BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2015-009957
Article Type:	Research
Date Submitted by the Author:	10-Sep-2015
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Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	General practice / Family practice, Epidemiology, Evidence based practice
Keywords:	risk prediction, clinical prediction rule, impact analysis

Title:

Impact analysis studies of clinical prediction rules relevant to primary care: a systematic review

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Abstract

Objectives: Following appropriate validation, clinical prediction rules (CPRs) should undergo impact analysis to evaluate their effect on patient care. The aim of this systematic review is to narratively review and critically appraise CPR impact analysis studies relevant to primary care.

Setting: Primary care

Participants: Adults and children

Intervention: Studies that implemented the CPR compared to usual care were included. Study design: randomised controlled trial (RCT), controlled before-after and interrupted time-series

Primary outcome: Physician behaviour and/or patient outcomes.

Results: A total of 18 studies, incorporating 14 unique CPRs, were included. The main study design was RCT (n=13). Overall, 10 studies reported an improvement in primary outcome with CPR implementation. Of six musculoskeletal studies, five were effective in altering targeted physician behaviour in ordering imaging for patients presenting with ankle, knee and neck musculoskeletal injuries. Of six cardiovascular studies, four implemented cardiovascular risk scores and three reported no impact on physician behaviour outcomes such as prescribing and referral or patient outcomes such as reduction in serum lipid levels. Two studies examined CPRs in decision-making for patients presenting with chest pain and reduced inappropriate admissions. Of five respiratory studies, two were effective in reducing antibiotic prescribing for sore throat following CPR implementation. Overall, study methodological quality was often unclear due to incomplete reporting.

Conclusions: Despite increasing interest in developing and validating CPRs relevant to primary care, relatively few have gone through impact analysis. To date research has focused on a small number of CPRs across few clinical domains only.

Keywords: Clinical prediction rule, Impact analysis, Risk prediction, Primary care

Strengths and limitations of this study

- Clinical prediction rules (CPRs) are increasingly developed and advocated for use in clinical practice. However, little is known regarding the effectiveness of these tools versus usual care for relevant clinical outcomes.
- This is the first systematic review of CPRs relevant to primary care that have gone through impact analysis.
- This systematic review forms part of a larger study which aims to develop a register of clinical prediction rules that are relevant to primary care. The methodological approach has been published in detail previously.
- In brief, an electronic search string for PubMed was developed to retrieve CPRs relevant to primary care from 30 pre-selected medical journals. This limit was necessary due to th e broad scope of the research question but may have resulted in relevant articles not being retrieved. However in addition secondary sources of CPRs were searched, author searches for key experts in the field were conducted and reference lists of each relevant impact analysis study were reviewed to identify possible additional studies.

Introduction

Clinical prediction rules (CPRs) are clinical tools that quantify the individual contributions that various components of the history, physical examination and investigations contribute towards diagnosis, prognosis, or likely response to treatment in a patient.(1) These tools attempt to formally test, simplify, and increase the accuracy of clinicians' diagnostic and prognostic assessments and management decisions.(1, 2) Well recognized examples of CPRs include the Framingham cardiovascular risk score, the Ottawa ankle rule and the Centor score for sore throat.

Developing and validating a CPR requires reference to specific methodological standards.(1, 3, 4) Conventionally, these tools go through three distinct stages prior to full implementation in a clinical setting.(1, 3, 4) The first stage is derivation, where the independent and combined effects of explanatory variables such as symptoms, signs and/or investigations, is established. The next stage is validation, where the final derived CPR is evaluated first in a similar clinical setting (narrow validation), followed by different clinical settings (broad validation). If following these stages predictive accuracy is established, then the final stage of evaluation is to test the impact of using the CPR in clinical practice, ideally in a randomized controlled trial (RCT) for relevant clinical outcomes.(1, 5, 6) Impact analysis aims to investigate if the implementation of a CPR in clinical practice is better than usual care for patient, process of care and/or cost outcomes.(7, 8)

Our research group recently published two studies detailing the development and content of an international register of CPRs relevant to primary care.(2, 9) With increasing interest in CPRs, large numbers have been derived but fewer have been validated or tested in an impact analysis study.(2) If CPRs are to truly improve the quality of patient care then evaluation of these tools is crucial.

The aim of this systematic review is to present a narrative and critical analysis of CPRs relevant to primary care which have gone through impact analysis.

Methods

The methods used for identifying CPRs from the literature and in developing a register of these tools relevant to primary care have been published in detail previously.(2, 9) These methods are summarised below.

Search strategy

An electronic search string for PubMed was developed to retrieve CPRs relevant to primary care from 30 pre-selected medical journals (See Appendix 1 for search string and journals included).(9) No restriction was placed on language. Original electronic searches were conducted from 1980-2009 and for the purposes of this review were updated to the end of 2013.(2) In addition, secondary sources of CPRs were searched including the Journal of the American Medical Association (JAMA) Rational Clinical Examination series, a handbook of CPRs and personal resources. (2, 9) Author searches for key experts in the field were also conducted for additional relevant articles. Furthermore, reference lists of each relevant impact analysis study were searched to identify possible additional studies.

Inclusion criteria

Studies were eligible for inclusion if they met following criteria;

1) Population: Relevant to primary care defined as "normally the point of first medical contact within the health care system, providing open and unlimited access to its users, dealing with all health problems regardless of the age, sex, or any characteristic of the person concerned. (10) Although studies may not have been conducted in a primary care setting, they were eligible for inclusion providing they were relevant to primary care. This inclusion criterion was designed to be broad to acknowledge variation in the same-day diagnostic tests that are available across different countries and the international variation in the role of primary care clinicians. Studies set in the emergency department were considered relevant to primary care if following application of the CPR the patient could be discharged home following application of the CPR.

2) Intervention: CPR defined as "a clinical tool that quantifies the individual contributions that various components of the history, physical examination, and investigations make toward the diagnosis, prognosis, or likely response to treatment in a patient."(1) Diagnostic, prognostic and management CPRs were included and screening questionnaires (i.e. applied

to apparently healthy people who may be at increased risk of a disease or condition) were excluded. A requirement for inclusion was that the CPR comprised the entire intervention. Studies where the CPR was implemented as part of a broader guideline, protocol or decision aid were excluded. Studies that used a CPR to determine eligibility for trial inclusion but were not part of the intervention were also excluded.

The following study designs were included: (cluster) RCT, controlled before-after or interrupted time series studies. Uncontrolled study designs were excluded.

3) Comparison: Usual care.

4) Primary Outcome: Physician behaviour e.g. ordering of diagnostic tests, process of care e.g. number of inpatient bed days and/or patient outcomes e.g. duration of symptoms.(1)

Data extraction

All articles were initially screened for inclusion according to title and abstract by one reviewer. Potentially relevant articles were then reviewed by a second reviewer with any disagreements resolved by a third independent reviewer. For each relevant article the following data was extracted: i) Name of CPR (ii) Type of CPR: prediction rule, decision rule or both; (iii) Clinical domain: using International Classification of Primary Care – second edition (ICPC-2)(11); (iv) Clinical setting; (v) Study population; (vi) Primary outcome of interest; (vii) Predictive accuracy of the CPR (measured by sensitivity/specificity (95% confidence intervals) where reported, otherwise the model's c-statistic was recorded); and (viii) Impact on primary outcome of interest.

