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How Safe is Primary Care? A Systematic Review

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ABSTRACT

Importance: Improving patient safety is at the forefront of policy and practice. While considerable progress has been made in understanding the frequency, causes, and consequences of error in hospitals, less is known about the safety of primary care.

Objective: We investigated how often patient safety incidents occur in primary care and how often these were associated with patient harm.

Evidence Review: We searched 18 databases and contacted international experts to identify published and unpublished studies available between January 1, 1980 and July 31, 2014. Patient safety incidents of any type were eligible. Eligible studies were critically appraised using validated instruments and data were descriptively and narratively synthesized.

Findings: Nine systematic reviews and 100 primary studies were included. Studies reported between <1 and 24 patient safety incidents per 100 consultations. The median from population-based record review studies was 2 to 3 incidents for every 100 consultations / records reviewed. It was estimated that around 4% of these incidents may be associated with severe harm, defined as significantly impacting on a patient's wellbeing, including long-term physical or psychological issues or death (range <1% to 44% of incidents). Incidents relating to diagnosis and prescribing were most likely to result in severe harm.

Conclusions and Relevance: Millions of people throughout the world use primary care services on any given day. This review suggests that safety incidents are relatively common, but most do not result in serious harm that reaches the patient. Diagnostic and prescribing incidents are the most likely to result in avoidable harm.

Systematic Review Registration: This systematic review is registered with the International Prospective Register of Systematic Reviews (PROSPERO CRD42012002304).

INTRODUCTION

Health services strive to provide good quality care, but sometimes people are inadvertently harmed.[1] Between 3% and 17% of people admitted to hospital may experience a safety incident,[1-6] and it is commonly reported that about 10% of hospitalized patients may experience harm.[7-9] Over the last two decades, a substantial body of work has been undertaken to understand the reasons that patient safety incidents occur in hospitals and the effectiveness of interventions to avoid and reduce the impact of such incidents.[10-15] Far less is known about the nature, causes or consequences of incidents in primary care.[16] This may be due to many factors, including the assumption that primary care is safer than hospital care, because primary care is in the early stages of development in some parts of the world, and because primary care medical records may not always be easily accessible, thus making it difficult to study patient safety incidents.

An important first step in preventing harm in primary care is to understand how often patient safety incidents occur, what type of incidents occur, and what impact they have. This is particularly important given the drive for universal access, which is predicated on enhanced provision of primary care.[17, 18] The global drive towards primary care-based models of care has been supported by the World Health Organization (WHO) in low- and middle-income countries and economic pressures in industrialized nations. This is particularly true in the US, which is expanding primary care through the creation of Accountable Care Organizations (ACOs) and Patient-Centered Medical Homes (PCMH). It is important to understand how this expansion can proceed in a safe, sustainable manner. We were commissioned by WHO to investigate the frequency of patient safety incidents in primary care and the resulting harm in order to set the scene for deliberations on how to prevent incidents and minimize their impact.

METHODS

This systematic review of published and unpublished literature was conducted according to PRISMA guidelines.[19] Our review is registered with the PROSPERO database (PROSPERO CRD42012002304). We provide a summary of our methods below. Readers are referred to full details about the methodology which are freely available online, including as part of the online supplement.[20]

Inclusion and Exclusion Criteria

Studies were eligible for inclusion if they were systematic reviews or primary research conducted in humans and focused on patient safety incidents in primary care. Box 1 outlines how we defined primary care, safety incidents, severity of harm, and other key terms. We were interested in studies that included data about one or more of the following:

1. Number of safety incidents
2. Type of safety incidents
3. Severity of harm associated with safety incidents

Primary care varies widely between and within countries so our search strategy covered a broad range of care delivered outside hospital.[21-27] However, for the purposes of this article, we focused on studies describing models of care that were comparable with US notions of primary care and incidents of commission rather than omission (see Box 1 for definitions). A broader range of studies were identified on topics such as community pharmacy, but these have not been summarized here. Similarly, studies with a broad 'ambulatory care' focus were not included if these combined settings such as hospital, outpatients and primary care. Only studies with a primary care focus were included where that focus could be ascertained from the title and from the abstract.

Studies that aimed to test an intervention and collected safety data incidentally were not included, because the aim was to investigate the frequency of safety incidents and harm in routine practice, not when an intervention was undertaken.

Published and unpublished research available between January 1, 1980 and July 31, 2014 was eligible. Eligible study types were 1) systematic reviews; 2) primary studies not included in the reviews; and 3) primary studies included in the reviews only if they contained empirical data to feed into the calculation of specific estimates of harm that were not available in the reviews themselves (33 studies). Non-systematic reviews, case series, or case reports were not eligible for inclusion and nor were studies included in other systematic reviews that did not contain exact rates of harms for use in our calculations

Box 1: Definitions of terms used in the review

Harm – no harm, low harm, moderate harm and severe harm

Harm was defined as impairing the structure or function of the body or mind. This may include pain, nausea, psychological distress, disability, or death. The criteria used in individual studies included in the review were extracted but we standardized the descriptors of harm based on methods suggested by the United Kingdom's (UK) National Patient Safety Agency:[35]

- No harm: any patient safety incident that had the potential to cause harm but was prevented, resulting in no harm, or that ran to completion but no harm occurred
- Low harm: required extra observation or minor treatment and caused minimal harm
- Moderate harm: resulted in a moderate increase in treatment and caused significant but not permanent harm (an example would be hospitalization)
- Severe harm: resulted in permanent harm such as disability, death, or long-lasting physical or mental consequences

Incidents of commission

Incidents of commission were defined as those occurring when something was actively done incorrectly or inappropriately, such as prescribing the wrong dose of medication.

Incidents of omission

Incidents of omission were defined as those occurring when there was a lapse in the quality of care. Such incidents were outside the scope of the review.

Patient safety incidents

Patient safety incidents were defined as any unintended or unexpected incident(s) that could have or were judged to have led to patient harm. 'Patient safety incident' is an umbrella term which is used to describe a single incident or a series of incidents that occur over time. The LINNAEUS taxonomy is a primary care patient safety classification system that categorizes incidents into 'Process incidents' or 'Knowledge or skill incidents' and then further divides these into sub-categories.[34] This taxonomy was used as an initial coding framework to group studies based on their primary focus of investigation. Studies including incidents that could not be classified in this way were categorized as 'Other.'

Primary care

Primary care was defined as 'first port of call' generalist care, delivered outside hospital inpatient settings. Although in some countries primary care includes, for example, community nursing and community pharmacy in addition to family practice clinics, for the purposes of this review we used the following definition of the US primary care workforce: "…includes the specialties of family practice, general practice, general internal medicine, and general paediatrics and, for women patients, obstetricians and gynaecologists."[35]

Search Strategy and Study Selection

Search terms were developed based on an international taxonomy for patient safety and previous work.[28-34, 36] Our search terms are available via the online supplement.[20]

Eighteen databases containing published and unpublished literature were searched, including: African Index Medicus, African Journals Online, Bioline International, CINAHL, Embase, IndMED, HINARI, Iran MEDEX, Korean MED, Latin American and Caribbean Health Sciences, Medline, NepJOL, PsycINFO, Thai Index Medicus, WHOLIS, Google Scholar, SIGLE. The final three databases in this list include gray literature. We also searched 'The Grey Literature Report' (http://www.greylit.org/). We also searched AHRQ Patient Safety Network (http://www.psnet.arhq.gov) which is a patient safety literature clearing house. WHO invited an international panel of primary care clinicians and policy-makers to identify additional published and unpublished studies. Further material was sought using the bibliographies of identified papers and by contacting experts through WHO's six regional offices.

Where primary studies appeared in the systematic reviews that met our inclusion criteria, these were not analysed separately.

Studies identified as potentially suitable were assessed for inclusion by two independent reviewers (SSP and AC-S), with arbitration by a third reviewer (AS), if necessary. The full text of all papers was rescreened by a third reviewer (DdS) when revising the manuscript.

Quality Assessment

Studies were quality appraised to assess internal and external validity[37] using the Critical Appraisal Skills Programme (CASP) for systematic reviews[38] and the Evidence Based Library and Information Practice (EBLIP) Critical Appraisal Checklist for epidemiologic studies.[39] An

overall grading of the individual components was given for each study. Quality appraisal was independently carried out by two reviewers (SSP and AC-S, or KC and SAS). Disagreements were resolved through discussion, with arbitration by an additional reviewer, if necessary (AS).

Data Extraction and Synthesis

Preliminary data were abstracted onto a customized data extraction sheet by two independent reviewers (SSP and AC-S, or KC and SAS), with arbitration by an additional reviewer if necessary (AS). Data were then re-extracted by a third reviewer (DdS) about country of origin; study design; measurement methods; frequencies of patient safety incidents, and burden of harm.

There was significant heterogeneity in the countries of origin, research methods used, type of safety incidents analyzed and metrics so it was not appropriate to combine the data using meta-analysis. A descriptive and narrative synthesis of the data was undertaken. The frequency of incidents and harm were tabulated and graphed. Median incident rates were calculated based on population-based record review studies.

This review does not aim to provide a definitive summary statistic for the frequency of incidents, but rather to show the range in estimates. The rate of per 100 consultations / people / prescriptions was either drawn directly from articles or calculated from data provided in the articles. For example, if articles provided a percentage, we reframed this as a rate out of 100. Equally, if articles provided a numerator and denominator, we converted this to a denominator of 100, if appropriate. This does not allow exact comparability because the unit of measurement differed between studies (people / prescriptions / consultations), but provides a summary of broad trends.

FINDINGS

Number, Type, and Setting of Studies Included

We screened 61,521 articles and 109 studies met our inclusion criteria: nine systematic reviews and 100 primary studies (see Figure 1). Eighty-eight percent of the systematic reviews (8/9) and 12% of the primary studies (12/100) were judged to be of high quality.

Thirty-six percent of studies were from the US or Canada (39/109), 39% were from Europe (43/109), 13% were from other Organization for Economic Co-operation and Development (OECD) countries (14/109), and 12% were from non-OECD countries (13/109). All studies focused on primary care / family practice / general practice clinics (or aggregated data drawn from these services). Most studies used record review or prescription review to measure safety incidents so they were using an epidemiologic measurement approach. A minority used incident reporting systems and very few used interviews or surveys. The online supplement provides a summary of the characteristics, methods and findings of each study.[20]

Frequency of Patient Safety Incidents in Primary Care

Fifty-nine studies (some of which were reported in more than one paper) provided an estimate of the frequency of patient safety incidents (see Table 1 in the online supplement). Twelve studies collating 'any type of patient safety incident' reported between <1 and 24 incidents per 100 consultations (see Figure 2). Most of the studies reporting incident rates were not of high quality, though most involved record review or review of prescriptions. Coupled with the large variation in estimates, this means that we cannot confidently state the rate of patient safety incidents in primary care. However, the median of studies based on record review was 2 to 3 incidents per 100 consultations / patient records reviewed.

Types of Safety Incidents

Studies documenting the type of safety incidents identified that the three most common categories were: administrative and communication incidents; diagnostic incidents; and prescribing and medication management incidents. Although some studies defined 'communication issues' as safety incidents, the majority of these incidents did not result in harm. The severity of harm associated with incidents is described below.

It is outside the scope of this review to comment about all the types of incidents and their relative frequency, but we provide some broad ranges to show the variation in research. For instance, the proportion of incidents relating to administrative and communication issues ranged between 6% and 67% of all incidents in individual studies.[40-49] Some studies estimated that administration incidents occurred in at least 6% of patient contacts.[50] Most of these incidents related to issues such as incomplete, unavailable, unclear or incorrect documentation;[7, 34, 51, 52] inappropriate monitoring of laboratory tests;[53] or insufficient communication between providers or between professionals and patients.[54]

Studies of incident reporting systems suggest diagnostic incidents were responsible for 4% to 45% of all reported patient safety related incidents.[51, 54, 55] Common diagnostic incidents related to misdiagnosis or missed diagnoses.

Thirty-five studies focused explicitly on prescribing incidents, where the rate was between 1 and 90 out of 100 prescriptions issued (see Table 2 in the online supplement). The figures were higher in studies that focused on particular subgroups, such as the elderly or those taking multiple medications.[56-59] It was difficult to compare these studies because they used different measurement approaches and focused on specific patient populations.

