

Estimating the frequency of errors and the global burden from iatrogenic harm in primary care: protocol for a systematic review and meta-analysis

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Summary

Background Interest in improving the safety profile of healthcare continues and notable developments have taken place in recent years in hospital settings, particularly in the developed world, to estimate the frequency of errors, understand causal factors, and to identify and test the effectiveness of ways of minimising risk of iatrogenic harm to patients. In contrast relatively little is known about the frequency and pattern of errors in primary care - where the majority of care is now delivered - and there is as a result little evidence on how to enhance the safety of primary care. There is therefore a need to estimate the frequency of errors and associated harm in primary care settings internationally, and to obtain insights into their aetiology and potential preventability in order to inform deliberations on how to improve the safety of care outside hospital.

Methods Two reviewers independently searched the following databases for published and grey literature: African Index Medicus, African Journals Online, Bioline International, CINAHL, EMBASE, Google Scholar, IndMED, HINARI, Iran MEDEX, Korean MED, Latin American and Caribbean Health Sciences, MEDLINE, NepJOL, PsycINFO, SIGLE, Thai Index Medicus and WHOLIS. The time frame for the searches was 1980 – 31st August 2011. We are in addition in the process of identifying unpublished material through contacting experts and working through the World Health Organization's regional offices. Data will be independently extracted onto a customised data extraction sheet. Studies will be critically appraised by two reviewers using the following instruments: the Critical Appraisal Skills Programme (CASP) for systematic reviews and qualitative studies, Cochrane risk of bias tool for experimental studies and the EBLIP Critical Appraisal Checklist for epidemiological studies. In order to map the diverse categories of errors onto a common framework, we will use the LINNAEUS Taxonomy; two independent reviewers will map any variables onto the 8 categories in the Taxonomy and resolve any disputes through mutual discussion and arbitration by a third reviewer. Data will be reported both using a narrative-based approach and meta-analyses using random effects modeling in order to derive summary estimates of the frequency of errors, the associated harm and estimates of preventability. This systematic review will be registered with the International prospective register of systematic reviews (PROSPERO).

Findings Our searches thus far have identified 47,223 potentially relevant studies from which 176 have been selected as satisfying our eligibility criteria. We are currently in the process of completing searches for unpublished data and undertaking critical appraisal of included studies. We anticipate that we will be able to report the results towards the end of September, 2012 using the PRISMA framework.

Interpretation This systematic review should provide a state-of-the-art synthesis of evidence in relation to the frequency of errors and the burden of associated iatrogenic harm in low-, middle- and high-income settings globally.

Funding: World Health Organization

Background

Errors are common in healthcare and often result in varying degrees of harm, including death of the patient. Unsafe care is responsible for a substantial disease burden, and this has been studied extensively in hospitals for the past decade; the prevalence of harm due to all episodes of secondary care has been estimated as ranging from 3.2 to 16.6%.^{1,2,3,4,5,6} Work from these specialist settings, where most of the research in patient safety has hitherto focused, has found clear patterns in errors.⁷ It has thus been possible to identify errors that most frequently lead to major harm and those that are most amenable to prevention.⁸ Many patient safety programmes have also attempted to adopt practices from other high-risk industries which have made great progress in managing the challenges of improving safety and reducing harmful events. These industries have all accepted that errors are inevitable and provide opportunities to learn and improve from them; they have built systems that reliably deliver what is required, identify errors that occur and mitigate risks to prevent errors causing harm.⁹

Resolution 55.18 of the Fifty-fifth World Health Assembly in 2002 called on member states to pay the closest possible attention to the problem of patient safety and to establish and strengthen science-based systems necessary for improving patient safety and the quality of health care.¹⁰ In 2004, the World Alliance for Patient Safety was created to take action forward. Several key pieces of work were undertaken by the Alliance, to focus on understanding the causality of errors and engineering appropriate solutions to reduce the burden of iatrogenic harm. Initiatives have include two global safety challenges – Clean Care is Safer Care¹¹ and Safe Surgery Saves Lives.^{12, 13} This work has largely focused on hospitals and recognising that the majority of patient-clinician interactions now take place in primary care, the WHO Patient Safety Programme has extended its perspective into this important care setting. Studies of risk in these settings pose unique challenges – primary care, is very heterogeneous in its manifestations, involves management of patients with a wide variety of undifferentiated complaints and is in many parts of the world still poorly regulated. The relationships that patients have with their primary care practitioner is furthermore different from other care settings in that it is, particularly in developed country contexts, often more personal and longer-term than that provided through secondary or tertiary care. Medical records through which many patient safety studies have been carried out are more limited, if they exist at all. Simplistic attempts at transferring lessons from specialist care settings to primary care are of limited value. The underpinning evidence-base, whether in terms of conceptual frameworks, typologies/taxonomies, epidemiology, risk factors or interventions all therefore potentially need to be developed in their own right in relation to primary care. It is also important, that this evidence base reflects the variations in primary care provision in different parts of the world.