Data analysis

i) Critical analysis of CPR impact analysis

Each article was critically appraised utilising a published framework for impact analysis of CPRs.(7) Developed in 2011 by an expert panel, this four-phase framework provides guidance for impact analysis studies (See Figure 1). The phases are as follows; 1) *Exploratory phase*; evaluate the level of evidence and predictive accuracy of the CPR; 2) *Preparation for impact analysis*; consider potential barriers, assess acceptability of the CPR to clinicians and local stakeholders and conduct a pilot study; 3) *Experimental phase*; evaluation of the CPR with monitoring of the use of the CPR in a clinical setting; 4) *Long-term implementation*

phase; examine if a CPR with reported positive impact on relevant clinical outcomes is implemented long-term and how this was achieved.(7)

ii) Summary of effect on process and outcome of care

Meta-analysis was not possible due to heterogeneity in CPRs and outcomes of interest, so a narrative analysis was conducted. In this section, where appropriate and where data was available, crude odds ratios and absolute risk reductions (ARR) were calculated.

Methodological quality assessment

The methodological quality of each impact analysis study was independently evaluated by two reviewers (MU, BC) and by a third reviewer if consensus was not reached (EW). For each study design, an appropriate quality assessment check list was used. RCTs and cluster RCTs were assessed through the Cochrane risk of bias tool.(12) Controlled before-after studies and interrupted time series studies were evaluated through Cochrane criteria for these study designs.(13)

Results

Overview of studies

Study identification

A flow diagram of the search strategy is presented in Figure 2. The PubMed search (1980-2013) and supplementary sources searches retrieved a total of 86,158 studies of which 1,111 CPR studies were identified following review of title and abstract. A total of 18 studies met the inclusion criteria for the systematic review.

Description of included impact analysis studies

A total of 14 unique CPRs were tested in 18 impact analysis studies (See Table 1 and Appendix 2). According to ICPC-2, these studies were classified into four broad clinical domains namely; musculoskeletal, most commonly the Ottawa ankle rule (14-19) (n=6); cardiovascular (20-26) (n=6) respiratory (27-31) (n=5), and neurological (32) (n=1). The majority of studies were conducted in North America (Canada n=10, United States n=4) with the remainder in the United Kingdom (n=2) and France (n=2). Most studies were set in the emergency department (ER) (n=9) and primary care (n=7). The remainder were carried out in the outpatient department (n=2).

Regarding study design, there were four cluster RCTs (14, 17, 26, 32), eight RCTs (21, 23-25, 27-31), one pilot RCT (22), three controlled before-after studies (15, 16, 18) and two interrupted time series' (19, 20). In a total of 16 studies, the intervention was the impact of the CPR alone (14-28, 31, 32), and two studies utilized different trial arms to test the CPR alone versus CPR and protocol versus usual care.(29, 30) Two studies integrated the CPR into a computerised clinical decision support system (CDSS). (19, 31) Two studies used real-time CPR reminders at the point of test ordering.(17, 32)

i) Critical analysis of CPR impact analysis studies

i) Preparation for impact analysis: level of evidence of CPR, consideration of potential barriers and assessment of CPR acceptability

Fifteen of 18 studies implemented a CPR that was broadly validated, while three studies tested a CPR that had been derived or internally validated only.(20, 29, 30) Ten studies reported the CPR's sensitivity from validation studies in identifying the target outcome which ranged from 85%-100%.(14-19, 27, 28, 30, 32) Five studies identified and addressed

potential barriers for implementation before impact analysis, most frequently through barriers analysis.(17, 19, 21, 31, 32) Six studies assessed the acceptability of the CPR to clinicians prior to the implementation phase of the study, usually through training sessions and engagement with local stakeholders. (14, 18, 21, 26, 31, 32) Seven studies reported that a pilot or simulation phase was conducted or there was a previous impact analysis on the same CPR by the same authors. (15-18, 20, 31, 32)

ii) Impact analysis phase: adherence with CPR use and reasons for non-adherence

Twelve studies tracked the use of the CPR during implementation, usually with standardised data collection forms or computerised tools.(14-17, 19, 21, 24, 25, 28, 30-33) Overall, adherence with CPR use varied between studies ranging from 57.5% to 100%, with reported reasons for non-adherence including fear of missing the diagnosis, preference for own clinical judgment and patient request.(19, 32) Clinicians' acceptability of CPR use during the intervention phase was evaluated in four studies (15, 16, 19, 32), of which two assessed the reported rate of comfort using a five-point likert scale.(15, 16)

iii) Post implementation phase: maintaining use of CPR

Of 10 studies with a positive impact on primary outcome, four evaluated the effect of the CPR in a post intervention phase ranging from 5 to 12 months. (14, 15, 17, 19) To maintain CPR use, two studies used a passive strategy of posters, one retained computerized clinical decision support and one did not employ any particular strategy. In all four studies the effect of CPR use was maintained.

Importance of study design in assessing the impact of CPRs

There were five uncontrolled before-after studies retrieved during the initial search, which were excluded from data analysis based on their uncontrolled study design (See Appendix 3).(34-38) These studies tested the impact of the Ottawa ankle rule (n=2), the Canadian C-spine rule (n=1), the CT head rule (n=1) and the Glasgow Blatchford bleeding score (n=1). All five studies demonstrated a positive impact on primary outcome, usually physician behaviour in ordering imaging.

ii) Effect on the process and outcome of care

Overall, ten studies reported that CPR implementation resulted in a positive impact on primary outcome while eight studies reported no impact versus usual care. Studies are

presented according to clinical domain. Table 2 presents a summary of the estimated effect sizes for the impact analysis studies.

Musculoskeletal (cluster RCTs n=2, Controlled before-after studies n=3, interrupted time-series n=1)

All six musculoskeletal studies focused on the implementation of CPRs for deciding upon further imaging for patients presenting with ankle, knee or neck injury.(14-19) All included musculoskeletal CPRs had reported sensitivities of 100% in their validation studies and all focused on physician behaviour in deciding to order imaging. Of these six studies, five reported a positive effect on reducing imaging with crude ORs ranging from 0.03 to 0.96.(14-17, 19) (See Table 2) All studies adopted an educational approach to encourage CPR use amongst clinicians, through use of educational meetings, posters and pocket cards. Of note three studies tested the impact of the Ottawa ankle rule; two controlled before-after trials in Canada and one cluster RCT in France.(14, 15, 18)

Cardiovascular (cluster RCT n=1, RCTs n=4, Interrupted time series n=1)

Of six cardiovascular studies, two implemented chest pain CPRs to assess the impact on physician decision-making regarding emergency admission for patients with suspected myocardial infarction.(20, 21) One of these studies reported a 30% relative reduction in patients admitted inappropriately.(20) The remaining four studies implemented cardiovascular risk scores in general practice. Three of these studies reported no impact on physician behaviour such as prescribing and referral to dieticians or on patient outcomes such as reduction in lipid levels.(22, 23, 26) However, in one large scale RCT (n=3,053), that published its findings in two separate articles; both patient lipid levels and physician antihypertensive prescribing were improved.(24, 25)