Estimates of the rate of dispensing incidents in primary care also varied widely, from less than 2% of prescriptions[51, 60-64] to up to 65%.[52] These variations are likely to reflect the different definitions used (such as whether or not 'not specifying the route of administration' was listed as an incident),[65] study designs,[51, 54, 67, 68] and focusing on certain sub-sets of patients such as those receiving psychotropic medications,[69] those with poly-pharmacy,[57] or those in care homes.[59]

Results varied depending on whether the studies were high or lower quality. For example, a systematic review found that retrospective studies yielded a lower estimate of adverse drug events (3%),[70] compared with prospective evaluations (10%).[71] Therefore, as with the overall rate of safety incidents, it is not possible to draw firm conclusions about the rate of consultations or people who experience diagnosis, communication, or medication incidents, but we can say that these three broad categories made up the bulk of incidents recorded.

Harm Associated with Patient Safety Related Incidents

Although patient safety incidents may be relatively common in primary care, many incidents did not result in actual harm. For instance, 'safety incidents' may include illegible handwriting on prescriptions, even if such incidents do not ultimately impact on wellbeing. The definition of 'safety incidents' often included processes rather than direct patient impacts.

As with estimates of the quantity and type of incidents in primary care, estimates of harm also varied widely. Table 3 (in the online supplement) lists the severity of harm recorded in 33 individual studies. Many of these studies reviewed incident reports. Serious incidents may be more likely to have been reported, so these studies probably over-estimated the severity of harm. Figure 3 illustrates the range of estimates from record review studies only. These types of studies are more likely to give a representative picture because they do not rely on incident

reports or significant event analysis. Studies based on record review had a median estimate of 4% of incidents being associated with severe harm, defined as significantly impacting on a patient's wellbeing, including long-term physical or psychological issues or death (range <1% to 44%).

Incidents Associated with Harm

Diagnostic and medication-related incidents were most commonly associated with harm to patients. For example, one study found that 58% of reported misdiagnoses were associated with harm (severity not described).[54] Between 8%[72] and 11%[73] of medication incidents were reported to result in harm (of any severity). These proportions varied depending on the population studied, research design, and outcome of interest. Results also varied depending on whether the studies were high or lower quality; however, the exact proportions are perhaps less important than the fact that it was diagnostic and prescribing errors that were associated with most severe harm.

DISCUSSION

Statement of Principal Findings

This extensive review suggests that patient safety incidents are a relatively frequent occurrence in primary care, but that most do not result in significant harm to patients. The heterogeneity of studies means that it is not possible to provide a point estimate of the frequency of incidents, but record review studies suggested a median of around 2 to 3 incidents per 100 consultations / patient records reviewed. About 4% of these incidents were associated with severe harm (median of record review studies). Diagnostic and medication incidents were most likely to result in harm and most likely to result in severe harm.

Strengths and Limitations

This is the most comprehensive synthesis of the evidence available about patient safety incidents in primary care. Our search strategy was broad and looked for published and unpublished studies, with particular effort made to identify research from low- and middle-income country settings (though few studies were found).

The review provides, for the first time, a comprehensive assessment of how common patient safety incidents are in core primary care contexts and how frequently these are associated with harm. When these estimates are considered in light of data about the high rates of use of primary care services,[74] the absolute burden of iatrogenic harm may be large and may increase if primary care expansion continues in a similar fashion to the current models of care.

Understanding the epidemiology of errors in primary care contexts is crucial to baselining, understanding risk factors, and ultimately developing and evaluating strategies to reduce the risk of iatrogenic harm. We have provided a baseline from which to work.

We have also identified some key methodological insights that need to be considered when planning future epidemiological studies. Key amongst these are the need for multi-stakeholder perspectives, validated tools, and longitudinal study designs in representative populations, with boosted samples in high-risk patients (e.g. those with multi-morbidity and/or poly-pharmacy).

An important issue is whether the findings of the review represent 'typical' primary care practice. To assist this we limited the review to studies focusing on primary care clinics similar to those run in a US context (rather than a wider definition of primary care as may be common in some parts of the world), but this means that other primary care contexts were excluded. It was sometimes differentiate studies for inclusion because they contained a mix of primary care and other care or because the definition and scope of ambulatory care was not included in papers.

A major limitation is that there is no widely used standardized taxonomy for classifying incidents in primary care settings.[8,75,76] This means that studies defined and measured incidents differently, resulting in variations in the estimated proportion of incidents and harms. Higher quality studies, those with a broad population focus, and those based on record review were more likely to have lower estimates of the frequency and severity of harm. Relationships between country, data quality, setting, and severe harm deserve further attention.

Most studies used a single method to assess the frequency of incidents, rather than a triangulation of approaches. This may under-estimate the frequency of incidents. The primary care record systems used to record incidents may also be open to coding errors.

As with all systematic reviews, publication bias may be present, whereby certain types of studies may be more likely to be published. We sought to address this by searching extensively for unpublished literature and by sense-checking findings with international experts. The large variability of findings suggests that our results were not unduly tarnished by only the highest levels of incidents or harms being reported. The variability of estimates remained regardless of whether studies were rated as high or low quality.

Our graphical representation of the severity of harm is based on studies that reviewed records, rather than relying on incident reports. This is because incident reports may be less likely to capture incidents that have low severity and people may be more likely to report some types of incidents than others. Studies of malpractice claims may be particularly open to bias so we excluded these when reporting median rates.

Recommendations for Policy, Practice, and Future Research

Patient safety is high on the policy radar when developing and rolling-out new models of primary care (e.g. PCMHs). But these 'solutions' can introduce new risks which need to be proactively identified. For example, health information technology (HIT) has been seen as an important solution to enhancing safety, but it is now appreciated that such technology can also introduce some new risks.[77] Having standardized methods to identify and quantify these risks is essential.

Key implications of this review include the need to develop a standardized set of definitions of core terminology, the need to promote mixed-methods evaluations that triangulate different sources of evidence, and a particular focus on diagnostic and medication errors, which appear to be most frequently associated with severe patient harm. There is also a need to better identify those at greatest risk of experiencing patient safety incidents and the nature of the incidents that occur, because such insights will be crucial to developing interventions to decrease the burden of iatrogenic harm.

A standardized taxonomy for classifying incidents and harm would allow comparisons across settings, countries, and over time. Longitudinal, multi-methods investigations would provide more insight into the extent of harm associated with different types of error. More in-depth analysis into particular areas of high risk is warranted, in particular people with multiple long-term conditions and associated poly-pharmacy. The paucity of evidence about low- and middle-income countries highlights the need for more work to understand the nature of incidents and the opportunities for prevention in these resource-scarce contexts.

The estimated proportion of patient safety incidents in primary care is generally lower than the estimated 10% of people who experience events in hospital,[9,78] but primary care and hospital encounters are not easily comparable because hospitalized patients experience multiple clinical encounters during a single admission. Furthermore, the overall volume of people using primary care is substantially higher than those using hospital services in many parts of the world, so even if incidents occur in a lower proportion of visits, this translates into a considerable burden of potential harm, though most is not severe.[79] However, incidents occur in all care settings so this finding is only useful if it prompts policy-makers and clinicians to do something about it.[80] Better prediction tools and more experimental studies are needed to understand which incidents we can avoid, and how best to do so.

It is important to consider whether adverse drug events and similar are 'incidents' if the medication was correctly prescribed, dispensed, and monitored. In this review, all incidents were counted, as it was not possible to distinguish 'correct' prescribing from individual studies. However, it may be more useful to consider whether incidents are preventable versus a result of proper care. Research has attempted to determine what proportion of safety incidents may be preventable. Most studies of this type relate to prescribing and medication management incidents,[53, 69, 78, 81, 82] and use observational cross-sectional designs, so it can be challenging to interpret the estimates. A small number of more robust before-and-after studies and randomized controlled trials have found that up to half of all incidents may be preventable using interventions such as pharmacist-led medication review, computerized physician order entry (CPOE) and computerized decision support (CDS) systems, error alert systems, and education of professionals.[83-91]

Conclusions

Primary care services are expanding globally, providing a first port of call to millions of people every day.[18] Universal access to healthcare remains firmly on the agenda of policy-makers however, these services are not without potential harms. This review has suggested major gaps in the evidence base which now need to be filled. WHO's forthcoming roadmap on *Safer Primary Care for All* will explore the most effective ways to prevent incidents, particularly those most likely to cause serious harm.

To further support this journey, there is a need for researchers to use existing well-developed definitions, taxonomies, and tools, such as the NPSA definition and the Linnaeus taxonomy,[35,92] to allow greater comparability between studies and research contexts. There is also a need for better quality epidemiological studies, but the review shows that focusing on diagnostic and prescribing errors – which are the most frequent and hence important sources of significant iatrogenic harm – needs to be a priority for research and policy.[93,94]

FIGURE LEGENDS

Figure 1: PRISMA diagram of studies included in the review

Figure 2: Safety incidents per 100 primary care consultations / records – results from 12 studies

Figure 3: Proportion of safety incidents in primary care resulting in severe harm – results from 7 studies based on record review

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Transparency declaration

Contributorship:

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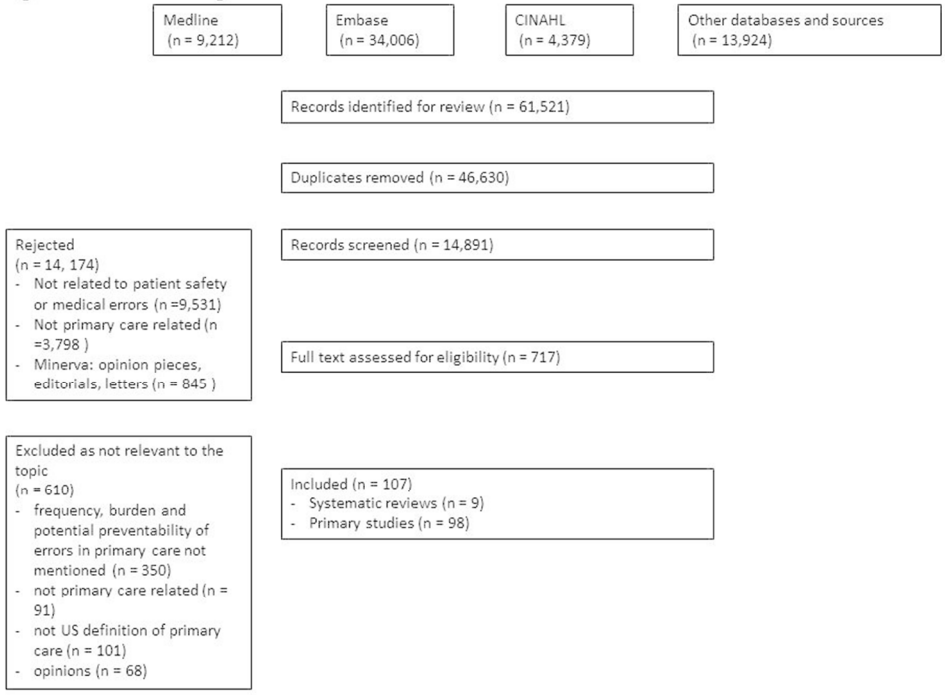
Figure 1: PRISMA diagram of studies included in the review



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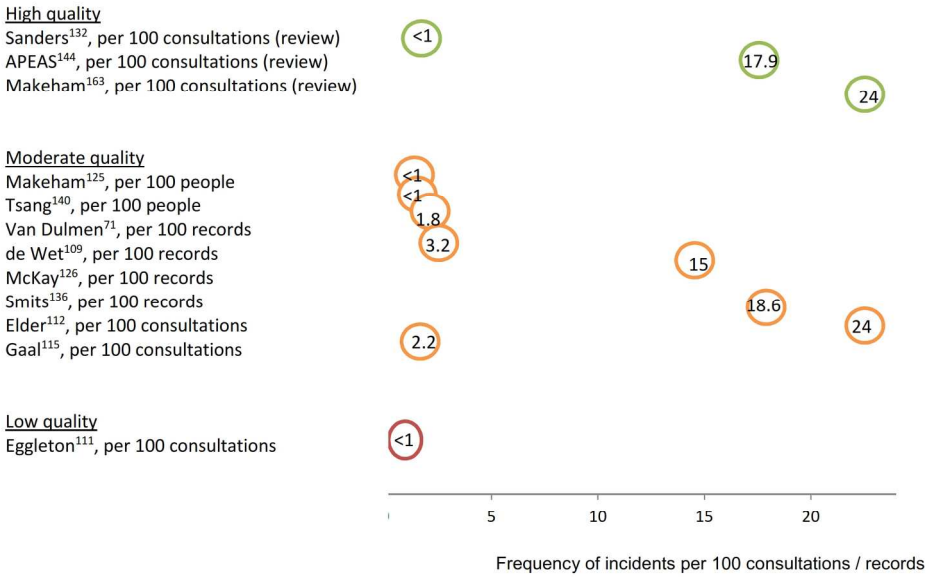

Note: the rate per 100 consultations, records, or people is provided as specified in the text next to the study (consultations / records / people). Details of the first author are provided to allow cross-checking to the study details in the online supplement. All studies were observational unless listed as a review. The quality rating is based on validated scales.