We have been commissioned by the World Health Organization (WHO) to conduct a systematic review on the global burden of harm in primary care. The key objectives are to:

- estimate the frequency of patient safety incidents and associated disease burden from iatrogenic harm in primary care
- describe approaches used to understand underlying causal factors and estimating the potential preventability of these patient safety incidents
- inform future work on developing methods to measure the global burden of harm in primary care and identify potential gaps and priority areas.

Methods

This systematic review will be carried out and reported using the methods detailed in the PRISMA guidelines.¹⁴

Definitions

Varying definitions exist for primary and ambulatory care and these are presented in Panel 1.^{15,16,17} After much deliberation, we opted to use the widely recognised definition proposed by the WHO's Declaration of Alma-Ata.¹⁵ This definition does not take into account primary care delivered in a private setting, a situation

that occurs to a certain extent in most countries, so will be included in our review. It is also important to include ambulatory care in our definition of primary care.¹⁶ Harm implies impairment of structure or function of the body and/or any deleterious effect arising there from, including disease, injury, suffering, disability and death, and may be physical, social or psychological. Disease is a physiological or psychological dysfunction. Injury is damage to tissues caused by an agent or event and suffering is the experience of anything subjectively unpleasant. Suffering includes pain, malaise, nausea, depression, agitation, alarm, fear and grief. Disability implies any type of impairment of body structure or function, activity limitation and/or restriction of participation in society, associated with past or present harm.¹⁸ Patient safety is the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum. An acceptable minimum refers to the collective notions of given current knowledge, resources available and the context in which care was delivered weighed against the risk of non-treatment or other treatment.¹⁸

Search strategy

An inclusive string of Medical Subject Headings (MeSH) and free terms was developed based on the current international taxonomy for patient safety (WHO 2009) and previous work undertaken by others.^{19,20,21} As noted above, the scope of primary care was broad and hence several of its constituents were identified and included in the search strategy using terms suggested by Pearson A *et al.*;²² these included physiotherapy, chiropractic services, occupational therapy, pharmacy, dentistry (including dental nurses), psychology, primary medical care, nursing, midwifery, home care, podiatry, speech therapy and optometry.

The following 18 databases were searched (dated from 1980 to 31 August 2011) for published and grey literature: African Index Medicus, African Journals Online, Bioline International, CINAHL, EMBASE, Google Scholar, IndMED, HINARI, Iran MEDEX, Korean MED, Latin American and Caribbean Health Sciences, MEDLINE, NepJOL, PsycINFO, SIGLE, Thai Index Medicus and WHOLIS. The search terms for CINAHL, EMBASE and MEDLINE are shown in Appendix 1. The search terms used for the larger databases such as CINAHL, EMBASE and MEDLINE can be found in Appendix 1. In addition, we developed a related comprehensive search strategy of the grey literature; sets of terms employed in the grey literature searches included “family practice” OR “primary care” OR “primary healthcare” OR “primary health care” OR “general practice” OR “ambulatory” in Set 1; and “harm” OR “safe” OR “error” OR “risk” OR “iatrogenic” in Set 2. These sets were combined with the Boolean operator AND.

A working group was convened at the WHO Head Quarters in Geneva on 27/28 February 2012, and experts were asked to identify additional studies assessing the global burden of harm due to patient safety incidents in primary care. We are currently identifying unpublished material again by contacting experts and working through the WHO’s six regional offices.

Study selection

The time frame for searches of the respective databases was from 1980 to 31st August 2011. No language restrictions were applied. Studies identified as potentially suitable were assessed for inclusion by two independent reviewers with arbitration by a third reviewer if necessary.

Inclusion and exclusion criteria

Our inclusion criteria are as follows:

- Studies have to be conducted in humans
- Primary research studies and systematic reviews that provide information on frequency, burden and potential preventability of errors in primary care.

Studies will be excluded if they fall outside our scope of interest and if they do not report on primary research or report the findings from a formal systematic review of the literature.

Quality assessment

Studies will be assessed for quality using the following tools: Critical Appraisal Skills Programme (CASP): systematic reviews and qualitative studies;²³ the Cochrane risk of bias tool for experimental studies;²⁴ and the EBLIP Critical Appraisal Checklist for epidemiological studies.²⁵ This will be carried out independently by two independent reviewers, with arbitration by a third reviewer if necessary. Studies will be graded as ‘low quality’ if $\leq 33\%$ of the quality criteria are fulfilled, ‘moderate quality’ if $>33\%$ but $\leq 67\%$ of the quality criteria are met and ‘high quality’ if $>67\%$ of all the quality criteria are noted. This method has been used elsewhere.²⁸

Data abstraction

Data will be abstracted onto a customised data extraction sheet by two independent reviewers, with arbitration by a third reviewer in necessary. Variables to be extracted include: title of the study, country of study, methods used to measure harm (study type), unit of harm, frequencies of unit of harm (to calculate incidences), burden of harm, preventability of harm and a quality assessment of the individual studies.