Respiratory (RCTs n=5)

Of five respiratory studies, four focused on physician behaviour in terms of antibiotic prescribing for sore throat in general practice.(27-29, 31) Of these four studies, only one reported significantly reduced antibiotic prescription rates in the intervention group (age-adjusted relative risk 0.74, 95% CIs 0.60-0.92) versus usual care.(31) The primary outcome in the fifth study was reported symptom severity in patients presenting with sore throat and

antibiotic prescribing was included as a secondary outcome.(30) This study found that use of the CPR alone or CPR in combination with a rapid antigen detection test (RADT) improved patient reported symptom severity and duration, and reduced antibiotic use by 29% (adjusted risk ratio 0.71, 95% CI 0.50-0.95).(30)

Neurological (cluster RCT n=1)

One study implemented the Canadian CT head rule, which guides the ordering of brain imaging in patients presenting following minor head injury.(32) Despite this CPR having 100% sensitivity in validation studies, it did not reduce imaging rates. In process evaluation, clinicians' reported unease with certain components of the rule and fear of missing a high-stakes diagnosis as reasons for not adopting the CPR.(32)

Methodological quality assessment of included studies

Studies were heterogeneous with regard to risk of bias. For the RCT designs (n=13), five studies were considered low risk of bias for random sequence generation and five were considered low risk in relation to allocation concealment (See Figure 3i). The remaining RCT studies had an unclear risk in these domains. Due to the nature of many of the interventions, it was not always possible to blind participants and research personnel, therefore, performance bias was judged to be unclear or high in over half of these studies. In the non-randomised study designs, the risk of selection bias was high in all studies while the risk of blinding and contamination was low in all studies (See Figure 3ii). Overall, six studies tested the impact of a CPR in which the authors were involved in developing. (16, 17, 21, 28, 30, 32) The impact that this may have in terms of bias is unclear.

Discussion

Summary of main findings

This review indicates that despite the increasing research interest in developing and validating CPRs, relatively few of these tools relevant to primary care have gone through impact analysis. Implementation has been restricted to a few clinical domains mainly musculoskeletal, cardiovascular and respiratory and certain CPRs have undergone multiple evaluations, for example, the Ottawa ankle rule. Of 18 studies meeting inclusion criteria, 10 demonstrated an improvement in primary outcome with CPR use when compared to usual care. Approximately half of these successful studies focused on changing physician behaviour in ordering imaging for patients presenting with ankle, knee and neck musculoskeletal injuries.(14-17, 19) Two studies implemented CPRs for managing patients presenting with chest pain and were successful in reducing unnecessary emergency admission.(20, 21) One study reported statistically significant improvements in participants' serum lipid profiles and appropriateness of antihypertensive medication following discussion of individualized cardiovascular risk with their general practitioner (GP).(24, 25) Four studies with a positive impact on the study's primary outcome successfully implemented post RCT measures to maintain the impact through both passive (posters) and active strategies (retention of computerized CDSS).(14, 15, 17, 19)

Studies which aimed to alter physician behaviour regarding prescribing were less successful with three of six such studies successful in reducing prescription rates.(22, 30, 31) Studies that reduced antibiotic prescription rates invested significant time before CPR implementation in assessing acceptability to clinicians' and also integrated the CPR into the clinical work flow through computerised clinical decision support or point of care reminders.(30, 31) The importance of this type of impact analysis preparation in adequately addressing barriers to implementation and in integrating the CPR into the clinical workflow has been highlighted.(5, 7, 39) In this review, ten studies considered barriers to implementation and/or gauged the acceptability of the CPR to clinicians' prior to impact analysis. However, only four studies integrated the CPR into clinical work flow using either computerized CDSS or point of care reminders.(17, 19, 31, 32)

The perceived seriousness of the target condition may also affect CPR implementation. For instance, the impact of the Canadian CT head rule was evaluated in the diagnostic pathway

of intracranial bleeding following minor head injury.(32) This CPR has 100% sensitivity and though implemented by an experienced CPR research group, this CPR did not impact on CT imaging rates.(32) In a parallel process evaluation, clinicians' reported unease with certain components of the rule and fear of missing a high-stakes diagnosis as reasons for not adopting the CPR.(32)

Overall, adherence with CPR use during implementation varied considerably between studies ranging from 57% to 100%. Reasons for non-adherence, established through process evaluation, related to fear of missing the diagnosis, preference for own clinical judgment and patient request for further investigation or management.

Comparison with existing literature

Previous CPR reviews relevant to inpatient and paediatric settings reported issues around the variability of methodological quality in conducting CPR studies and a paucity of impact analysis studies.(3, 6, 40) The issue of methodological quality has recently been addressed with the publication of two standardized reporting guidelines for CPR derivation and validation studies and systematic reviews of CPRs.(41, 42) These publications will have an important role to play in standardising CPR research and in promoting robust validation of CPRs which should then be prioritised for evaluation in future impact analysis studies.

CPRs, which demonstrate improvements in the process of care and/or patient outcomes, should then be considered for inclusion in relevant clinical guidelines to facilitate dissemination into clinical practice. A recent survey which examined the use of CPRs in clinical practice by GPs in the United Kingdom reported that GPs most often used cardiovascular, depression, fracture and atrial fibrillation CPRs.(43) CPR use was dictated by perceived clinical utility, familiarity and local policy requirements. In a supplementary review of clinical guidelines very little inter-guideline consistency was found to guide clinicians in terms of which, if any, of these tools to use in practice.(43) Prioritising the evaluation of a few adequately validated CPRs with proven predictive accuracy in relevant clinical settings would add significantly to this evidence base and facilitate, if appropriate, the inclusion of certain CPRs into future clinical guidelines.

Implications for clinical practice and research

CPR research is a relatively new methodological discipline and a challenging area of research.(2) In the conduct of this review several uncontrolled before-after impact analysis studies were retrieved. While these studies have a role in contributing to the overall evidence base, they are not a substitute for carefully conducted RCTs in determining the effectiveness of CPRs on clinically relevant outcomes.(6) In this review the majority of included RCTs focused on physician behaviour or process of care as the primary outcome. This is not surprising considering how challenging it is to demonstrate differences in patient outcomes, requiring much larger sample sizes which significantly increase running costs.(44) In addition, contextual issues which exist between countries, due to differences in healthcare delivery, healthcare systems and incentives, render process of care outcomes difficult to generalise.(5, 6)

Certainly CPR impact needs to be considered early in the development phase of any new CPR. For instance, Irish research shows high levels of GP referrals to symptomatic breast units.(45) Recent research efforts have focused on the development of a breast cancer CPR for use in primary care to aid these referral decisions.(46) However, although this CPR underwent methodologically robust development and demonstrates good predictive accuracy it is unlikely its use will impact on referral rates. This is due largely to the existence of a low risk threshold for referral driven by a combination of factors including patient expectation, media interest and fears of medico-legal ramifications for clinicians if a diagnosis is missed. So when considering an impact analysis RCT in this clinical domain, these contextual issues would need to be addressed in tandem with validation and impact analysis studies.

