO recommends 'partnering between patients, families, caregivers and health care professionals to agree on treatment plans, ensure patients are equipped to manage their medications safely, and ensure patients have an up-todate medication list' [5]. There have been many attempts to include patients in electronic discharge[123-125], and WHO has developed a free 'Medsafe' app (https://www.iapo.org.uk/news/2019/jul/18/who-medsafe-app) to support patients holding an up-to-date medicines record.

We know that current self-reporting systems (National Reporting and Learning System, NRLS) are thought to detect only 7-15% of all incidents including medication errors [126]. Continuing to change cultures to remove personal blame may improve self-reporting figures and allow systems to be improved.

UK-based studies are needed examining the proportion of patients undergoing medicines reconciliation, how long from admission this occurs, and patient risk factors (such as polypharmacy, high risk conditions and medicines). Audits need to be carried out to measure the number of transition medication errors including at inter- and intra-hospital transfer. These data are needed both prior to and after ISN DAPB4013 implementation to be able to assess the impact on both transition medication errors and medicines reconciliation capacity.

5.5. CONCLUSION

Medication transition errors persist despite standard medicines reconciliation, and the improved interoperability from planned ISN DAPB4013 implementation will substantially reduce transition medication error prevalence, and associated harm and cost. These estimates relate to transition medication errors occurring at hospital admission or discharge, and intra-hospital or inter-hospital transfer. Due to lack of direct data on the burden of transition medication error to the NHS, we assumed that definitely avoidable ADEs are a proxy for medication error. Given the quality of the data available, there is a high level of uncertainty around presented estimates of benefit. We have had to exclude many transitions and use conservative parameter estimates so these estimates presented might be lower than the real impact on medication transition error rates, and associated effectiveness of ISN DAPB4013 implementation.

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