Data synthesis

We will initially conduct a narrative synthesis of the literature. This will involve use of the LINNAEUS Taxonomy as shown in Figure 1 for classifying errors as studies have used different terms for describing errors.²⁶

This Taxonomy uses two discrete categories to classify errors:

- Process errors
 - Office administration
 - Investigations
 - Treatments
 - Communications
 - Payment
- Knowledge and skill errors
 - Execution of a clinical task
 - Mis-diagnosis
 - Wrong treatment decision¹⁴

Key findings from each study will be summarised and presented in tables. Two independent reviewers will code the variables based on the LINNAEUS Taxonomy and resolved any disputes through mutual discussion and arbitration by a third reviewer. Those variables that cannot be mapped onto the Taxonomy will be placed in a newly created category ‘Other’. A similar approach will be used to standardise the descriptors of harm based on methods suggested by the National Patient Safety Agency in its key document *Seven Steps to Patient Safety*.²⁸

We anticipate undertaking meta-analyses of data for proportions (incidences) of errors in primary care in each of the LINNAEUS categories. We will calculate proportions of frequency, burden of harm and preventability and attempt to stratify the data by the quality of the studies and the income-setting (low, middle and high). Random effects modelling will be used to synthesise data.²⁹ Pooled incidences will be presented as proportions with 95% confidence intervals (CIs). We will use Comprehensive Meta-Analysis version 2 (Biostat™, USA) to undertake analyses. We will in addition provide a narrative summary of the different methods used to study patient safety incidents in primary care settings together with a critique of these methodologies.

Funding

This work was funded by the Patient Safety Research section of the World Alliance for Patient Safety, WHO

Results

To date, our searches have revealed a total of 47,223 references from which we screened 15,624 titles. We have selected 167 primary studies and 9 systematic reviews as shown in the PRISMA flow diagram. (Figure 2) So far, we have been able to show that high-income countries contribute almost 20 times as much to the understanding of harm caused by patient safety incidents in primary care (158/167, 94.6%) as shown in Figure 3.

Discussion

This work should provide a definitive assessment of the frequency of errors and associated burden of iatrogenic harm in primary care settings globally. We anticipate reporting in September 2012.

Authors' contributions: AS is the senior author and will oversee all aspects of the work. SSP, AC-S, SAS, KC, ST, BP, SPS, RG, YY, MCAL will be responsible for extracting and synthesising the data and drafting earlier versions of the manuscript. IL, AT, LD and DB have and will continue to provide critical intellectual content.

Conflict of interest: MCAL and IL work for the WHO. DB is external lead for patient safety research, WHO

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Panel 1: Definitions of safer care available in the literature

The Institute for Healthcare Improvement (IHI) defines medical harm as the “*unintended physical injury resulting from or contributed to by medical care (including the absence of indicated medical treatment), that requires additional monitoring, treatment or hospitalisation, or that results in death. Such injury is considered harm whether or not it is considered preventable, whether or not it resulted from a medical error, and whether or not it occurred within a hospital.*” (IHI) “*Patient safety is the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum. An acceptable minimum refers to the collective notions of given current knowledge, resources available and the context in which care was delivered weighed against the risk of non-treatment or other treatment.*”¹⁴

*“Primary health care is essential health care based on practical, scientifically sound and socially acceptable methods and technology made universally accessible to individuals and families in the community through their full participation and at a cost that the community and country can afford to maintain at every stage of their development in the spirit of self reliance and self-determination. It forms an integral part both of the country's health system, of which it is the central function and main focus, and of the overall social and economic development of the community. It is the first level of contact of individuals, the family and community with the national health system bringing health care as close as possible to where people live and work, and constitutes the first element of a continuing health care process.”*¹¹

Ambulatory care includes single- or multi-disciplinary diagnostic, therapeutic, and adjunct secondary prevention and educational services for non-admitted patients that are hospital- or community-based, or offered in partnership with other organisations; and which are managed by the hospital with funding from either global budgets or from multiple cost centres.¹²