Certain clinical domains have seen a proliferation of CPR research, particularly musculoskeletal and cardiovascular conditions. The publication of several carefully conducted impact analysis trials for CPRs relating to knee, ankle and neck injuries is largely due to one Canadian research group while historically the availability of large UK population datasets facilitated the development of cardiovascular prognostic CPRs.(14-17, 47, 48) In this review five impact analysis studies (two were uncontrolled before-after studies detailed in Appendix 3) focused on the impact of the Ottawa ankle rule in emergency room settings, three of which were conducted in the same country.(14, 15, 18, 34, 35) Ideally CPR

development and impact analysis should be aligned with clinical need rather than developing or testing the effectiveness of CPRs when accurate tools already exist.(43)

The relatively small number of impact analysis studies retrieved means it is not possible to make firm conclusions about the overall effectiveness of these tools in primary care. However, certain CPRs such as the Ottawa ankle and knee rules are appropriate for use in clinical practice and have a role in reducing unnecessary imaging rates. Future research should focus on conducting RCTs of broadly validated CPRs with consideration of contextual and local implementation factors.(7) Pertinent issues include how best to integrate the CPR into clinical workflow and the potential benefits of embedding CPRs as part of computerised clinical decision support.

Study limitations

Although this review was conducted systematically and multiple resources searched to retrieve relevant articles, electronic searches were limited to 30 pre-selected journals and as a result it is possible relevant studies were not retrieved. However, to the best of our knowledge, this review is the first to analyse in detail CPR impact analysis studies relevant to primary care. The broad definition of primary care used for this review led to the inclusion of impact analysis studies conducted in the emergency room setting. This was necessary to account for the variation in primary care services and access internationally. Studies that implemented CPRs as part of a broader guideline, protocol or decision aid were excluded. Finally, due to the heterogeneous nature of the included studies, meta-analysis was not possible.

Conclusion

Impact analysis of CPRs in primary care has to date focused on a small number of CPRs in a limited number of clinical domains. Future research should focus on prioritising well-validated and accurate CPRs for impact analysis to determine if these tools impact on the process of clinical care and patient outcomes.

Contributorship statement

Emma Wallace wrote the manuscript, acted as a reviewer during the systematic review and contributed to the results. Maike Ujen contributed to writing the manuscript, acted as a reviewer for the systematic review, contributed to the results and did methodological quality assessment Barbara Clyne acted as a reviewer for the systematic review, contributed to the results and completed the methodological quality assessment of included articles. Atieh Zarabzadeh acted as a reviewer for the systematic review and contributed to the results. Claire Keogh ran the original electronic searches, acted as a reviewer and contributed to the results and discussion. Rose Galvin acted as a reviewer and contributed to the results and discussion. Susan M Smith acted as a reviewer and contributed to the results and discussion. Tom Fahey conceived the idea, oversaw the project and acted as a reviewer. All authors read and approved the final manuscript.

Declaration of competing interests

"All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare that all authors had grant funding from the Health Research Board (HRB) of Ireland through the HRB Centre for Primary Care Research (Grant No. HRC/2007/1) for the submitted work; there are no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; there are no other relationships or activities that could appear to have influenced the submitted work."

Funding sources

This research was funded by the Health Research Board (HRB) of Ireland through the HRB Centre for Primary Care Research, Grant No. HRC/2007/1.

Data sharing

The authors' are happy to share data about this manuscript via the Dryad data repository.

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Figures

Figure 1: Framework for the impact analysis and implementation of CPRs(7)