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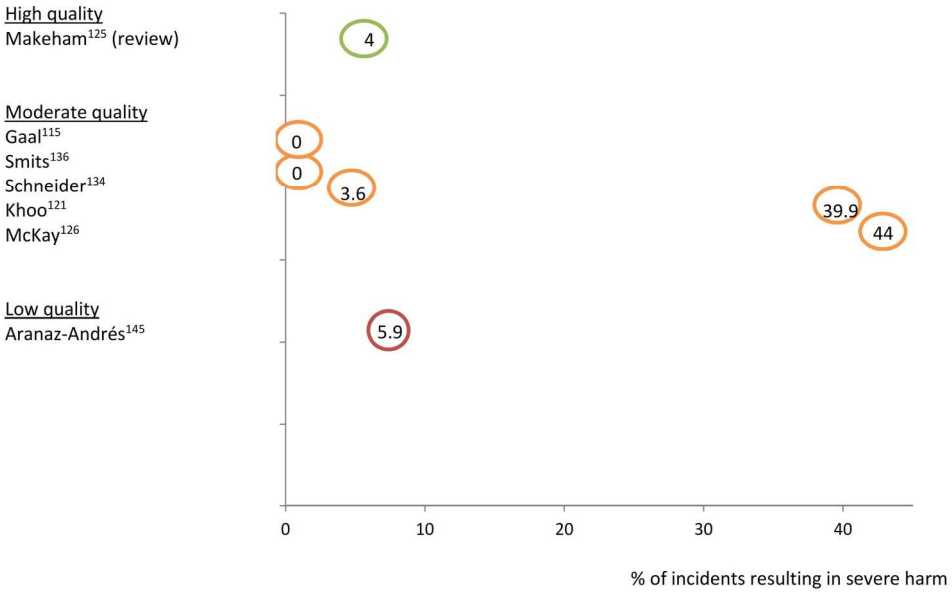

Note: Details of the first author are provided to allow cross-checking to the individual study details in the online supplement. All studies were observational unless listed as a review. The quality rating is based on validated scales.

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How Safe is Primary Care? A Systematic Review

ONLINE SUPPLEMENT: TABLES

Table 1: Summary of studies about frequency of safety incidents in primary care

Author	Study type	Number analyzed	Region	Type of incidents	Rate	Study quality
Bregnhoj L 2007[106]	Observational	1621	OECD	Prescribing / medication	39.5 per 100 medicines	High
Gurwitz JH 2003[117]	Observational	30397	OECD	Prescribing / medication	5 per 100 people	High
Honigman B 2001[66]	Observational	25056	OECD	Prescribing / medication	5.5 per 100 people	High
Lund BC 2010[125]	Observational	236	OECD	Prescribing / medication	14.4 per 100 people	High
Olaniyan JO 2014[82]	Systematic review	33	OECD	Prescribing / medication	1 to 90 out of 100 prescriptions	High
Sandars J 2003[133]	Systematic review	280	OECD	Prescribing / medication	11 per 100 prescriptions	High
Tsang C 2012[140]	Systematic review	15	OECD	Prescribing / medication	0.49 per 100 people aged 65+	High
Abramson 2012[95]	Observational	9385	OECD	Prescribing / medication	36.7 per 100 prescriptions	Moderate
Al Khaja KA 2011[81]	Observational	2773	Other	Prescribing / medication	26.4 per 100 prescriptions	Moderate
Al Khaja KAJ 2007[65,98]	Observational	2282	Other	Prescribing / medication	90.5 per 100 prescriptions	Moderate
Al Khaja KAJ 2010[99]	Observational	86	Other	Prescribing / medication	87.2 per 100 prescriptions	Moderate
Avery AJ 2013[103]	Observational	6048	OECD	Prescribing / medication	4.9 per 100 prescribed items	Moderate
Bradbury F 2004[104]	Observational	8830	OECD	Prescribing / medication	16.6 per 100 people	Moderate
Bradley MC 2012[105]	Observational	166108	OECD	Prescribing / medication	34 per 100 people	Moderate
Brekke M 2008[107]	Observational	86000	OECD	Prescribing / medication	18.4 per 100 people	Moderate
Brenner S 2012	Observational	516	OECD	Prescribing / medication	15 per 100 records	Moderate
Clark RC 2007[109]	Observational	127582000	OECD	Prescribing / medication	3.1 per 100 people	Moderate
De Wilde S 2007[111]	Observational	171690	OECD	Prescribing / medication	32.2 per 100 people	Moderate
Field TS 2004[115]	Observational	31757	OECD	Prescribing / medication	4.8 per 100 people	Moderate
Howard M 2004[118]	Observational	777	OECD	Prescribing / medication	16.3 per 100 people	Moderate
Khoja T 2011[120]	Observational	5299	Other	Prescribing / medication	18.7 per 100 prescriptions	Moderate
Khoo	Observational	1753	Other	Prescribing /	41.1 per 100	Moderate

Author	Study type	Number analyzed	Region	Type of incidents	Rate	Study quality
2012[122]				medication	records	
Martinez Sanchez A 2011[71]	Observational	23995	OECD	Prescribing / medication	1.5 per 100 prescriptions	Moderate
Ryan C 2009[132]	Observational	500	OECD	Prescribing / medication	13 per 100 people	Moderate
Schneider JK 1992[135]	Observational	463	OECD	Prescribing / medication	21 per 100 people	Moderate
Straand J 1999[138]	Observational	16774	OECD	Prescribing / medication	13.5 per 100 prescriptions	Moderate
Tomlin A 2012[139]	Observational	173478	OECD	Prescribing / medication	14.4 per 100 people	Moderate
Van Der Hooft CS 2005[142]	Observational	25258	OECD	Prescribing / medication	20 per 100 older people	Moderate
Weingart SN 2005[144]	Observational	661	OECD	Prescribing / medication	4.7 per 100 people	Moderate
Abramson EL 2013[96]	Observational	1905	OECD	Prescribing / medication	3.8 per 100 prescriptions	Low
Khoja TA 1996[121]	Observational	6350	Other	Prescribing / medication	11.6 per 100 prescriptions	Low
Koper 2013[123]	Observational	169	OECD	Prescribing / medication	56.2 per 100 people	Low
Neville RG 1989[128]	Observational	15916	OECD	Prescribing / medication	3.2 per 100 prescribed items	Low
Nicholson D 2006[129]	Observational	24	OECD	Prescribing / medication	91.7 per 100 clinicians prescribing	Low
Paille F 1995[130]	Observational	4080	OECD	Prescribing / medication	32.5 per 100 prescriptions	Low
Sayers YM 2009[134]	Observational	3948	OECD	Prescribing / medication	12.4 per 100 prescriptions	Low
Apeas 2008[101,102]	Observational	96047	OECD	Any safety incident	0.8 to 17.93 per 100 consultations	High
Makeham M 2008[126]	Systematic review	49	OECD	Any safety incident	0.0004 to 24 per 100 consultations	High
Makeham MA 2006[70]	Observational	166569	OECD	Any safety incident	0.2 per 100 people	High
De Wet C 2009[110]	Observational	500	OECD	Any safety incident	9.4 per 100 records	Moderate
Elder NC 2004[113]	Observational	351	OECD	Any safety incident	24 per 100 consultations	Moderate
Gaal S 2011[116]	Observational	8401	OECD	Any safety incident	2.2 per 100 consultations	Moderate
Smits M 2010[137]	Observational	145	OECD	Any safety incident	18.6 per 100 records	Moderate
Tsang C 2013[141]	Observational	74763	OECD	Any safety incident	0.6 per 100 people	Moderate
Van Dulmen SA 2011[72]	Observational	1000	OECD	Any safety incident	1.8 per 100 records	Moderate
Eggleton KS 2014[112]	Observational	170	OECD	Any safety incident	7 per 100 consultations	Low
McKay J 2013[127]	Observational	520	OECD	Any safety incident	15 out of 100 records	Low

Author	Study type	Number analyzed	Region	Type of incidents	Rate	Study quality
A-Elgayoum SME 2009[97]	Observational	3203	Other	Diagnosis	70 per 100 blood smears	Moderate
Illboudo TP 2012[119]	Observational	1331	Other	Diagnosis	94.1 per 100 people	Moderate
Leon AC 1999[124]	Observational	1000	OECD	Diagnosis	16 out of 100 people	Moderate
Wahls TL 2007[143]	Observational	9116	OECD	Diagnosis	0.7 per 100 people	Moderate
Casalino LP 2009[108]	Observational	1889	OECD	Failure to notify of abnormal result	7.1 per 100 abnormal results	Moderate
Al-Agilly S 2007[100]	Observational	258	OECD	Inaccurate records	27.5 per 100 records	Moderate
Farrow SC 1999[114]	Observational	82	OECD	Infection control	24.4 per 100 practices	Low
Pandit NB 2008[131]	Observational	182	Other	Injection practices	77 out of 100 clinics	Low
Smith PC 2005[136]	Observational	1614	OECD	Missing information	13.6 per 100 consultations	Moderate

Note: Studies are arranged in order of type of incident, followed by study quality. Harm rates were devised by extracting figures directly from articles. No recalculations were performed. If studies used slightly different terminology to the definitions of severity of harm listed in Box 1, then the data were categorized into the Box 1 definitions based on descriptions in the articles themselves. For example, if an article stated that 10% of incidents resulted in hospitalization, this would be listed as a moderate harm. Death rates were reported separately where available.

Table 2: Prescribing incidents in primary care per 100 prescriptions / people – results from 33 studies arranged in order of study quality

Study	Study type	Prescribing incidents	Study quality
Bregnhoj[106]	Observational	39.5 / 100 medicines	High
Gurwitz[117]	Observational	5 / 100 people	High
Honigman[66]	Observational	5.5 / 100 people	High
Lund[125]	Observational	14.4 / 100 people	High
Olaniyan[82]	Systematic review	90 / 100 prescriptions	High
Sandars[133]	Systematic review	11 / 100 prescriptions	High
Tsang[140]	Systematic review	0.49 / 100 people	High
Abramson[95]	Observational	36.7 / 100 prescriptions	Moderate
Al Khaja[65]	Observational	90.5 / 100 prescriptions	Moderate
Al Khaja[81]	Observational	26.4 / 100 prescriptions	Moderate
Al Khaja[98]	Observational	87.2 / 100 prescriptions	Moderate
Avery[94]	Observational	4.9 / 100 prescribed items	Moderate
Bradbury[104]	Observational	16.6 / 100 people	Moderate
Bradley[105]	Observational	34 / 100 people	Moderate
Brekke[107]	Observational	18.4 / 100 people	Moderate
Clark[108]	Observational	3.1 / 100 people	Moderate
De Wilde[111]	Observational	32.2 / 100 people	Moderate
Field[115]	Observational	4.8 / 100 people	Moderate
Howard[118]	Observational	16.3 / 100 people	Moderate
Khoja[120]	Observational	18.7 / 100 prescriptions	Moderate
Khoo[122]	Observational	41.1 / 100 records	Moderate
Martinez Sanchezy[71]	Observational	1.5 / 100 prescriptions	Moderate
Ryan[132]	Observational	13 / 100 people	Moderate
Schneider[135]	Observational	21 / 100 people	Moderate
Straand[138]	Observational	13.5 / 100 prescriptions	Moderate
Tomlin[139]	Observational	14.4 / 100 people	Moderate
Van Der Hooft[142]	Observational	20 / 100 people	Moderate
Weingart[144]	Observational	4.7 / 100 people	Moderate
Abramson[95]	Observational	3.8 / 100 prescriptions	Low
Khoja[120]	Observational	11.6 / 100 prescriptions	Low
Koper[123]	Observational	56.2 / 100 people	Low
Neville[128]	Observational	3.2 / 100 prescribed items	Low
Nicholson[129]	Observational	91.7 / 100 clinicians	Low

Note: the number per 100 prescriptions, medications prescribed, or people is provided as specified. Details of the first author are provided to allow cross-checking to the individual study. Details are in the online supplement.[20] The quality rating is based on validated scales.