Figure 1: the LINNAEUS Taxonomy

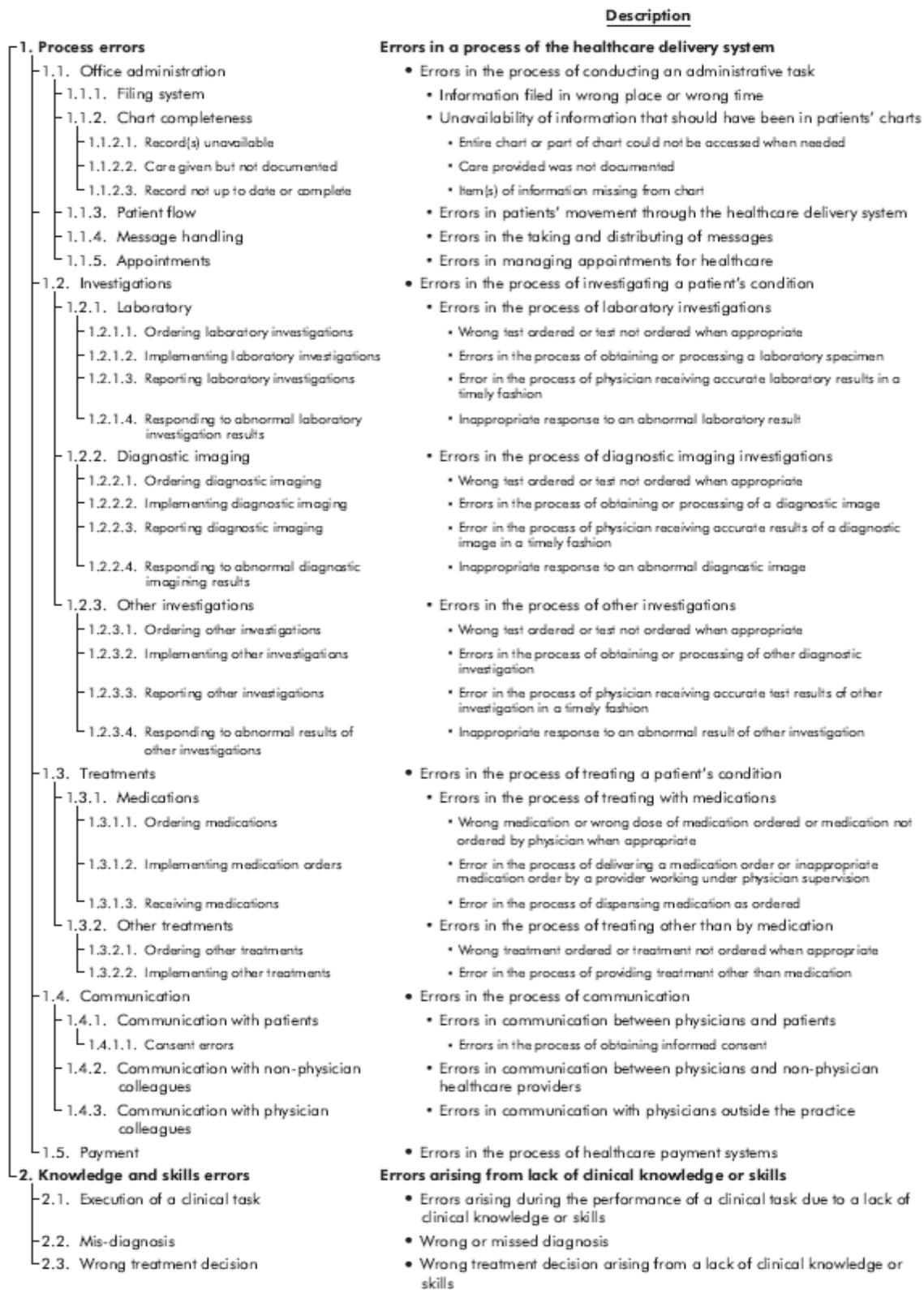


Figure 1 Taxonomy of errors recognized in family medicine.