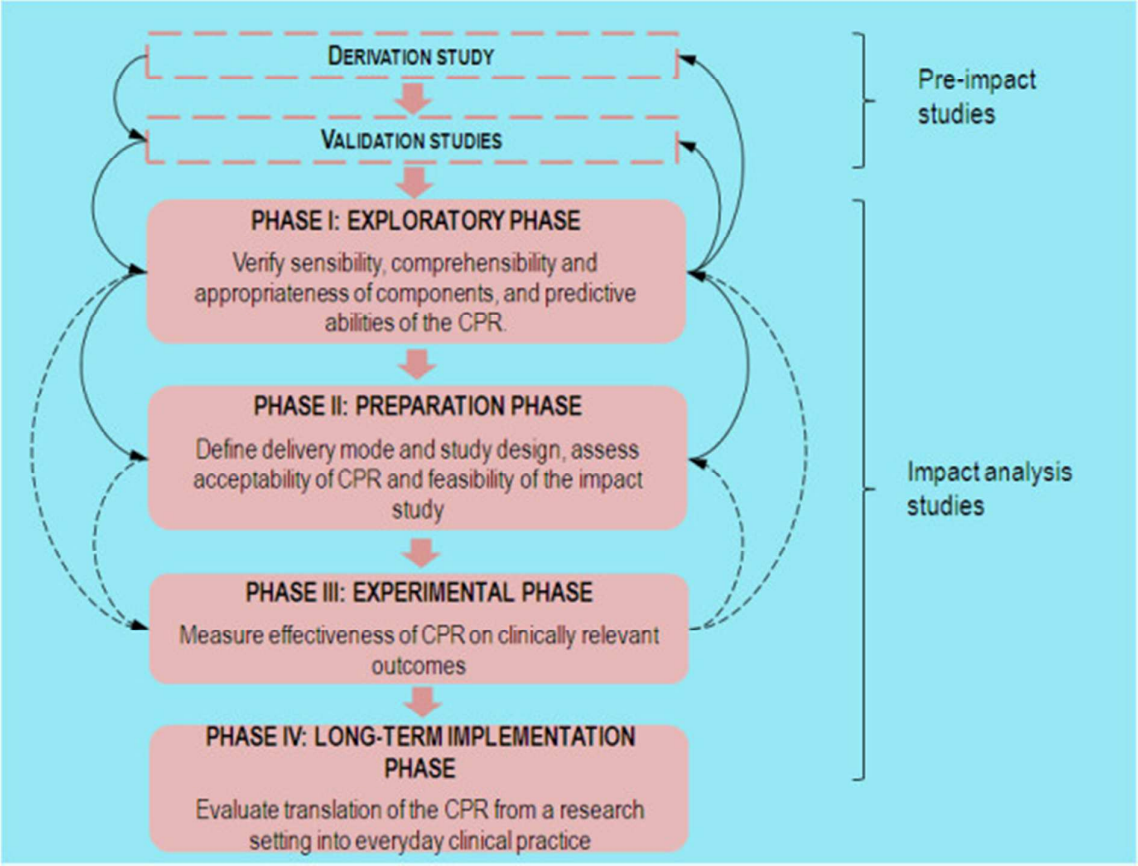

Figure 2: Flow diagram of search strategy

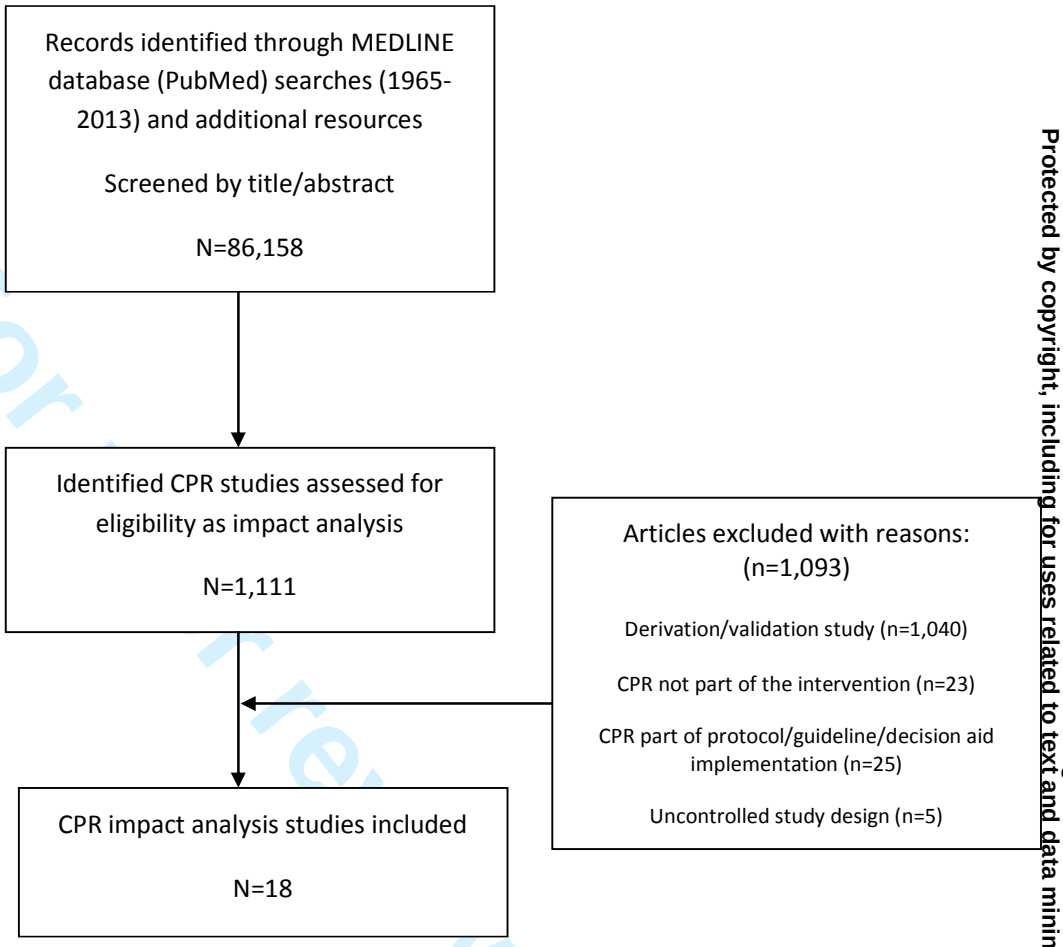

Figure 3i): Methodological quality assessment of impact analysis studies with RCT study design

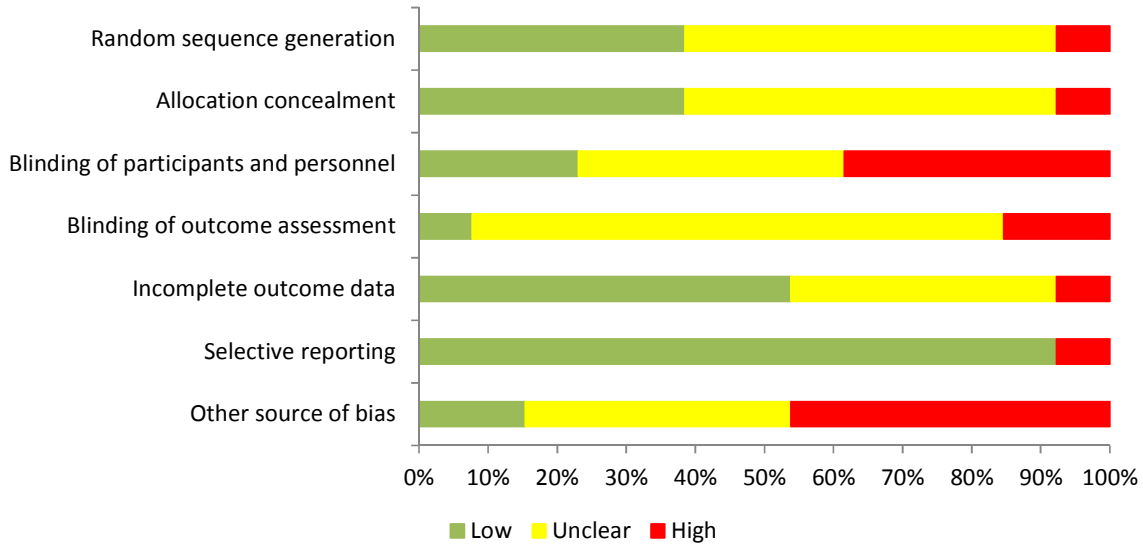

Figure 3ii) Methodological quality assessment of impact analysis studies with controlled before-after study design