Table 3: Summary of studies about severity of harm from safety incidents in primary care

Author	Study type	Number of events analyzed	Region	Severity of harm found in studies based on chart review	Severity of harm found in studies based on prescription reviews	Severity of harm found in studies based on incident reports / claims
Apeas 2008[145]	Observational	1108	OECD			23.6% no harm 38.6% low harm 32% moderate harm 5.8% severe harm 70.2% preventable
Aranaz-Andrés JM 2012[146]	Observational	773	OECD	5.9% severe harm 64.3% preventable		
Avery AJ 2013[147]	Observational	6048	OECD		0.2% severe harm	
Beyer M 2005[148]	Observational	85	OECD			34% temporary or permanent harm
Bhasale A 1998[149]	Observational	142	OECD			42.3% no harm 25.4% low harm 10.6% moderate harm 8.5% severe harm 13.4% death
De Wet C 2009[150]	Observational	500	OECD	82.9% low to moderate harm		
Dovey SM 2002[33]	Observational	330	OECD			55.8% no harm 12.1% low harm 7.0% moderate harm 5.5% severe harm 0.3% death
Elder NC 2004[151]	Observational	351	OECD			24% actual harm (severity not specified)
Fernald DH 2004[152]	Observational	209	OECD			64.1% no harm 15.3% low harm 10.1% moderate harm 10.5% severe harm

Author	Study type	Number of events analyzed	Region	Severity of harm found in studies based on chart review	Severity of harm found in studies based on prescription reviews	Severity of harm found in studies based on incident reports / claims
Gaal S 2011[153]	Observational	1000	OECD	38.6% no harm 50.5% low harm 6.9% moderate harm 4.0% 'unknown harm'		
Gurwitz JH 2003[154]	Observational	30397	OECD			38% severe harm (serious, life threatening or fatal)
Hickner J 2010[155]	Observational	507	OECD			1.6% severe harm
Hoffmann B 2008[156]	Observational	78	OECD			3.9% no harm 25.6% actual harm (severity unknown)
Kennedy AG 2008[157]	Observational	216	OECD			90% no harm 8.7% low harm 1.8% moderate harm 0% severe harm
Khoja T 2011[158]	Observational	5299	Other		53.2% no harm 8.7% low harm 37.3% moderate harm 0.8% severe harm	
Khoo 2012[159]	Observational	1753	Other	39.9% severe harm 93.5% preventable		
Kingston-Reichers J 2010[160]	Systematic review	Review	OECD	9% to 52% harm (severity not specified) 42% to 83% preventable		
Kostopoulou O 2007[161]	Observational	78	OECD			3.9% no harm 16.7% severe harm or death
Kuo GM 2008[162]	Observational	194	OECD			41% no harm 35% low harm 21% moderate harm 3% severe harm

Author	Study type	Number of events analyzed	Region	Severity of harm found in studies based on chart review	Severity of harm found in studies based on prescription reviews	Severity of harm found in studies based on incident reports / claims
Kuzel AJ 2004[163]	Observational	170	OECD			76.9% harm (severity unknown)
Makeham M 2008[164]	Systematic review	Review	OECD	17% to 39% harm (severity not specified) 0% to 4% severe harm 45% to 76% preventable		
Makeham MA 2006[70]	Observational	166569	OECD			0.25% harm (severity not specified)
McKay J 2009[165]	Observational	191	OECD			57.1% no harm 7.3% low harm 11.5% moderate harm 4.7% severe harm 1.6% death 17.8% not classified
McKay J 2013[166]	Observational	520	OECD	44% moderate to severe harm 45% preventable		
Murie J 2003[167]	Observational	55	OECD			47.3% no harm 9.1% low harm 3.6% moderate harm 18.2% severe harm 21.8% death
O'Beirne M, 2013[168]	Observational	264	OECD			50% harm (any type) 1% severe harm 93% preventable
Pearson A 2009[169]	Systematic review	Review	OECD	24% to 42% harm (severity not specified)		
Phillips Jr RL 2004[170]	Observational	26126	OECD			18.7% low harm 26.0% moderate harm 19.0% severe harm 36.3% death

Author	Study type	Number of events analyzed	Region	Severity of harm found in studies based on chart review	Severity of harm found in studies based on prescription reviews	Severity of harm found in studies based on incident reports / claims
Phillips RL 2006[171]	Observational	701	OECD			20.7% no harm 30.0% low harm 30.0% moderate harm 14.3% severe harm 8.1% death
Schneider JK 1992[172]	Observational	332	OECD	3.6% severe harm		
Singh H 2013[173]	Observational	190	OECD	86% moderate or severe harm		
Smits M 2010[174]	Observational	145	OECD	29.6% moderate harm 0% death		
Statham MO 2008[175]	Observational	123	OECD			51.2% low harm 39.8% moderate harm 8.9% severe harm 11.6% preventable

Online Supplement

Summary of studies included in the review

This supplement provides a summary of each of the studies identified for the review and their quality (rated using validated appraisal tools).

For systematic reviews, quality was assessed using the Critical Appraisal Skills Programme (CASP) tool. For observational (epidemiological and other) studies, quality was assessed using the Evidence Based Library and Information Practice (EBLIP) Critical Appraisal Checklist.

The table is ordered alphabetically.

Findings are listed in terms of:

- the number of safety incidents
- the type of safety incidents
- the level of harm associated with incidents

Not all studies included findings in each of these areas, so parts of the table are left blank if there were no relevant key findings.

Studies included in systematic reviews

Studies summarized in systematic reviews identified as part of this review are listed in alphabetical order. This is to illustrate the range of studies drawn on, even if the original primary studies were not incorporated into the narrative synthesis for our review.

Online content

The final page of this document lists where the full protocol can be found online (including the full search terms and search strategy) as well as where freely available online content can be sourced.

Online table 1: Summary of key findings of studies included in the review

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Abramson 2012[1]	Observational	Primary care clinic	USA	Review of prescriptions	Reviewed 9385 prescriptions from 78 providers and found 36.7 prescribing incidents per 100 prescriptions (95% CI 30.7 to 44.0), excluding incidents associated with legibility. Non-legibility incidents were found in 175.0 per 100 prescriptions (95% CI 169.1 to 181.3), inappropriate abbreviation incidents in 13.4 and direction incidents in 4.2 per 100 prescriptions. The majority of incidents were judged to be preventable.			Moderate
Abramson EL 2013[2]	Observational	Primary care	USA	Record review	Chart review of patient notes from 16 clinicians over a three month period analysed 1905 prescriptions. The prescribing incident rate was 3.8 per 100 prescriptions (95% CI 2.8 to 5.1).			Low
A-Elgayoum SME 2009[3]	Observational	Primary care clinic	Sudan	Test review	3203 blood smears from patients clinically suspected to have malaria were examined. Of these 2253/3203 (70.3%) were found to be a misdiagnosis.			Moderate
Al Khaja KA 2011[4]	Observational	Primary care clinics and pharmacy	Bahrain	Review of prescriptions	Audited prescriptions issued by 20 primary care centers and found 733/2773 (26.4%) medical prescribing incidents.			Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Al Khaja KAJ 2007[5]	Observational	Primary care clinics	Bahrain	Review of prescriptions		Incidents in prescriptions included 4972/7139 (69.7%) incidents of omission such as strength/dose: 573/4972 (11.5%); dosage form: 2815/4972 (56.6%); dosage frequency: 261/4972 (5.3%); and length of treatment: 1323/4972 (26.6%). Incidents of commission accounted for 1759/7139 (24.6%) of incidents in prescriptions. These included dosage form: 159/1759 (9.0%); dosage frequency: 105/1759 (6.0%); and length of treatment: 1419/1759 (80.7%).		Moderate
Al Khaja KAJ 2007[6]	Observational	Primary care clinic	Bahrain	Review of prescriptions	2282 prescriptions dispensed for infants for corticosteroids were analyzed. The frequency of dosing and length of therapy were not stated in 21.6% and 43.6% of prescriptions, respectively.			Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Al Khaja KAJ 2007[7]	Observational	Primary care clinic	Bahrain	Review of prescriptions	Reviewed prescriptions for infants. Drug-related incidents were present in 2066/2282 (90.5%) of the prescriptions reviewed. 5745 prescribed drug items were reviewed. There were 4282/5745 (74.5%) drug-related incidents.	Incidents of omission accounted for 4146/5745 (72.2%) of drug-related incidents. The breakdown of this category was: strength/dose: 424/4146 (10.2%); dosage form: 979/4146 (23.6%); dosage frequency: 621/4146 (15.0%); and length of treatment: 2122/4146 (51.2%). Incidents of commission accounted for 3338/5745 (58.1%). The breakdown of this category was: dosage form: 1354/3338 (40.6%); dosage frequency: 4/3338 (0.1%); length of treatment: 1594/3338 (47.8%); and incidents of commission: 386/3338 (11.6%). Incidents of integration accounted for 183/5745 (3.2%).		Moderate
Al Khaja KAJ 2010[8]	Observational	Primary care clinics and pharmacy	Bahrain	Review of prescriptions	Audited prescriptions issued by 20 primary care centers for pediatric iron preparations. Found 75/86 (87.2%) of prescriptions contained omission incidents.	Omission incidents were subcategorized as: unclear names of iron preps: 15/75 (20.0%); prescriptions without specifying the daily dosage of iron: 4/75 (5.3%); prescriptions without stating the daily dosage of iron: 42/75 (56.0%); and prescriptions without specifying the duration of therapy: 14/75 (18.7%).		Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Al-Agilly S 2007[9]	Observational	General practice	UK	Record review	Patients were invited to check their records. 187 out of 258 patients (72.5%) said their records were accurate. There were 89 inaccuracies reported by patients. 42 (47%) were of obvious clinical importance including wrongly entered diagnoses, or missing major morbidity such as an operation, or incidents in repeat medication. There were 47 (53%) inaccuracies in lifestyle data (smoking, alcohol history or weight), or dates of illnesses.			Moderate
Apeas 2008[10]	Observational	Primary care clinic	Spain	Incident reporting system	Of 96,047 visits, the health care professional detected some possible adverse effect in 1,932 visits, generating a total of 2,059 reports. A total of 1,074 adverse effects were identified corresponding to 971 different patients. The prevalence of adverse effects per visit was 11.18% (1,074/96,047, 95% CI 10.52% to 11.85%). The prevalence of visits which experience some adverse event was 17.93% (1,722/96,047, 95% CI 17.09% to 18.77%).	The causes of these incidents included medication (534/1180. 45.3%), provision of care (285/1080, 26.4%), communication (273/1080, 25.3%), diagnosis (159/1080, 14.7%) and management (99/1080, 9.2%).	In 23.6% of the cases, the consequences of the adverse effect did not affect the care provided, in 33.1% a higher level of observation and monitoring were required, in the remaining 7.5%, the adverse effect required an additional test and in 17.1%, an additional medical or surgical treatment was performed. In 14.9%, the consequence of the adverse effect required another visit or referral to specialized care (without hospitalization), and in 5.8% hospitalization of the patients for some life support treatment was required. 778 / 1108 (70.2%) adverse events were deemed to be preventable and 330/1108 (29.8%) could not have been prevented.	High