Figure 2: PRISMA flow diagram

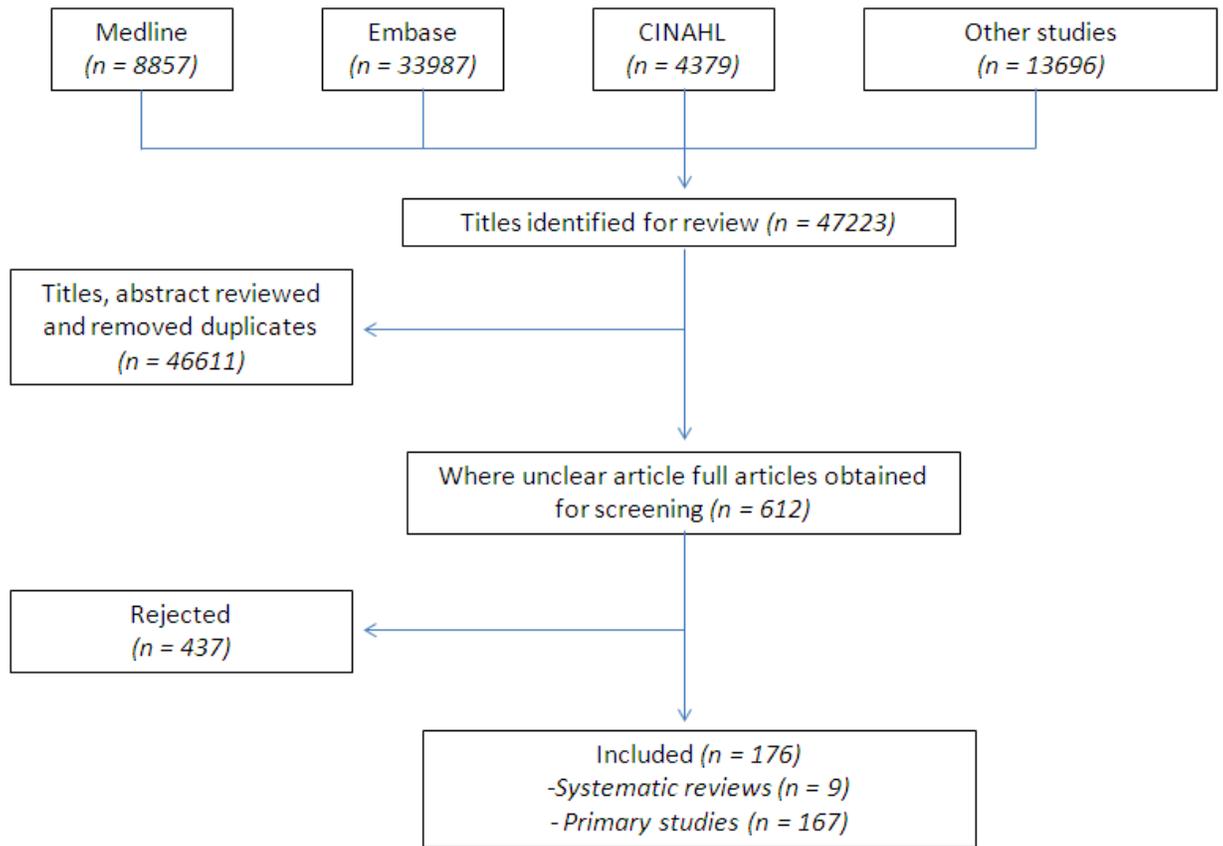
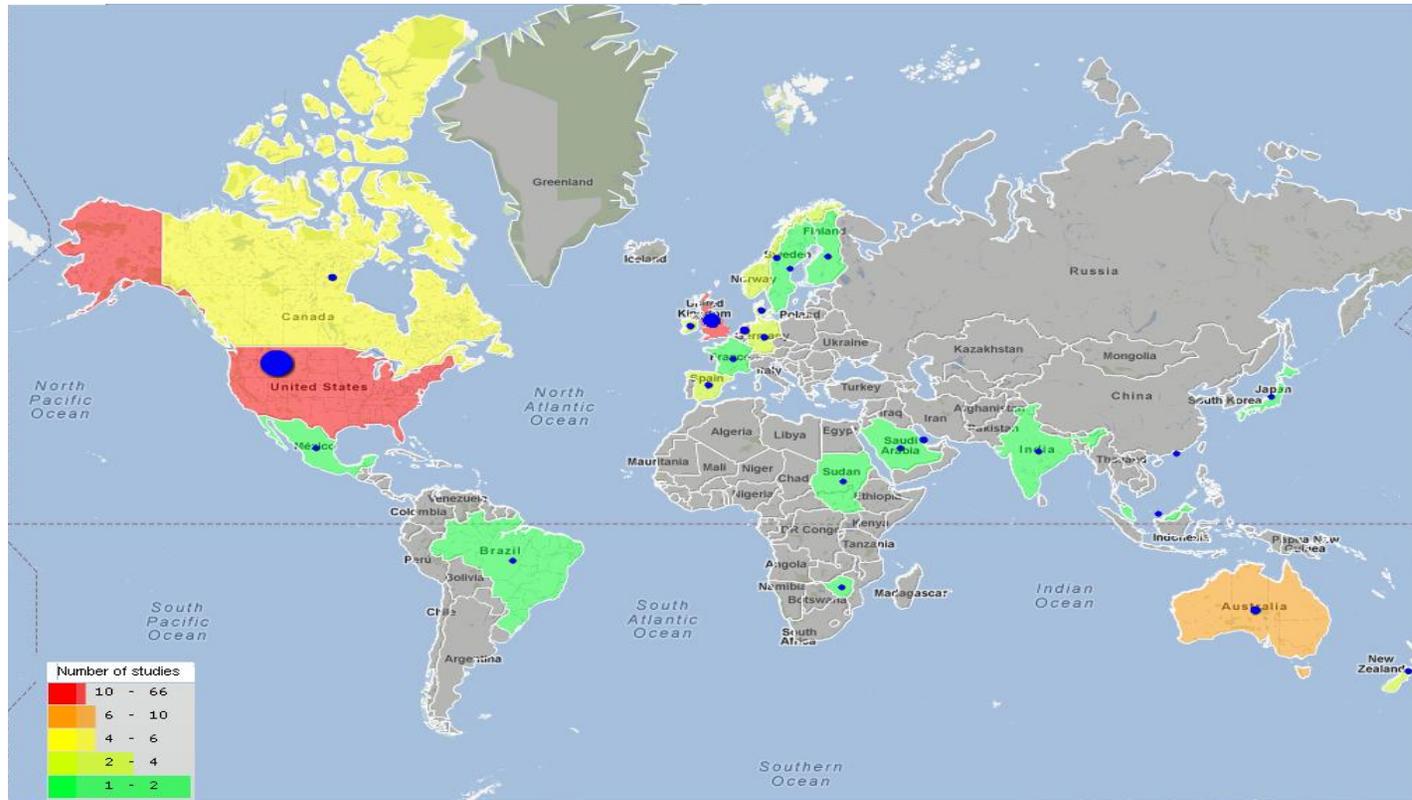


Figure 3: Global participation in patient safety research associated with primary care