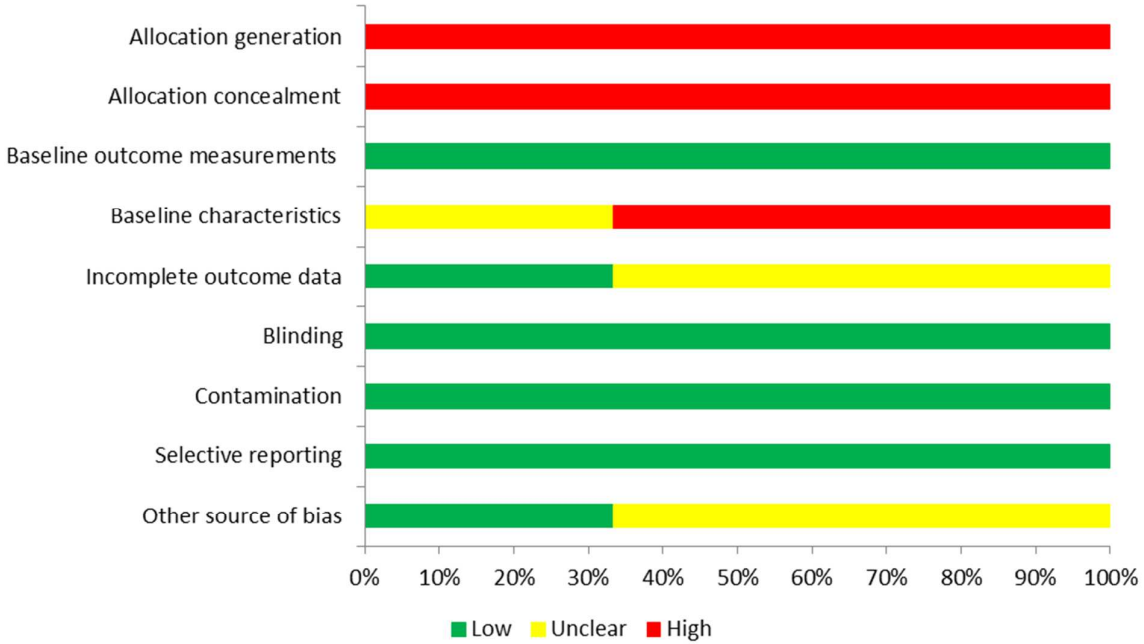

Table 1: Summary of impact analysis studies of CPRs relevant to primary care

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)
Auleley, 1997, France (14)	Ottawa ankle rule Sensitivity 100% (95-100%), Specificity 50% (46-55%) Cluster RCT	4980, ≥ 18 years, emergency departments of 5 Paris university teaching hospitals	**Intervention:** educational intervention to encourage CPR use (i.e. posters, pocket cards, and data forms) **Post-intervention:** only posters alone used to sustain the intervention effect. **Comparison:** Usual care	**Physician behaviour:** Referral for radiography (ankle/foot)	Relative reduction intervention site: 22.4% (95% CI 19.8-24.9), control group increase of 0.5% (95% CI 0-1.4).
Cameron, 1999, Canada, (18)	Ottawa Ankle Rule Sensitivity 100% (95-100), Specificity 50% (46-55%) Controlled before-after	1648, ≥18 years, Male 885, Female 763, Mean age 38 (18-91), emergency departments in 10 hospitals	**Group A:** little or no prior use of the CPR and educational intervention (educational meeting, posters, pocket cards and patient information leaflets) **Group B:** some prior use of the CPR and educational intervention **Group C:** active local implementation of the CPR and no educational intervention.	**Physician behaviour:** Referral for ankle X-ray	No reduction referral for ankle X-rays: intervention before 73%, after 78%, p=0.11, control: before 75%, after 65%, p=0.022

Stiell, 1994, Canada, ER(15)	Ottawa ankle rule Controlled before-after Sensitivity 100% (95-100), Specificity 50% (46-55%),	2342, ≥ 18 years, emergency departments of 2 hospitals	**Intervention:** educational intervention to encourage CPR use (i.e. lecture, pocket cards, and posters) **Post-intervention:** posters remained in ER **Comparison:** Usual care	**Physician behaviour:** Referral for radiography (ankle/foot)	*Ankle x-ray:* Relative reduction 28% in intervention group, increase of 2% in control group (p<0.001). *Foot X-ray:* Relative reduction of 14 % intervention group, increase of 13% in control group (p<0.05).
Boutis, 2013, Canada, ER(19)	Low Risk Ankle Rule Sensitivity 100% [93.3-100) Specificity NR ITS	2151, children aged 3-16, emergency departments of six hospitals	**Phase 1:** no intervention **Phase 2:** educational interventions to encourage CPR use (i.e. physician education, pocket cards, posters) and CDSS **Phase 3:** CDSS only **Comparison:** Usual care	**Physician behaviour:** Referral for ankle X-ray	Relative reduction in ankle x-rays in intervention sites compared to control sites. RR: 21.9% (95% CI 15.2-28.6)
Stiell, 1997, Canada, ER(16)	Ottawa Knee Rule Sensitivity 100% (94-100), Specificity 49% (46-52%), Controlled before-after	3907, ≥ 18 years, emergency departments of 4 hospitals (2 community and 2 teaching)	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters). **Comparison:** Usual care	**Physician behaviour:** Referral for knee radiography	Relative reduction of 26.4% of patients referred for knee x-ray in intervention group (77.6% vs. 57.1% (p<0.001), vs. relative reduction of 1.3% in control group (76.9% vs. 75.9%, p=0.6)
Stiell, 2009, Canada, ER(17)	Canadian C-spine Rule Sensitivity 99% (96-	11824, ≥ 16 years, emergency departments of 6 hospitals	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters) and	**Physician behaviour:** Diagnostic imaging rate of cervical spine	Relative reduction of 12.8% for cervical spine imaging (95% CI 9-16%) intervention group. Control group showed a relative increase of 12.5%

	100%), Specificity 45% (44-46%) Cluster RCT		CDSS at point of requesting imaging **Comparison:** Usual care		(95% CI 7-18%)
McIsaac, 2002, Canada, Primary care(28)	McIsaac Sensitivity 83% (no CIs), Specificity 94% (no CIs) RCT	621, ≥ 3 years, general practice, 97 participating GPs,	**Intervention:** mailed educational intervention (published score with summary explanation with pocket card). Physicians were provided with a sticker to apply to the encounter form that listed the score and management approach. **Comparison:** Physicians only received the education material.	**Physician behaviour:** Unnecessary antibiotic prescriptions (negative throat swab)	Non-significant difference intervention vs. control groups in unnecessary antibiotic prescription (20.4% vs. 16.1%, p=0.29)
McIsaac, 1998, Canada, Primary care(27)	Centor score Sensitivity 90% (no CIs), Specificity 92% (no CIs) RCT	396, ≥ 15 years, general practice, 450 participating GPs	**Intervention:** mailed CPR with summary explanation and patient information. Physicians asked to complete an encounter form. **Comparison:** mailed educational intervention and a control form with no score or management actions.	**Physician behaviour**: Antibiotic prescription	Non-significant reduction in antibiotic prescription in intervention group (27.8%) vs. control (35.7%) (p=0.09)
McGinn,	1) Walsh rule for	168 Primary care	**Intervention:** education	**Physician behaviour**:	Intervention group significantly less

2013, USA, (31)	streptococcal pharyngitis 2) Heckerling rule for pneumonia Walsh rule: c-statistic: 0.71 [95% CI, 0.67-0.74) Heckerling rule: c-statistic 0.82 (0.74-0.9) RCT	providers, 2 large academic ambulatory care centres in New York	session and computerised CDSS with CPRs embedded promoting physician to calculate scores of both CPRs and receive management recommendations. **Comparison:** Usual care with background information on CPRs	Change in antibiotic prescription	likely to order antibiotics than control (age-adjusted RR, 0.74; 95% CI, 0.60-0.92). Absolute risk difference 9.2%.
Worrall, 2007, Canada, (29)	Modified Centor score Sensitivity 90% (no CIs), Specificity 92% (no CIs) RCT	533, ≥ 19 years, 37 practices in eastern Newfoundland CPR:170 RADT: 120 RADT+CPR:102 Control:141	**CPR group**: decision rules only **RADT group**: rapid antigen test only **RADT+CPR group**: decision rules and antigen test combined **Comparison:** Usual care	**Physician behaviour**: Prescribing rate of antibiotics	Prescription rates: CPR alone - 55% RADT - 27% (NS) RADT+CPR -38% (p<0.001) Control: 58%
Little, 2013, UK (30)	FeverPAIN c-statistic: 0.71 RCT	631, ≥ 3 years, general practice (48 UK practices)	**CPR group:** CPR was applied and antibiotic prescribed according to the score. **CPR+RADT group:** CPR was applied and antibiotic prescribed or RADT carried out according to the score.	**Patient behaviour:** Patient reported symptom severity days 2-4 after consultation on a 7-point Likert scale	Greater improvements in symptom severity for CPR group compared to control (−0.33, 95% CI −0.64 to −0.02)