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Aranaz-Andrés JM 2012[11]	Observational	General practice	Spain	Record review and survey	Data were collected for 52 healthcare professionals who attended 96,047 consultations. 773 adverse events were identified, giving a point prevalence of 0.8% (95% CI 0.76 to 0.85).	55.5% (429) of the AE stemmed from problems with the medication prescribed; 17.1% (132) involved a worsening of the clinical course of the underlying disease; 7.8% (60) involved complications from a medical procedure; 7.4% (57) involved health care-related infection; and 6.1% (50) stemmed from problems with the care dispensed (wound cures, catheter care, etc).	Most adverse events (64.3%) were considered preventable and only 5.9% were severe, usually related to medication (odds ratio 4.6; 95% CI 2.1 to 10.3).	Low
Avery AJ 2013[12]	Observational	General practice	UK	Record review	6048 unique items prescribed over a 12 month period for 1777 patients were examined. 4.9% of all prescription items had a prescribing or monitoring incident (95% CI 4.4% to 5.5%).		Most incidents were of mild to moderate severity. 0.2% were classed as severe. Children under 15 years, adults over 64 years and people with higher numbers of unique medication items prescribed were at greater risk of incidents.	Moderate
Beyer M 2003[13]	Observational	General Practice	Germany	Incident reporting system		Examined 51 medication incidents. These were subcategorized as follows: failure to give medicine: 3/51 (5.9%); wrong medication: 8/51 (15.7%); wrong dose: 9/51 (17.7%); drug omitted: 1/51 (2.0%); adverse events: 6/51 (11.8%); drug interactions: 6/51 (11.8%); other: 10/51 (19.6%); no indication: 8/51 (15.7%).		Low

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Beyer M 2005[14]	Observational	General practice	Germany	Incident reporting system		Analyzed 85 incident reports. These included wrong diagnosis: 17/85 (20.0%); wrong clinical decision: 9/85 (11.0%); not applicable: 1/85 (1.0%); administration incidents: 9/85 (11.0%); investigation incidents: 2/85 (2.0%); treatment incidents: 23/85 (27.0%); communication incidents : 18/85 (21.0%); wrong payment: 4/85 (5.0%); wrong treatment: 2/85 (2.0%).	34% of incidents caused temporary or permanent harm.	Moderate
Bhasale A 1998[15]	Observational	General practice	Australia	Incident reporting system		Types of diagnostic incident included: missed diagnosis: 59/142 (41.6%); misdiagnosis: 38/142 (26.8%); delayed diagnosis: 31/142 (21.8%); and diagnostic procedural complication: 18/142 (12.7%). Contributing factors were listed as: incident in judgment: 63/142 (44.4%); failure in recognizing signs and symptoms: 57/142 (40.1%); poor communication between patient and health team: 33/142 (23.2%); poor communication between health professionals: 30/142 (21.1%); inappropriate action of others: 30/142 (21.1%); inappropriate patient assessment: 27/142 (19.0%); inappropriate follow up of patient: 19/142 (13.4%); and inappropriate second opinion : 33/142 (23.2%).	60/142 (42.3%) patients suffered no harm; 36/142 (25.4%) suffered low harm; 15/142 (10.6%) suffered moderate harm; 12/142 (8.5%) suffered severe harm; and that 19/142 (13.4%) patients died.	Moderate
Bradbury F 2004[16]	Observational	General practice	Ireland	Record review	Of the 8830 patient records reviewed for people using NSAIDs, 1462/8830 (16.6%) showed evidence of an adverse drug reaction.			Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Bradley MC 2012[17]	Observational	Primary care	UK	Database	The overall prevalence of potentially inappropriate prescribing in over 70 year olds (n =166,108) was 34%.			Moderate
Bregnhoj L 2007[18]	Observational	General Practice	Denmark	Records review	212 older people with polypharmacy were prescribed 1621 medications by their GPs. 640/1621 (39.5%) of the medications were likely to be inappropriate. Most of the patients (200/212, 94.3%) had one or more inappropriate ratings among their medications.			High
Brekke M 2008[19]	Observational	General practice	Norway	Record review	15,790/86,000 (18.4%) elderly people received one or more potentially harmful medications / inappropriate prescriptions from their GP.			Moderate
Brenner S 2012[20]	Observational	Primary and urgent care	US	Record review	A trigger tool identified that 15% of patients had adverse drug events.	54% of adverse drug events occurred during medication monitoring, and 45% during patient self-administration.		Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Britt H 1997[21]	Observational	General practice	Australia	Incident reporting system		Examination of 500 incident reports found pharmacological treatments: 259/500 (51.8%); non-pharmacological treatments: 183/500 (36.5%); diagnostic incidents; 142/500 (28.3%); equipment incidents: 26/500 (5.2%); poor communication: 130/500 (26.0%); incident in judgment: 120/500 (24.0%); action of others: 120/500 (24.0%); poor communication between health professionals: 100/500 (20.0%); patient consulted other medical officer: 80/500 (16.0%); failure to recognize symptoms: 70/500 (14.0%); patients history not adequately reviewed: 55/500 (11.0); omission of checking procedure: 55/500 (11.0%); and GP tired/rushed/running late: 50/500 (10.0%).		Moderate
Casalino LP 2009[22]	Observational	Primary care	USA	Record review	Retrospective medical record review of 5434 randomly selected patients aged 50 to 69 years in 19 community-based and 4 academic medical center primary care practices found the rate of apparent failures to inform people of an abnormal test result or to document informing the patient was 7.1% (135 failures / 1889 abnormal results), with a range of 0% to 26.2%.			Moderate
Clark RC 2007[23]	Observational	General practice	UK	Record review	127,582,000 patient records were reviewed and adverse drug reactions were found in 3,968,000/127,582,000 (3.1%) cases.			Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Cox SJ 2004[24]	Observational	General practice	UK	Significant Event Audit		This study analyzed significant events. Administrative incidents made up the highest proportion of events: 95/337 (28.2%). Other events were categorized as follows: other medical: 70/337 (20.8%); prescribing-related events: 46/337 (13.7%); missed new cancer diagnosis: 32/337 (9.5%); other: 28/337 (8.31%); nursing-related events: 23/337 (6.8%); patient complaint: 17/337 (5.0%); avoidable death where terminal care took place at home: 15/337 (4.5%); section under Mental Health Act: 8/337 (2.4%); and suicide: 3/337 (0.89%).		Low
De Wet C 2009[25]	Observational	General practice	UK	Record review	Review of 500 records found an adverse event in 47 records (9.4%), indicating that harm occurred at a rate of one event per 48 consultations. A further 17 records (3.4%) contained evidence of a potential adverse event.	Incident and harm rates were higher in those aged >60 years, and most were medication-related (59%).	Harm severity was low to moderate for most patients (82.9%).	Moderate
De Wilde S 2007[26]	Observational	General practice	UK	Record review	Looked at 171,690 records of elderly people and found 55,325 / 171,690 (32.2%) patients received potentially inappropriate medications.			Moderate
Diamond MR 1995[27]	Observational	General practice	Australia	Interviews		Interviews with 39 trainees in general practice found that of 180 incident reports 70/180 (38.9%) were related to communication; 17/180 (9.4%) were related to management; 56/180 31.11% to diagnosis; 17/180 9.44% to administration; and 20/180 11.11% were classified as 'other'.		Low

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Dovey SM 2002[28]	Observational	Family practice	USA	Incident reporting system		Knowledge and skills incidents made up 46/330 (13.9%) of medical incidents. Process incidents accounted for 284/330 (86.1%) of medical incidents. The process incidents were further broken down as: office administration: 102/284 (35.9%); investigations: 82/284 (28.9%); treatment 76/284 (26.8%); communication: 19/284 (6.7%); and insurance-related incidents: 1/284 (0.4%). When looking at incident reports, process incidents made up 284/330 (86.1%) of incident reports. The process incidents were further broken down as: office administration: 102/284 (35.9%); investigations: 82/284 (28.9%); other investigations: 6/284 (2.11%); treatments: 76/284 (26.8%); communication: 19/284 (6.7%); payment: 4/284 (1.4%). Knowledge and skill incidents made up 46/330 (13.9%) of incident reports.	184/330 (55.8 %) incident reports recorded that the patient suffered no harm; 40/330 (12.1%) reports showed that the patient suffered low harm; 23/330 (7.0%) reports showed that the patient suffered moderate harm; 18/330 (5.5%) reports showed that the patient suffered severe harm; and 1/330 (0.3%) report recorded the death of a patient.	Moderate
Eggleton KS 2014[29]	Observational	General practice	New Zealand	Record review	Harm was identified in 46 out of 170 patient records (27%). This equates to 7 occurrences of harm per 100 consultations.	All harms related to medication use.		Low

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Elder NC 2002[30]	Systematic review	Primary care	USA	Various		Four studies described medical incidents and adverse events in primary care, and three other studies peripherally addressed primary care medical incidents. There were three main types of preventable adverse events: diagnosis, treatment, and preventive services. Process incidents were classified into four categories: clinician, communication, administration and blunt end.		High
Elder NC 2004[31]	Observational	Family practice	USA	Survey	Fifteen physicians in 7 practices completed forms for 351 visits. Incidents and preventable adverse events were identified in 24% of these visits. There was wide variation in how often individual physicians identified incidents (3% to 60% of visits).	57/351 (16.2%) of the reports related to office administration incidents. Of these, 37/57 (64.9%) related to charting; and general office administration accounted for 21/57 (36.8%) incidents. Physician-related incidents accounted for 28/351 (8.0%); patient communication incidents accounted for 16/351; and 15/351 (4.3%) related to preventable adverse events.	Harm was believed to have occurred as a result of 24% of the incidents, and was a potential in another 70%.	Moderate
Ely JW 2012[32]	Observational	Primary care	USA	Survey		200 family physicians, general internists and general pediatricians were surveyed about diagnostic incidents. Common presenting complaints included abdominal pain (n = 27 of 202 patients, 13%); fever (n =19; 9%); and fatigue (n = 15, 7%).		Low

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Farrow SC 1999[33]	Observational	General practice	UK	Survey	This study looked at infection control in general practice. In the 82 practices, it found the following issues. Failure to access an autoclave: 56/82(68.3%); failure to have an autoclave with maintenance contract: 34/82 (41.5%); lack of access to Central Sterile Supply Department: 16/82 (19.5%); ineffective decontamination: 20/82 (24.4%); and inappropriate use of chemical disinfectants: 33/82 (40.24%). It also found a lack of hepatitis B vaccination in exposed staff in 31/82 (37.8%) practices; no infection control guidelines/sharps injury protocols in 60/82 (73.2%) practices; and a lack of training in 54/82 (65.85%) practices.			Low

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Fernald DH 2004[34]	Observational	Primary care	USA	Incident reporting system		Examined reports to primary care incident report system. Diagnostic testing incidents accounted for 325/708 (45.0%) of all incident reports. This was further broken down into: blood test: 129/325 (39.7%); other specimen: 67/325 (20.6%); imaging: 58/325 (17.9%); and 'other or unspecified test': 31/325 (9.5%). Medication incidents accounted for 165/708 (23.3%) of all incident reports. This category was further categorized as follows: wrong drug: 32/165 (19.4%); right drug: wrong dose or timing: 99/ 165 (60.0%); right drug: wrong administration or dispensing: 39/165 (23.6%); drugs not prescribed: 6/165 (3.64%). Communication incidents accounted for 437/708 (61.7%) of all incident reports.	134/209 patients (64.1%) suffered no harm; 32/209 (15.3%) suffered low harm; 21/209 patients (10.1%) suffered moderate harm; and 22/209 patients (10.5%) suffered severe harm.	High
Field TS 2004[35]	Observational	Primary care clinic	USA	Record review and incident reports	Among 31,757 older people, 1,523 adverse drug events were identified, a rate of 48.0 per 1,000 person-years. The rate of preventable adverse drug events was 13.3 per 1,000 person-years.			Moderate