There are two multicentre studies not listed on the map: the first study included Australia, Canada, Netherlands, New Zealand, the United Kingdom and the United States of America (10); the second study included Canada, England, the Netherlands, New Zealand, the United States of America and Australia. (104)

The size of the dot ● represents the number of primary studies undertaken in these geographical locations

Appendix 1: Sample search strategies CINAHL, EMBASE and MEDLINE

CINAHL

1. "family practice".ab,ti
2. "general practice".ab,ti
3. "primary care".ab,ti
4. "primary health care".ab,ti
5. "primary healthcare".ab,ti
6. "primary medical care".ab,ti
7. physiotherapy.ab,ti
8. "physical therapy".ab,ti
9. chiropractic.ab,ti
10. "occupational therapy".ab,ti
11. pharmacy.ab,ti
12. dispensing.ab,ti
13. dispensary.ab,ti
14. polypharmacy.ab,ti
15. dentistry.ab,ti
16. dental care.ab,ti
17. psychology.ab,ti
18. psychotherapy.ab,ti
19. midwifery.ab,ti
20. "prenatal care".ab,ti
21. "postnatal care".ab,ti
22. "perinatal care".ab,ti
23. "obstetric care".ab,ti
24. "maternity care".ab,ti
25. "home care".ab,ti
26. "respite care".ab,ti
27. rehabilitat*.ab,ti
28. podiatry.ab,ti
29. "speech pathology".ab,ti
30. "speech-language pathology".ab,ti
31. optometry.ab,ti
32. lenses.ab,ti
33. "ambulatory care".ab,ti
34. "outpatient care".ab,ti
35. family practice/
36. primary health care/
37. physical therapy/
38. chiropractic/
39. occupational therapy/
40. polypharmacy/
41. dentistry/
42. dental care/
43. psychology/
44. psychotherapy/
45. midwife/
46. prenatal care/
47. postnatal care/
48. perinatal care/
49. obstetric care/
50. home health care/
51. respite care/
52. podiatry/
53. speech-language pathology/
54. optometry/
58. ambulatory care/
59. dentist.ab,ti
60. dentists.ab,ti
61. "dental nurse*".ab,ti
62. midwife*.ab,ti
63. midwives.ab,ti
64. midwife.ab,ti
65. "community pharmacist*".ab,ti
66. "community nurse*".ab,ti
67. "general practitioner*".ab,ti
68. "family practitioner*".ab,ti
69. "family doctor*".ab,ti
70. optician*.ab,ti
71. optometrist*.ab,ti
72. dentist/
73. midwives/
74. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73
75. "medical error*".ab,ti
76. "medication error*".ab,ti
77. "diagnostic error*".ab,ti
78. "iatrogenic disease".ab,ti
79. malpractice.ab,ti
80. "safety culture".ab,ti
81. "near failure".ab,ti
82. "near miss".ab,ti
83. "patient safety".ab,ti

84. "safety event report*".ab,ti
85. "safety manage*".ab,ti
86. "risk manage*".ab,ti
87. "adverse drug reaction".ab,ti
88. medication error/
89. diagnostic error/
90. iatrogenic disease/
91. malpractice/
92. patient safety/
93. risk management/
94. adverse drug event/
95. 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94
96. exp health care errors/
97. "analytical stud*".ab,ti
98. "comparative stud*".ab,ti
99. "epidemiologic stud*".ab,ti
100. "intervention stud*".ab,ti
101. "follow-up stud*".ab,ti
102. "prospective stud*".ab,ti
103. "cross-sectional stud*".ab,ti
104. "evaluation stud*".ab,ti
105. "cohort stud*".ab,ti
106. "case-control stud*".ab,ti
107. "delphi stud*".ab,ti
108. "delphi technique".ab,ti
109. "clinical trial*".ab,ti
110. "controlled clinical trial*".ab,ti
111. "double-blind design".ab,ti
112. "double-blind method".ab,ti
113. "single-blind design".ab,ti
114. "single-blind method".ab,ti
115. "randomized controlled trial*".ab,ti
116. review*.ab,ti
117. "systematic review*".ab,ti
118. "narrative review*".ab,ti
119. "meta-analysis".ab,ti
120. comparative studies/
121. prospective studies/
122. cross sectional studies/
123. case control studies/
124. delphi technique/
125. clinical trials/
126. double-blind studies/
127. single-blind studies/
128. randomized controlled trials/
129. systematic review/
130. meta analysis/
131. 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130
132. 74 and 95 and 131
133. 74 and 96 and 131
134. 132 or 133 (years limited to 1980 -2011)