			Comparison: Delayed prescribing		
Pozen, 1984, USA, ER(20)	Pozen score for chest pain Sensitivity 94% (no CIs), Specificity 78% (no CIs) ITS	2320, aged ≥30 male and ≥40 female, emergency departments of 6 US hospitals	**Intervention:** Research assistant presented physicians with the CPR probability score. **Comparison:** Usual care, the CPR probability was calculated but not presented to the physicians.	**Physician behaviour:** Appropriate admission/discharge	30% relative reduction in patients admitted to CCU who did not have acute coronary syndrome
Kline, 2009, USA, ER(21)	Kline chest pain CPR c-statistic 0.74 (0.65-0.82) RCT	369 adults presenting with chest pain, one emergency room in an academic urban US hospital	**Intervention:** Clinicians and patients received a printout of CPR result displayed numerically and graphically. **Comparison:** Usual care, no printout was provided to clinicians or patients.	**Physician behaviour**: Hospital admission with no significant cardiovascular diagnosis	No significant decrease for patients admitted with no CVD diagnosis: 11% vs. 5% (95% CI -0.2%-11%), p=0.059
Persell, 2012, primary care(26)	Framingham risk estimate and global cardiovascular risk score Cluster RCT	N=14 physicians, n=218 adult patients randomised to intervention, n=15 physicians, n=217 adults patients randomised to control, US primary care	**Intervention**: Individualised CVD risk estimate posted to high-risk patients and their physicians alerted by secure email Control: usual care	**Patient:** Reduction in LDL-cholesterol level by 30mg/dl	No difference in the primary outcome (11% vs. 11.1% OR 0.99, 95% CI 0.56, 1.74, p=0.96) but intervention patients were more likely to receive a prescription for a statin (11.9% vs. 6%, OR 2.13, 95% CI 1.05, 4.32, p=0.038)
Grover	Framingham risk	N=3,053 adults	**Intervention:** Patients	**Patient outcomes:**	1. Statistically significant reduction in

2007 and 2008, primary care(24, 25)	score RCT	mean age 56.4, male 66.9%, n=230 primary care physicians, 10 provinces in Canada primary care	identified as high risk and randomised to intervention had their individualised coronary risk profile discussed **Control:** usual care, coronary risk profile withheld	1. Reduction in LDL-cholesterol level 2. Reduction in BP	LDL and total cholesterol-HDL ratio in intervention vs. control and patients were more likely to reach lipid targets 2. Patients in intervention group were more likely to receive appropriate antihypertensive treatment and more likely to start or modify treatment
Hall, 2003, UK, (22)	New Zealand cardiovascular risk score NR Pilot RCT	323, aged 35-75 years, patients with no history of cardiovascular or renal disease, one UK hospital outpatient department (OPD) clinic	**Intervention:** Risk scores were clearly documented at the front of the notes of patients. **Comparison:** Usual care	**Physician behaviour:** 1. Prescription of risk modifying drugs 2. Management of CVD risk factors	3. No significant between group differences: change in diabetes treatment 42% (95% CI 34-50) vs. 58 (95 CI 29-45%), change in antihypertensive drugs 26 (95% CI 10-22%) vs. 10% (95% CI 5-16%), change in lipid lowering drugs: 12% (7-17%) vs. 9% (95% CI 4-14%) 4. Referral to dietician 10% (95% CI 6-15%) vs. 13% (95% CI 7-19%)
Hanon, 2000, France (23)	Framingham risk score NR RCT	1243, aged 18 -75 years with hypertension attending a general physician	**Intervention:** Physicians knowledge of the calculated risk score. **Comparison:** Usual care	**Patient and Physician behaviour:** Change in BP, patients prescribed dual therapy	No difference in BP (patients with BP <140/90 mmHg intervention: 64%, control 62%) or % patients on dual therapy (41% intervention vs. 46% control)
Stiell, 2010, Canada, ER(32)	CT head rule Sensitivity 100% (96-100%), Specificity 51%	4531, alert and stable adults with minor head injury aged ≥ 16 years, 12	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters) and real-	**Physician behaviour:** Proportion of patients referred for CT imaging	Increased proportion of patients referred for CT imaging intervention: before: 62.8%, after: 76.2% (difference: 13.3% (95% CI 9.7%-

	(48-53%) Cluster RCT	emergency departments in three provinces of Canada (6 teaching sites, 6 community sites)	time reminder at point of requesting imaging **Comparison:** Usual care		17.0%) Control: before: 67.5%, after: 74.1% (difference: 6.7% (95% CI 2.6-10.8)

***NR=Not reported, **NA=Non-applicable, ***NS=Non-significant, $ CPR predictive accuracy as referenced in the impact analysis study**

Table 2: Table of estimated effect sizes for impact analysis studies

Author, Year CPR name	Study design (n)	Sample size calculation reported (n)	Primary outcome	Effect size: Crude odds ratio (OR) of improvement in primary outcome in intervention versus control (95% CI)	Absolute risk reductions (95% CI)
Auleley, 1997(14) Ottawa ankle rule	Cluster RCT (4980)	Yes (900)	**Physician behaviour:** Referral for radiography (ankle/foot)	Crude OR 0.03 (0.01-0.06)	22.8% (20.0-25.7)
Stiell, 1994(15) Ottawa ankle rule	Controlled before-after (2342)	NA	**Physician behaviour:** Referral for radiography (ankle/foot)	*Ankle X-ray:* Crude OR 0.11 (0.08-0.16) *Foot X-ray:* Crude OR 0.73 (0.57-0.94)	33.4% (28.9-37.9) 6.6% (1.1-11.7)
Cameron, 1999(18) Ottawa Ankle Rule	Controlled before-after (1648)	NA	**Physician behaviour:** Referral for ankle X-ray	Crude OR 0.96 (0.60-1.55)	0.8% (-8.5 – 9.8)
Boutis, 2013(19) Low Risk Ankle Rule	ITS (2151)	NA	**Physician behaviour:** Referral for ankle X-ray	[#]NA	[#]NA
Stiell, 1997(16) Ottawa Knee Rule	Controlled before-after (3907)	NA	**Physician behaviour:** Referral for knee radiography	Crude OR 0.42 (0.35-0.51)	18.8% (14.7-22.9)
Stiell, 2009(17) Canadian C-spine Rule	Cluster RCT (11824)	Yes (9600)	**Physician behaviour:** Diagnostic imaging rate of cervical spine	Crude OR 0.82 (0.74-0.90)	5% (2.5-7.5)
Pozen, 1984(20) Pozen score for	ITS (2320)	NA	**Physician behaviour:** Appropriate admission	[#]NA	[#]NA

chest pain					
Kline, 2009(21) Kline chest pain CPR	RCT (369)	Yes (400)	**Physician behaviour**: Admission with no significant cardiovascular diagnosis	Crude OR 0.47 (0.22-1.04)	5.4% (-0.2 – 10.9)
Persell, 2012(26) Framingham risk score	Cluster RCT (425)	Yes (406)	**Patient:** Proportion of patients with a reduction in LDL-cholesterol level by 30mg/dl	Crude OR 0.99 (0.55-1.81)	0.1% (-0.0 – 0.0)
Grover, 2007 and 2008 (24, 25) Framingham risk score	RCT (3053)	Yes (3000)	**Patient:** 1. Reduction in LDL-cholesterol level	*Reduction in LDL-cholesterol level: mean difference −0.33mg/dl (−0.5.4 to −1.1; P=0.02)*	NA
Hall, 2003(22) New Zealand cardiovascular risk score	Pilot RCT (323)	NA	**Physician behaviour:** Prescription of risk modifying drugs, management of CVD risk factors	*Diabetes treatment:* Crude OR 1.28 (0.82-2.01) *Antihypertensive drugs:* Crude OR 1.62 (0.84-3.12) *Lipid lowering drugs:* Crude OR 1.48 (0.72-3.04) *Referral to dietician:* Crude OR 0.78 (0.40-1.54)	-6.0% (-16.6-4.7) -5.5% (-12.9-1.9) -3.7% (-10.3-3.0) 2.5% (-4.47-9.57)
Hanon, 2000(23) Framingham risk score	RCT (1243)	No	**Patient and Physician behaviour:** BP, patients prescribed dual therapy	*Normal BP:* Crude OR 1.09 (0.87-1.38) *Dual therapy:* Crude OR 0.82 (0.65-1.02)	- 2.1% (-7.4-3.3) 4.9% (-0.6-10.4)
McIsaac, 2002(28) McIsaac	RCT (621 patients, 97	Yes (850 patients, 85 physicians)	**Physician behaviour:** Unnecessary antibiotic prescriptions (negative throat swab)	Crude OR 0.71 (0.47-1.08)	4.9% (-1.1 – 10.9)