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Gaal S 2011[36]	Observational	General practice	Netherlands	Record review	A random sample of 1,000 patients from 20 general practices was obtained. The 1,000 patient records included a total of 8,401 patient contacts with the practice. A total of 211 patient safety incidents were identified (95% CI 185 to 241). These incidents concerned 186 patients. In other words, a total of 1 to 4 patient safety incidents per patient were detected per year for a prevalence of 2.2% for all patient contacts (186/8401).	116/211 (55.0%) adverse events were related to poor organization. 31/211 (14.7%) were related to treatments; 26/211 (12.3%) were related to communication issues; 21/211 (10.0%) were related to diagnosis; 14/211 (6.6%) were categorized as 'prevention'; and triage accounted for 3/211 (1.4%) adverse events. In terms of cause, 4/358 (1.1%) were categorized as technical; 176/358 (49.2%) as human; 97/358 (27.1%) as organizational; and 81/358 (22.6%) as patient-related.	58 out of 211 patient safety incidents affected patients; seven were associated with hospital admission; none resulted in permanent disability or death. 51/101 (50.5%) of patients suffered low harm; 39/101 (38.6%) suffered no harm; 7/101 (6.9%) suffered moderate harm; and 4/101 (4.0%) were categorized as 'unknown harm'.	Moderate
Garfield S 2009[37]	Systematic review	Primary care	UK	Various		Review of 27 papers to map the medicines management system in primary care in the UK. The proportion of incidents in managing medicines in primary care was high. Several stages of the process had incident rates of 50% or more: repeat prescribing reviews, interface prescribing and communication and patient adherence.		High

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Gehring 2012[38]	Observational	General practice	Switzerland	Survey		Cross-sectional survey of 630 nurses and doctors in 472 practices asking about the occurrence of patient safety incidents and analyzed data from the Swiss primary care critical incident reporting systems. The incidents with highest frequency were incomplete, unavailable, unclear, or incorrect patient documentation (88.4%); missing, incomplete, or erroneous information from external providers (81.7%); and required medication was not prescribed, administered, or dispensed (80.6%).		Low
Gurwitz JH 2003[39]	Observational	Ambulatory care clinic (including primary care)	USA	Record review and incident reports	In 30,397 older person-years there were 1523 adverse drug events. The overall rate of adverse drug events among older people was 50.1 per 1000 person-years, with a rate of 13.8 preventable adverse drug events per 1000 person-years.	Incidents associated with preventable drug events were most often related to prescribing and monitoring.	38% (578) of drug events were categorized as serious, life threatening or fatal.	High
Hansen LB 2006[40]	Observational	Primary care	USA	Survey		22 practices recorded 567 clarification calls over a two week period from pharmacies, most frequently for prior authorization issues (n = 209; 37%), formulary issues (n = 148; 26%), and unclear/missing prescription dosages (n = 117; 21%). Drug classes most frequently requiring clarifications were gastrointestinal (n = 122; 21.7%), cardiovascular (n = 278; 13.9%), and analgesic / anesthetic (n = 74; 13.2%) agents.		Low

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Hickner J 2008[41]	Observational	Family practice	USA	Incident reporting system		Examined 590 event reports of 966 testing process incidents. Incidents occurred in ordering tests (12.9%), implementing tests (17.9%), reporting results to clinicians (24.6%), clinicians responding to results (6.6%), notifying patient of results (6.8%), general administration (17.6%), communication (5.7%) and other categories (7.8%). Charting or filing incidents accounted for 14.5% of incidents.		Moderate
Hickner J 2010[42]	Observational	Primary care clinic	USA	Incident reporting system		507 anonymous event reports were submitted by 24 practices. Of these reports, 357 (70%) included medication incidents only, 138 (27%) involved adverse drug events only, and 12 (2.4%) included both.	Eight (1.6%) of the reported events led to hospitalization.	High
Hildebrandt DE 2006[43]	Observational	Family practice	USA	Record review			Examined level of harm suffered when people were not appropriately triaged when they rang primary care for help out of hours. 31/119 (26.1%) patients suffered low harm (discomfort due to pain); and 4/119 (3.4%) patients suffered moderate harm.	Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Hoffmann B 2008[44]	Observational	General practice	Germany	Incident reporting system		Most of the incident reports (52/78, 66.7%) – related to 'appropriate care obstructed or delayed/inappropriate care provided'. Within this category, 'prescribing or medication review' accounted for 11/52 (21.2%) reports; 10/52 (19.2%) reports related to 'delays or inappropriate care in hospital. 'Lack of information, communication failures' were responsible for 7/52 (13.5%) reports. The rest of the breakdown is as follows: dealing with test results or hospital correspondence: 5/52 (9.6%) reports; referrals (delayed/forgotten): 5/52 (9.6%) reports; vaccination/ drug administration: 4/52 (7.7%) reports; judging urgency of patient's condition: 2/52 (3.9%) reports; external factors/equipment failures: 3/52 (5.8%) reports; failing to home visit: 2/52 (3.85%); dispensing incidents: 2/52 (3.9%).	'Actual or potential consequence' related to 20/78 (25.6%) incident reports. 'No apparent potential for harm to patients' related to 3/78 (3.9%) reports; and 3/78 (3.9%) were labelled as 'other'.	Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Holden J 1998[45]	Observational	General practice	UK	Record review		Audit of 1263 deaths found that GP factors occurred in 65/1263 (5.2%) cases. Within this category, the highest proportion was 25/65 (38.5%) reports related to delayed referral, diagnosis, treatment. This was followed by non-prescription of aspirin: 22/65 (3.9%) reports; failure to check/control blood pressure: 12/65 (18.5%) reports; side-effects from aspirin: 3/65 (4.6%) reports; poor diabetic control: 1/65 (1.5%) report; failure to challenge hospital drug treatment: 1/65 (1.5%) report; and failure to treat osteoporosis: 1/65 (1.5%)		Moderate
Honigman B 2001[46]	Observational	Primary and ambulatory care	USA	Record review	There were adverse drug events in 864/25056 (3.5%) of cases. The adverse drug event rate was rate was 5.5 (95% CI 5.2 to 5.9) per 100 patients coming for care.			High
Howard M 2004[47]	Observational	Family practice	Canada	Record review	127/777 (16.3%) older people were prescribed one or more potentially inappropriate medications.			Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Illboudo TP, 2012[48]	Observational	Primary care clinic	Burkina Faso	Record review	This study assessed the correctness of diagnoses from 12 health centers among patients with severe malaria and pneumonia. Among the 457 malaria cases affecting children under five, 66 cases (14.4%) were correctly diagnosed and of those 66 correctly diagnosed cases, 40 cases (60.6%) received an appropriate referral decision from their providers. Among the adult pneumonia cases, 5.9% (79/1331) of the diagnoses were correctly diagnosed; however, the appropriateness rate of the provider's referral decision was 98.7% (78/79).			Moderate
Kennedy AG 2008[49]	Observational	Primary care	USA	Incident reporting system			216 incident reports were submitted. Nearly 90% (142/165) were incidents that did not reach the patient (low severity). Nineteen incidents reached the patient without causing harm (8.7%) and 4 incidents caused temporary harm requiring intervention (1.8%)..	Moderate
Khoja T 2011[50]	Observational	Primary care	Saudi Arabia	Review of prescriptions	This study looked at 5299 prescriptions and found prescription incidents in 990/5299 (18.7%) of cases.		8/990 (0.8%) were classified as serious, and were potentially life-threatening incidents; 369/990 (37.3%) were classified as 'major nuisance'; 86/990 (8.7%) were classified as 'minor nuisance'; and 527/990 were classified as trivial (53.2%).	Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Khoja TA 1996[51]	Observational	Primary care	Saudi Arabia	Review of prescriptions	Out of 6350 prescriptions, 11.6% were found to have at least one incident.	Of 20320 individual drug entries, incidents included strength not stated: 772/20320 (3.8%); wrong dose: 329/20320 (1.6%); tablet instead of capsule: 197/20320 (1.0%); quantity and/or frequency missing: 652/20320 (3.2%); drug interactions: 24/20320 (0.1%); contraindication: 59/20320 (0.3%); wrong drug: 193/20320 (1.0%); incomplete drug: 136/20320 (0.7%); frequency of the daily dose missing: 18186/20320 (89.5%); generic name of the drug missing: 17475/20320 (86.0%); strength missing: 15504/20320 (76.3%); illegible/incomplete personal and diagnostic data: 12801/20320 (63.0%); duration of treatment missing: 7681/20320 (37.8%); poor/fair handwriting and abbreviations: 3861/20320 (19.0%); very poor handwriting and abbreviations: 3658/20320 (18.0%); and form of the drug missing: 2723/20320 (13.4%).		Low

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Khoo 2012[52]	Observational	Primary care clinic	Malaysia	Record review	A sample of 1753 medical records from 12 primary care clinics were scanned for diagnostic, management and documentation incidents. They found that 3.6% of medical records contained diagnostic incidents (95% CI 2.2 to 5.0), 53.2% contained management incidents (95% CI 46.3 to 60.2), 41.1% contained medication incidents (95% CI 35.8 to 46.4), 21.7% contained investigation incidents (95% CI 16.5 to 26.8), and 14.5% contained decision-making incidents (95% CI 10.8 to 18.2).		39.9% (95% CI 33.1 to 46.7) of incidents were potentially seriously harmful and nearly all (93.5%) were considered preventable.	Moderate
Kingston-Reichers J 2010[53]	Systematic review	Primary care	Canada	Various		Two major forms of harm were missed or delayed diagnosis and medication harm.	Included 46 studies. Proportion of incidents associated with harm was between 9% and 52% in individual studies. Between 42% and 83% were thought to be preventable.	High
Koper 2013[54]	Observational	General practice	Austria	Review of prescriptions	Examined medications of 169 patients with polypharmacy in 22 GP clinics. 74 patients (56.2%) had at least one dosing incident, four patients (2.4%) had at least one interaction in the most severe category. 158 patients were elderly (≥65 years), and of these 37.3% (n = 59) had at least one potentially inappropriate medication for the elderly.			Low

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Koper D 2013[55]	Observational	General practice	Austria	Record review	The medications of 169 patients with polypharmacy treated in 22 GP surgeries were analysed. Patients took an average of nine medicines each day. At least one dosing incident was found in 56% of patients.			Low
Kostopoulou O 2007[56]	Observational	General practice	UK	Incident reporting system		'Appropriate care obstructed or delayed/inappropriate care provided' accounted for 52/78 (66.7%) reports.	78 incident reports were relevant to patient safety and analysable. They included 21 (27%) adverse events and 50 (64%) near misses. 16.7% (13/71) had serious patient consequences, including one death. 75.7% (59/78) had the potential for serious patient harm. 'No apparent potential for harm to patients' accounted for 3/78 (3.9%) incident reports.	Moderate
Kuo GM 2008[57]	Observational	Family practice	USA	Incident reporting system		126 out of 194 (70%) medication incidents were prescribing incidents, 17 (10%) were medication administration incidents, 17 (10%) documentation incidents, 13 (7%) dispensing incidents and 5 (3%) were monitoring incidents. Adverse drug events resulted from 16% of reported medication incidents.	Harm from reported incidents was categorised as: prevented and did not reach patients, (72, 41%), reached patients but did not require monitoring (63, 35%), reached patients and required monitoring (15, 8%), reached patients and required intervention (23, 13%) and reached patients and resulted in hospitalisation (5, 3%). No deaths were reported.	Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Kuzel AJ 2004[58]	Observational	Primary care	USA	Interviews		People identified 221 events. The highest proportion of adverse events reported were related to breakdowns in the clinician-patient relationship: 82/221 (37.1%). This was followed by access breakdown: 63/221 (28.5%); and technical incident: 54/221 (24.4%). Communication breakdown related to 17/221 (7.7%) of adverse events; with inefficiency of care accounting for 5/221 (2.3%) of adverse events.	107/221 events had harm (76.9%). 119/170 (70.0%) of the harms were psychological. 39/170 of the harms were physical (22.9%).	Moderate
Leon AC 1999[59]	Observational	Primary care	USA	Interviews	This study examined the diagnosis of mental health issues in primary care. It found: misdiagnosis of major depression in 160/1000 (16.0%) patients; and misdiagnosis of panic disorder in 96/1001 (9.6%) patients.			Moderate
Lund BC 2010[60]	Observational (part of trial)	Primary care	USA	Survey	Of 236 patients, 34 (14.4%) experienced an adverse drug event.			High
Makeham M 2008[61]	Systematic review	Primary care	Australia	Various	Review of 49 studies found estimates of patient safety incidents in primary care were 0.004 to 240 per 1000 primary care consultations.	26% to 57% of incidents involved diagnostic “incidents”; 7% to 52% involved treatment; 13% to 47% involved investigations; 9% to 56% involved office administration; 5% to 72% were communication incidents.	45% to 76% of all ‘incidents’ were preventable. Harm from safety incidents ranged from 1.3 significant minor incidents per 1000 treatments to 4% of incidents resulting in death, 17% to 39% resulting in harm, and 70% to 76% had potential for harm.	High