EMBASE

1. family practice.ab,ti.
2. general practice.ab,ti.
3. primary care.ab,ti.
4. primary health care.ab,ti.
5. primary healthcare.ab,ti.
6. primary medical care.ab,ti.
7. physiotherapy.ab,ti.
8. physical therapy.ab,ti.
9. chiropractic.ab,ti.
10. occupational therapy.ab,ti.
11. pharmacy.ab,ti.
12. dispensing.ab,ti.
13. dispensary.ab,ti.
14. polypharmacy.ab,ti.
15. dentistry.ab,ti.
16. dental care.ab,ti.
17. psychology.ab,ti.
18. psychotherapy.ab,ti.
19. midwifery.ab,ti.
20. prenatal care.ab,ti.
21. postnatal care.ab,ti.
22. perinatal care.ab,ti.
23. obstetric care.ab,ti.
24. maternity care.ab,ti.
25. home care.ab,ti.
26. respite care.ab,ti.
27. rehabilitat\$.ab,ti.
28. podiatry.ab,ti.
29. speech pathology.ab,ti.
30. speech-language pathology.ab,ti.
31. optometry.ab,ti.
32. lenses.ab,ti.
33. ambulatory care.ab,ti.
34. outpatient care.ab,ti.
35. general practice/
36. primary medical care/
37. primary health care/
38. physiotherapy/
39. chiropractic/
40. occupational therapy/
41. pharmacy/
42. polypharmacy/
43. dentistry/
44. dental care/
45. psychology/
46. psychotherapy/
47. midwife/
48. prenatal care/
49. postnatal care/
50. perinatal care/
51. obstetric care/
52. home care/
53. respite care/
54. rehabilitation/
55. podiatry/
56. optometry/
57. spectacles/
58. ambulatory care/
59. outpatient care/
60. dentist.ab,ti.
61. dentists.ab,ti.
62. dental nurse\$.ab,ti.
63. midwife\$.ab,ti.
64. midwives.ab,ti.
65. midwife.ab,ti.
66. community pharmacist\$.ab,ti.
67. community nurse\$.ab,ti.
68. general practitioner\$.ab,ti.
69. family practitioner\$.ab,ti.
70. family doctor\$.ab,ti.
71. optician\$.ab,ti.
72. optometrist\$.ab,ti.
73. dentist/
74. dental assistant/
75. general practitioner/
76. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75
77. medical error\$.ab,ti.
78. medication error\$.ab,ti.
79. diagnostic error\$.ab,ti.
80. iatrogenic disease.ab,ti.
81. malpractice.ab,ti.
82. safety culture.ab,ti.
83. near failure.ab,ti.
84. near miss.ab,ti.
85. patient safety.ab,ti.
86. safety event report\$.ab,ti.

87. safety manage\$.ab,ti.
88. risk manage\$.ab,ti.
89. adverse drug reaction.ab,ti.
90. medical error/
91. medication error/
92. diagnostic error/
93. iatrogenic disease/
94. malpractice/
95. patient safety/
96. risk management/
97. adverse drug reaction/
98. 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97
99. exp safety/
100. err\$.ti,ab.
101. 99 or 100
102. health care quality/
103. 101 and 102
104. exp safety/
105. safe\$.ti,ab.
106. err\$.ti,ab.
107. adverse.ti,ab.
108. 104 or 105 or 106 or 107
109. exp health care organization/
110. health\$.ti,ab.
111. 109 or 110
112. 108 and 111
113. 103 or 112
114. analytical stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title,
- device manufacturer, drug manufacturer, device trade name, keyword]
115. comparative stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
116. epidemiologic stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
117. intervention stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
118. follow-up stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
119. prospective stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug
- manufacturer, device trade name, keyword]
120. cross-sectional stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
121. evaluation stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
122. cohort stud\$.mp.
123. case-control stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
124. delphi stud\$.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
125. delphi technique.mp.
[mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug

manufacturer, device trade name, keyword]
126. clinical trial\$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
127. controlled clinical trial\$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
128. double-blind design.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
129. double-blind method.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

130. single-blind design.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
131. single-blind method.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
132. randomi?ed controlled trial\$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
133. review\$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
134. systematic review\$.mp. [mp=title, abstract, subject

headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
135. narrative review\$.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
136. meta-analys?s.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
137. 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136
138. 76 and 98 and 137
139. 76 and 113 and 137
140. 138 or 139
141. limit 140 to yr="1980 - Current"