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Makeham MA 2002[62]	Observational	General practice	Australia, Canada, Netherlands, New Zealand, UK, USA	Incident reporting system		Of 132 incident reports, 104/132 (78.8%) were related to process incidents. Of these, 26/104 (25.0%) related to incidents in office administration; 17/104 (16.4%) related to investigation incidents; 38/104 (36.6%) related to treatment incidents; 20/104 (19.2%) related to communication incidents; 1/104 (1.0%) related to payment incidents; and incidents in health care workforce management accounted for 2/104 (1.9%) of reports. 28 of the 132 incident reports were related to knowledge and skill incidents (21.2%). These were further broken down into: incidents in execution of a clinical task 7/28 (25.0%); incidents in diagnosis: 18/28 (64.3%); wrong treatment decision with right diagnosis: 3/28 (10.7%).		Moderate
Makeham MA 2006[63]	Observational	General Practice	Australia	Incident reporting system	84 GPs submitted 418 incident reports, claimed for 490864 consultations and saw 166569 individuals in one year. The incidence of reported incident per consultation per year was 0.078 (95% CI 0.076% to 0.080%). The incidence of reported incidents per patient seen per year was 0.24% (95% CI 0.235% to 0.245%). Two incidents are reported for every 1000 individual patients seen by a GP.		418/166,569 (0.25%) incidents led to patient harm.	High

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Makeham MA 2008[64]	Observational	General Practice	Australia	Incident reporting system		Incidents relating to the processes of healthcare (n=365, 69.5%) were more common than those relating to deficiencies in the knowledge and skills of health professionals (n=160, 30.5%).		High
Martinez Sanchez A 2011[65]	Observational	Community pharmacy (review of primary care prescriptions)	Spain	Review of prescriptions	Review of community pharmacy records for primary care indicated prescription incidents in 355/23995 cases (1.5%).	Most incidents were due to incomplete/incorrect information or prescribed items being unavailable: 247/355 (69.6%). Inappropriate doses accounted for 27/355 incidents (7.6%); and inappropriate direction or instruction accounted for 25/355 incidents (7.0%).		Moderate
McKay J 2009[66]	Observational	General practice	UK	Significant Event Audit		259 significant event analyses were reviewed with the following breakdown of incidents: disease diagnosis and disease management: 46/259 (17.8%); prescribing, dispensing and other drugs 46/259 (17.8%); patient and relatives: 43/259 (16.6%); investigations and results: 37/259 (14.29%); communication: 23/259 (8.88%); administration: 16/259 (6.18%); medical records and confidentiality: 15/259 (5.79%); appointments and surgeries: 12/259 (4.63%); home visits and external care: 10/259 (3.86%); equipment: 7/259 (2.70%); miscellaneous: 2/259 (0.77%); health and safety: 2/259 (0.77%).	191 reports were reviewed regarding harm. Most patients did not suffer any harm: 109/191 (57.1%); low harm occurred in 14/191 cases (7.33%); moderate harm in 22/191 cases 11.52%); and severe harm in 9/191 cases (4.71%). Three deaths occurred overall: 3/191 (1.57%). 34/191 (17.80%) cases were not classified. The 109 incidents (57.1%) which did not lead to any harm were made up of incidents which had the potential to cause patient harm but were prevented, or incidents that ran to completion without harm occurring – 'near misses'.	Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
McKay J 2013[67]	Observational	General practice	UK	Record review	Twenty-one GP trainees attended a two hour workshop about how to use a trigger tool to identify patient safety incidents and then reviewed 25 clinical records each. 80 out of 520 records (15%) identified previously undetected patient safety incidents.		30 out of these 80 incidents were judged potentially preventable (45%). 35 were judged to cause moderate to severe harm (44%).	Low
Miller GC 2006[68]	Observational	General practice	Australia	Incident reporting system	852/8215 patients (10.4%) suffered adverse events.		Harm to patients was recorded as: mild: 297/551 (53.9%); moderate: 197/551 (35.8%); severe: 55/551 (10.0%); and 'don't know': 2/551 (0.4%).	Low
Montastruc P 1993[69]	Observational	Primary care clinic	France	Record review		49 adverse events identified in a rural area over a one year period were reviewed. Cutaneous adverse drug reactions accounted for 15/49 (30.6%) events. This was followed by digestive adverse drug reactions: 14/49 (28.6%); neurological adverse drug reactions: 11/49 (22.5%); pulmonary adverse drug reactions: 3/49 (6.1%); cardiovascular adverse drug reactions: 2/49 (4.1%); and others: 4/49 (8.2%).		Low
Murie J 2003[70]	Observational	General practice	UK	Significant Event Audit		Looked at 55 significant events: operational accounted for 24/55 (43.6%), followed by clinical 20/55 (36.4%); strategic failures: 9/55 (16.4%); human resources: 2/55 (3.6%); environmental: 3/55 (5.5%); political: 1/55 (1.8%) and legislative: 1/55 (1.8%).	Of the 55 cases reviewed, 12/55 (21.8%) resulted in death; 10/55 (18.2%) resulted in severe harm; 2/55 (3.6%) resulted in moderate harm; 5/55 (9.1%) resulted in low harm; and 26/55 (47.3%) resulted in no harm.	Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Neville RG 1989[71]	Observational	General practice	UK	Review of prescriptions	There were a total of 504 incidents from 15,916 prescription items (3.17%) during a three month observation period at one clinic.	212/504 incidents (42.1%) related to dose. This was further broken down as: strength of preparation not stated: 162/212 (76.4%); dose wrong by multiple of 10: 4/212 (1.9%); and other incorrect dose: 46/212 (21.7%). 187/504 (37.1%) related to quantity (wrong pack size). 40/504 (7.9%) related to naming of drugs, further subcategorized as follow: incomplete description: 33/40 (82.5%); confusion of similar names: 3/40 (7.5%); wrong drug: 3/40 (7.5%); and controlled drug regulations not followed: 1/40 (2.5%). 57/504 (11.3%) of the prescription incidents related to formulation. 8/504 (1.6%) related to 'limited list (prep not available on NHS)'.		Low
Nicholson D 2006[72]	Observational	Primary care	USA	Record review	Of the 24 participating physicians, 22/24 (91.7%) made at least one prescribing incident over the seven month period that led to an adverse event. All of the incidents leading to an adverse event were described as preventable or ameliorable.			Low
O'beirne M, 2013[73]	Observational	Family practice	Canada	Incident reporting system		264 incident reports were submitted by 191 practices. The top four types of incidents reported were documentation (41.4%), medication (29.7%), clinical administration (18.7%) and clinical process (17.5%).	Most reported incidents were judged to have 'virtually certain evidence of preventability' (93%). Harm was associated with 50% of incidents. Only 1% of the incidents had a severe impact.	Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Olaniyan JO 2014[74]	Systematic review	Primary care	UK	Various	Thirty-three studies estimating the incidence of medication incidents in primary care were identified and thirty-six studies evaluated the impact of incident-prevention interventions. Medication incidents were found to be common, with incident rates ranging from less than 1% to more than 90%, depending on the definitions and methods used.	The prescribing stage was most susceptible to incidents. Those aged over 65 years and children were more likely to experience significant incidents.		High
Paille F 1995[75]	Observational	General practice	France	Review of prescriptions	Focused on incidents for people with hypertension. Found that 1324/4080 (32.5%) prescriptions contained potentially inappropriate medications.			Low
Pandit NB 2008[76]	Observational	Primary care	India	Survey	Reviewed 182 organizations. 77% of had unsafe injection practices, including the use of a boiling pan for sterilisation, recapping of needles and exposure to body fluids. The prevalence of needle stick injuries among service providers was 52.2% and the annual incidence of needle stick injuries was 19%.			Low
Pariser RJ 1987[77]	Observational	Primary care	USA	Record review		Reviewed 319 medical incidents in 260 patients with skin conditions. 281/319 (88.0%) were diagnosis incidents.		Low
Pearson A 2009[78]	Systematic review	Primary care	Australia	Various		Incidents related to administration, knowledge and skills, prescribing, processes and communication.	Review of 33 studies found that harm rates ranged from 24% to 42%.	High

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Phillips Jr RL 2004[79]	Observational	Primary care clinic	USA	Malpractice claims			26,126 peer-reviewed malpractice claims were reviewed. 5921/26126 (22.7%) were assessed as negligent claims. The malpractice claims data identified the following levels of harm to patients. 2148/5921 (36.3%) resulted in a death; 1124/5921 (19.0%) resulted in severe harm; 1542/5921 (26.0%) resulted in moderate harm; and 1107/5921 (18.7%) resulted in low harm.	Moderate
Phillips RL 2006[80]	Observational	Family medicine clinics	USA	Incident reporting system		Examined reports to primary care incident report system. 898/935 (96.0%) were process incidents and 37/935 (4.0%) were knowledge and skill incidents.	145 / 701 (20.7%) incidents resulted in no harm to the patient, 196/701 (30.0%) in low harm, 203/701 (30.0%) in moderate harm, 100/701 (14.3%) in severe harm and 57 / 701 (8.1%) in death.	High
Rosser W 2005[81]	Observational	Family medicine clinics	Canada, England, Netherlands, New Zealand, USA, Australia	Incident reporting system		Examined 508 incident reports. The most common cause of incident was classified as office processes: 160/508 (31.5%). This was followed by: treatment incidents: 109/508 (21.5%); clinical knowledge: 89/508 (17.5%); external investigations: 73/508 (14.4%); communication: 62/508 (12.2%); work force management: 10/508 (2.0%); and financial accounting: 5/508 (1.0%).		High

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Rubin G 2003[82]	Observational	General practice	UK	Incident reporting system		Examined 940 incident reports. These were subcategorized as follows: prescription incidents: 397/940 (42.2%); communication incidents: 282/940 (30.0%); equipment incidents: 153/940 (16.3%); appointments incidents: 63/940 (6.7%); clinical incidents: 24/940 (2.6%); other incidents: 21/940 (2.2%).		Low
Ryan C 2009[83]	Observational	General practice	Ireland	Record review	Records of 500 elderly people were screened. One tool found 69 medicines were prescribed inappropriately in 65 patients (13%). Another tool identified 63 potentially inappropriate medicines in 52 patients (10.4%).			Moderate
Sandars J 2003[84]	Systematic review	Primary care	UK	Various	Review of 280 studies found wide differences in rates of incidents in primary care, varying from five to 80 per 100,000 consultations. Prescribing and prescription incidents have been found to occur in up to 11% of all prescriptions, mainly related to incidents in dose.	Incidents related to diagnosis were the most common across all studies, varying from 26% to 78% of identified incidents. Incidents associated with diagnosis, either delayed or missed, were most likely to result in major harm.		High

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Sayers YM 2009[85]	Observational	General practice	Ireland	Review of prescriptions	From a total of 3,948 prescriptions, 491 12.4%) contained one or more incidents. From a total of 8,686 drug items, 546 (6.2%) contained one or more incidents.	The most common incident was 'no direction': 226/491 (46.0%), followed by 'other prescription-related cause': 93/491 (18.9%). The rest of the breakdown was as follows: not dated: 71/491 (14.46%); inadequate information: 60/491 (12.2%); mix up of prescriptions: 51/491 (10.4%); wrong dose: 43/491 (8.8%); no age given: 37/491(7.5%); CD incident: 27/491 (5.5%); illegible: 27/491 (5.5%); off market: 20/491 (4.1%); not signed: 17/491 (3.5%).		Low
Schiff GD 2013[86]	Observational	Primary care	USA	Malpractice claims		Examined 551 malpractice claims from primary care. Allegations were related to diagnosis (72.1%), medications (12.3%), other medical treatment (7.4%), communication (2.7%), patient rights (2.0%), and patient safety or security (1.5%).		Low
Schneider JK 1992[87]	Observational	General medicine	USA	Record review	Records for 332 elderly people who attended a general medical clinic and 131 who attended a geriatric clinic showed potential drug interactions in 143 people (31%). There were 107 documented adverse drug reactions in 97 patients (21%). Of these patients, 86 were noted by doctors as having had a reaction.		Twelve reactions led to hospitalization.	Moderate
Schweppach DL 2012[88]	Observational	Primary care	Switzerland	Survey		630 doctors and nurses were surveyed and 391 (31%) described 936 threats to patient safety. Safety of medication (8.8%), triage by nurses (7.2%) and drug interactions (6.8%) were the threats cited most frequently.		Low

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Shaughnessy AF 1989[89]	Observational	Family practice	USA	Review of prescriptions		1814 prescriptions by family medicine residents were reviewed and incidents were categorized as: omissions: 707/1814 (38.97%); incorrect dosage: 254/1814 (14.00%); legal issues: 109/1814 (6.01%); non-prescription based: 417/1814 (22.99%); inaccurate/vague quantity: 218/1814 (12.02%); and incomplete direction: 109/1814 (6.01%).		Moderate
Singh H 2013[90]	Observational	Primary care clinic	USA	Record review		Reviewed 190 diagnostic incidents identified at two primary care facilities. Found missed diagnoses in 68 cases, relating to pneumonia (6.7%), decompensated congestive heart failure (5.7%), acute renal failure (5.3%), cancer (5.3%), and urinary tract infection or pyelonephritis (4.8%). These were due to issues in one or more of the following: the clinical encounter (78.9%), referrals (19.5%), patient-related factors (16.3%), follow-up (14.7%), and diagnostic tests (13.7%).	86% of incidents were classed as potentially moderately or severely harmful.	Moderate
Smith PC 2005[91]	Observational	Primary care	USA	Survey	253 clinicians were surveyed about 1614 patient visits. Clinicians reported missing clinical information in 13.6% of visits.	Missing information included laboratory results (6.1% of all visits), letters/dictation (5.4%), radiology results (3.8%), history and physical examination (3.7%), and medications (3.2%).		Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Smits M 2010[92]	Observational	Family practice	Netherlands	Record review	145 patient records were reviewed and 27/145 (18.6%) patient safety incidents were identified.	15/27 incidents (55.6%) related to inadequate or suboptimal treatment; 9/27 (33.3%) related to triage incidents; and 6 /27 (22.2%) related to wrong or misguided diagnosis.	Of the 27 identified patient safety incidents, 8/27 (29.6%) had consequences for patients: an extra intervention was needed in 6/27 (22.2%) cases, and 2/27 (7.4%) patients had to be admitted to a hospital. No incidents resulted in permanent harm or death.	Moderate
Statham MO 2008[93]	Observational	General practice	Australia	Record review			1062 people with acute eye disease were assessed. Incorrect diagnoses accounted for 642/1062 (60.5%) patients. conditions that were misdiagnosed and subsequently associated with servere adverse patient outcome occurred in 91/123 (74.0%) patients. The remainder had a correct initial diagnosis, but subsequent incorrect treatment: 32/123 (26.0%). 63/123 (51.2%) suffered low harm; 49/123 (39.8%) suffered moderate harm; and 11/123 (8.9%) suffered severe harm. There were judged to be 123/1062 (11.6%) patients who suffered preventable adverse outcomes.	Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Stewart L, 2012[94]	Observational	Primary care clinic	USA	Interviews		Of 219 patients interviewed to compare their medication use with their medical record, 162 (74%) had at least one discrepancy. The most common type of discrepancy was an incorrect medication documented on the chart. The most common reasons included over-the-counter (OTC) use of medications and patients not reporting use of medications.		Low
Straand J 1999[95]	Observational	General practice	Norway	Review of prescriptions	Reviewed 16774 prescription incidents among elderly people. 13.5% of prescriptions met criteria for inappropriate prescribing.			Moderate
Tam KWT 2008[96]	Observational	Primary care	Hong Kong	Record review and incident reports		Of the 132 adverse drug events in four clinics, 108/132 (81.82%) were categorized as actual adverse drug events (as opposed to potential adverse drug events). Of these, 5/108 (4.6%) were preventable; and 103/108 (95.4%) were non-preventable. Of the 108 adverse drug events, 5/108 (4.6%) were detected as preventable.		Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Taylor LK 2005[107]	Observational	Primary care clinic	USA	Incident reporting system		Looked at alerts generated by prescriptions over a nine-month period, and found alerts for prescription incidents in 6428/22419 (28.7%) cases. These were subcategorized as: drug-disease contraindication : 2644/6428 (41.1%); drug-drug interactions: 1522/6428 (23.7%); potential toxicity: 1022/6428 (16.0%); drug duplication: 731/6428 (11.4%); contraindicated for patient age: 249/6428 (3.9%); potential dosing incident: 221/6428 (3.4%); and other: 39/6428 (0.6%).		Low
Tilyard M 2005[97]	Observational	General practice	Australia, Canada, Netherlands, New Zealand, UK, USA	Incident reporting system		431 incident reports which were categorized as: treatment process incident: 110/431 (25.5%); office administration incident: 82/431 (19.0%); investigation process incident: 73/431 (16.9%); communication incidents: 62/431 (14.4%); wrong diagnosis: 54/431 (12.5%); and other: 50/431(11.6%).		Moderate
Tomlin A, 2012[98]	Observational	General practice	New Zealand	Record review	During a 6-year period, 173,478 patients from 30 practices received 4,811,561 prescriptions. There were 37,397 allergies, adverse events and other warnings recorded for 24994 patients (14%).			Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Tsang C 2012[99]	Systematic review	Primary care	UK	Various	Review of 15 studies of the types of adverse events that are routinely recorded in primary care found about 6.5% of adult emergency admissions were due to drug-related events. Between 0.7% and 2.3% of deaths following adverse events were attributed to treatment in primary care. In patients aged >65 years, the occurrence of adverse drug events was estimated at 4.9 per 1000 population			High
Tsang C 2013[100]	Observational	General practice	UK	Record review	Examined 74,763 people's records. Incidence was 6 adverse events per 1000 person-years (95% CI 5.74 to 6.27), which is equivalent to 8 adverse events per 10,000 consultations. Those at greatest risk were patients aged 65-84 years, those with the most consultations, five or more emergency admissions, and those with the greatest number of conditions. People registered at their practice for the longest periods of time had a lower risk of an adverse event.			Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Tse J, 2011[101]	Observational	General practice	Australia	Record review		33 patient records were reviewed. High levels of accuracy were found in the area of demographic details (94%). Moderately high levels of accuracy were reported for allergies (61%) but also a considerable percentage of non-recorded information was present (36%). Inaccuracies in medication lists were reported in 51% of records reviewed with 32.1% of all medications being inaccurately recorded. While over 91% of participants had a history summary with eight or less items present, omissions were reported for one in every five participants.		Low
Van Der Hooft CS 2005[102]	Observational	Primary care	Netherlands	Record review	Looked at the risk of inappropriate drug prescriptions. In the calendar year 2001, found the risk of receiving at least one inappropriate drug prescription in older adults was 5052/25258 (20%). Between 1997 and 2001, the 1-year risk of receiving at least one inappropriate drug prescription for older adults ranged between 16.8% (95% CI: 16.3–17.3%) and 18.5% (18.3–18.7%).			Moderate
Van Dulmen SA 2011[103]	Observational	Primary care	Netherlands	Record review and incident reports	1000 records were reviewed from 20 practices. In 18 out of 1000 (1.8%; 95% CI 1.0 to 2.6) records an incident was detected.	The main causes of incidents were incidents in clinical decisions (89%), communication with other healthcare providers (67%), and monitoring (56%).		Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Wahls TL 2007[104]	Observational	Primary care	USA	Survey	Diagnostic incidents associated with the failure to follow up on abnormal diagnostic studies ("missed results") are a potential cause of treatment delay. 106 clinicians were surveyed who saw an average of 86 patients per two week period. Providers encountered 64 patients with missed results during the two week period leading up to the study and 52 patients with treatment delays.	The most common missed results included imaging studies (29%), clinical laboratory (22%), anatomic pathology (9%), and other (40%). The most common diagnostic delays were cancer (34%), endocrine problems (26%), cardiac problems (16%), and others (24%).		Moderate
Wallace F 2013[105]	Systematic review	Primary care	Ireland	Various		Examined the epidemiology of malpractice claims in primary care (written demands for compensation for medical injury). Studies reporting on original data with ten or more cases were eligible. Thirty-four studies were included. Twenty-eight studies included data from medical indemnity malpractice claims databases and six studies reported survey data. Fifteen studies were from the USA, nine from the UK, seven from Australia, two from France and one from Canada. Diagnosis incidents were the most common, accounting for 26% to 63% of all claims. Medication incident was the second most common, accounting for 5.6% to 20% of all claims.		Low

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Weingart SN 2005[106]	Observational	Primary care	USA	Record review and interviews	661 patients who received prescriptions from 4 primary care practices were interviewed and their records reviewed. Patients' failure to discuss 90 medication symptoms resulted in 19 (21%) ameliorable and 2 (2%) preventable adverse drug events. Physicians' failure to change therapy in 48 cases resulted in 31 (65%) ameliorable adverse drug events.			Moderate
Wetzels R 2009[107]	Observational	General practice	Netherlands	Record review and incident reporting system		31 incidents were identified and classified as follows: Practice administration incidents accounted for 10/31 (32.3%). This was subcategorized as medical records: 7/10 (70.0%); appointments: 2/10 (20.0%); other – administration: 1/10 (10.0%). Diagnostic incidents accounted for 6/31 (19.4%). Broken down as: wrong diagnosis: 1/6 (16.7%); delayed diagnosis: 4/6 (66.7%); other diagnosis: 1/6 (16.7%). Therapeutic incidents accounted for 7/31 (22.6%). Subcategorized as: wrong, incomplete treatment: 5/7 (71.4%); other treatment: 2/7 (28.6%). Communication incidents accounted for 8/31 (25.8%). Subcategorized as: communication with patients: 3/8 (37.5%); and communication with caregivers: 5/8 (62.5%).		Moderate

First author	Study type	Setting	Country	Measurement method	Number of safety incidents	Type of safety incidents	Harm associated with incidents	Quality rating
Woolf SH 2004[108]	Observational	Family medicine clinics	USA	Incident reporting system		Examined incident reports. Process incidents accounted for 135/184 (73.4%) of reports. Process incidents were further subcategorized as follows: treatment: 50/135 (37.0%); office administration: 33/135 (24.4%); investigations: 27/135 (20.0%); communication: 23/135 (17.0%); and insurance-related incidents: 2/135 (1.5%). Knowledge and skill incidents accounted for 49/184 (26.6%) of incident reports. These were further broken down into the below categories: execution of a clinical task: 6/49 (12.2%); wrong diagnosis: 26/49 (53.0%); and wrong treatment decision: 17/49(34.7%).		High
Zavaleta-Bustos M 2008[109]	Observational	Primary care clinic	Mexico	Review of prescriptions		Reviewed 370 prescriptions. The most common incident was found to be inappropriate prescriptions: 268/370 (72.4%). This was followed by inappropriate dosage regime: 102/268 (38.1%); inappropriate indication: 92/268 (34.3%); unnecessary medications: 24/268 (9.0%); medication duplicity: 14/268 (5.2%); potential drug-drug interactions: 23/268 (8.6%); missing medication: 8/268 (3.0%); and inappropriate administration route: 5/268 (1.9%).		Moderate

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  http://www.crd.york.ac.uk/PROSPEROFILES/2304_PROTOCOL_20120323.pdf

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