MEDLINE

1. family practice.ab,ti.
2. general practice.ab,ti.
3. primary care.ab,ti.
4. primary health care.ab,ti.
5. primary healthcare.ab,ti.
6. primary medical care.ab,ti.
7. physiotherapy.ab,ti.
8. physical therapy.ab,ti.
9. chiropractic.ab,ti.
10. occupational therapy.ab,ti.
11. pharmacy.ab,ti.
12. dispensing.ab,ti.
13. dispensary.ab,ti.
14. polypharmacy.ab,ti.
15. dentistry.ab,ti.
16. dental care.ab,ti.
17. psychology.ab,ti.
18. psychotherapy.ab,ti.
19. midwifery.ab,ti.
20. prenatal care.ab,ti.
21. postnatal care.ab,ti.
22. perinatal care.ab,ti.
23. obstetric care.ab,ti.
24. maternity care.ab,ti.
25. home care.ab,ti.
26. respite care.ab,ti.
27. rehabilitat\$.ab,ti.
28. podiatry.ab,ti.
29. speech pathology.ab,ti.
30. speech-language pathology.ab,ti.
31. optometry.ab,ti.
32. lenses.ab,ti.
33. ambulatory care.ab,ti.
34. outpatient care.ab,ti.
35. Family Practice/
36. General Practice/
37. Primary Health Care/
38. "Physical Therapy (Specialty)"/
39. Chiropractic/
40. Occupational Therapy/
41. Pharmacy/
42. Community Pharmacy Services/
43. Polypharmacy/
44. Dentistry/
45. Dental Care/
46. Psychology/
47. Psychotherapy/
48. Midwifery/
49. Prenatal Care/
50. Postnatal Care/
51. Perinatal Care/
52. Obstetrics/
53. Maternal Health Services/
54. Home Care Services/
55. Respite Care/
56. Rehabilitation/
57. Podiatry/
58. Speech-Language Pathology/
59. Optometry/
60. Lenses/
61. Ambulatory Care/
62. dentist.ab,ti.
63. dentists.ab,ti.
64. dental nurse\$.ab,ti.
65. midwife\$.ab,ti.
66. midwives.ab,ti.
67. midwife.ab,ti.
68. community pharmacist\$.ab,ti.
69. community nurse\$.ab,ti.
70. general practitioner\$.ab,ti.
71. family practitioner\$.ab,ti.
72. family doctor\$.ab,ti.
73. optician\$.ab,ti.
74. optometrist\$.ab,ti.
75. Dentists/
76. Dental Assistants/
77. General Practitioners/
78. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77
79. medical error\$.ab,ti.
80. medication error\$.ab,ti.
81. diagnostic error\$.ab,ti.
82. iatrogenic disease.ab,ti.
83. malpractice.ab,ti.

84. safety culture.ab,ti.	substance word, subject	heading word, unique
85. near failure.ab,ti.	heading word, unique	identifier]
86. near miss.ab,ti.	identifier]	117. prospective stud\$.mp.
87. patient safety.ab,ti.	112. comparative stud\$.mp.	[mp=protocol supplementary
88. safety event report\$.ab,ti.	[mp=protocol supplementary	concept, rare disease
89. safety manage\$.ab,ti.	concept, rare disease	supplementary concept, title,
90. risk manage\$.ab,ti.	supplementary concept, title,	original title, abstract, name of
91. adverse drug reaction.ab,ti.	original title, abstract, name of	substance word, subject
92. Medical Errors/	substance word, subject	heading word, unique
93. Medication Errors/	heading word, unique	identifier]
94. Diagnostic Errors/	identifier]	118. cross-sectional stud\$.mp.
95. Iatrogenic Disease/	113. exp Epidemiologic	[mp=protocol supplementary
96. Malpractice/	Studies/	concept, rare disease
97. Safety Management/	114. epidemiologic stud\$.mp.	supplementary concept, title,
98. Risk Management/	[mp=protocol supplementary	original title, abstract, name of
99. Drug Toxicity/	concept, rare disease	substance word, subject
100. 79 or 80 or 81 or 82 or 83	supplementary concept, title,	heading word, unique
or 84 or 85 or 86 or 87 or 88	original title, abstract, name of	identifier]
or 89 or 90 or 91 or 92 or 93	substance word, subject	119. evaluation stud\$.mp.
or 94 or 95 or 96 or 97 or 98	heading word, unique	[mp=protocol supplementary
or 99	identifier]	concept, rare disease
101. safe\$.ab,ti.	115. intervention stud\$.mp.	supplementary concept, title,
102. exp Safety/	[mp=protocol supplementary	original title, abstract, name of
103. err\$.ab,ti.	concept, rare disease	substance word, subject
104. adverse.ab,ti.	supplementary concept, title,	heading word, unique
105. 101 or 102 or 103 or 104	original title, abstract, name of	identifier]
106. exp *Risk Management/	substance word, subject	120. exp Cohort Studies/
107. exp *Medical Errors/	heading word, unique	121. cohort stud\$.mp.
108. *Safety Management/	identifier]	122. exp Case-Control
109. 106 or 107 or 108	116. follow-up stud\$.mp.	Studies/
110. 105 and 109	[mp=protocol supplementary	123. case-control stud\$.mp.
111. analytical stud\$.mp.	concept, rare disease	[mp=protocol supplementary
[mp=protocol supplementary	supplementary concept, title,	concept, rare disease
concept, rare disease	original title, abstract, name of	supplementary concept, title,
supplementary concept, title,	substance word, subject	original title, abstract, name of
original title, abstract, name of		substance word, subject

heading word, unique identifier]

124. delphi stud\$.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

125. delphi technique.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

126. clinical trial\$.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

127. exp Clinical Trial/
128. controlled clinical trial\$.mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

129. exp Random Allocation/
130. exp Double-Blind Method/
131. double-blind design.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

132. exp Single-Blind Method/
133. single-blind design.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

134. randomi?ed controlled trial.mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

135. review\$.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

136. systematic review\$.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

137. narrative review\$.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

138. meta-analys?s.mp.
[mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

139. 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136 or 137 or 138

140. 78 and 100 and 139

141. 78 and 110 and 139

142. 140 or 141

143. limit 142 to yr="1980 - Current"