	physicians)				
McIsaac, 1998(27) Centor	RCT (396)	Yes (800)	**Physician behaviour**: Antibiotic prescription	Crude OR 0.69 (0.45-1.05)	8.1% (-1.0-17.3)
McGinn, 2013(31) 1) Walsh rule (streptococcal pharyngitis) 2) Heckerling rule (pneumonia)	RCT (168)	No	**Physician behaviour**: Change in antibiotic prescription	Crude OR 0.66 (0.50-0.86)	9.3% (3.2 – 15.3)
Worrall, 2007(29) Modified Centor score	RCT (533)	Yes (196)	**Physician behaviour**: Prescribing rate of antibiotics	Crude OR 0.89 (0.57-1.40)	2.9% (-8.2 – 13.9)
Little, 2013(30) FeverPAIN	RCT (6131)	Yes (909)	**Patient behaviour:** Patient reported symptom severity	Adjusted mean difference−0.33 (−0.64 to −0.02; P=0.04)	NA
Stiell, 2010(32) CT head rule	Cluster RCT (4531)	Yes (4800)	**Physician behaviour:** Proportion of patients referred for CT imaging	Crude OR 0.81 (0.69-0.96)	4.7% (1.0-8.4)

Appendix 1: Journal selection criteria and search strategy

Thirty journals relevant to primary care listed below were purposively chosen through various methods, including:

(1) The ISI Web of Knowledge Journal Citation Reports, listed under the category ‘‘medicine, general, and internal’’ and mentioned primary care, family medicine, or family practice in their title

(2) The 15 highest-ranked journals according to impact factor ratings in this same category

(3) Specialist journals that are known to publish CPRs (based on type of journal/expert opinion)

(4) A list of recommendations generated by an information specialist

(5) An expert consensus meeting attended by primary care clinicians, academics, and information specialists. (T.F., B.D.D., S.M.S., K.K.O.B., P.J.M., and B.Mc.G.)

Journal titles

Academic Emergency Medicine

Family Medicine

American Family Physician

Family Practice

American Journal of Medicine

Journal of American Medical Association

Annals of Emergency Medicine

Journal of the American Board of Family Medicine

Annals of Family Medicine

Journal of Clinical Epidemiology

Annals of Internal Medicine

Journal of Family Practice

Annals of Medicine

Journal of Internal Medicine

Annual Review of Medicine

Lancet

Archives of Internal Medicine

Medical Care

BMC Family Practice

Medical Decision Making

British Medical Journal

Medicine

British Journal of General Practice

New England Journal of Medicine

Canadian Family Physician

Public Library of Science Medicine

Canadian Medical Association Journal

Primary Care

Cochrane Database Systematic Reviews

Scandinavian Journal of Primary Health Care

Search on MEDLINE (PubMed)

Search 1: 30 journals, no limits

("American family physician"[Jour] OR "Annals of family medicine"[Jour] OR "The British journal of general practice : the journal of the Royal College of General Practitioners"[Jour] OR "Canadian family physician Medecin de famille canadien"[Jour] OR "Family medicine"[Jour] OR "Family practice"[Jour] OR "Journal of the American Board of Family Medicine : JABFM"[Jour] OR "The Journal of family practice"[Jour] OR "Primary care"[Jour] OR "Scandinavian journal of primary health care"[Jour] OR "BMC family practice"[Jour] OR "The New England journal of medicine"[Jour] OR "Lancet"[Jour] OR "JAMA : the journal of the American Medical Association"[Jour] OR "Annals of internal medicine"[Jour] OR "Annual review of medicine"[Jour] OR "PLoS medicine"[Jour] OR "British medical journal"[Jour] OR "Archives of internal medicine"[Jour] OR "Canadian Medical Association journal"[Jour] OR "Annals of medicine"[Jour] OR "The American journal of medicine"[Jour] OR "Medicine (Baltimore)"[Journal] OR "Cochrane database of systematic reviews (Online)"[Jour] OR "Journal of clinical epidemiology"[Jour] OR "Medical decision making : an international journal of the Society for Medical Decision Making"[Jour] OR "Medical care"[Jour] OR "Academic emergency medicine : official journal of the Society for Academic Emergency Medicine"[Jour] OR "Annals of emergency medicine"[Jour] OR "Journal of Internal Medicine"[Jour]) OR ("Br Med J"[Journal] OR "Br Med J (Clin Res Ed)"[Journal] OR "BMJ"[Journal] OR ("british"[All Fields] AND "medical"[All Fields] AND "journal"[All Fields]) OR "british medical journal"[All Fields]) OR ("Can Med Assoc J"[Journal] OR "CMAJ"[Journal] OR ("canadian"[All Fields] AND "medical"[All Fields] AND "association"[All Fields] AND "journal"[All Fields]) OR "canadian medical association journal"[All Fields])

AND

Search 2: CPR search terms

"clinical prediction"[All Fields] OR "clinical model*"[All Fields] OR "clinical score*"[All Fields] OR "decision rule*"[All Fields] OR "diagnostic accuracy"[All Fields] OR "diagnostic rule*"[All Fields] OR "diagnostic score*"[All Fields] OR "diagnostic value"[All Fields] OR "predictive outcome*"[All Fields] OR "predictive rule*"[All Fields] OR "predictive score*"[All Fields] OR "predictive value"[All Fields] OR "predictive risk*"[All Fields] OR "prediction outcome*"[All Fields] OR "prediction rule*"[All Fields] OR "prediction score*"[All Fields] OR "prediction value*"[All Fields] OR "prediction risk*"[All Fields] OR "risk assessment"[All Fields] OR "risk score*"[All Fields] OR (validation[All Fields] AND decision[All Fields]) OR (validation[All Fields] AND rule[All Fields]) OR "validation score*"[All Fields] OR (derivation[All Fields] AND validation[All Fields]) OR (("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) AND ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields])) OR (("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "symptoms"[All Fields] OR "diagnosis"[MeSH Terms] OR "symptoms"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "signs"[All Fields] OR "diagnosis"[MeSH Terms] OR "signs"[All Fields]))

AND

Search 3: limit to humans

NOT

Search 4: Publication type

(News[ptyp] OR Comment[ptyp] OR Editorial[ptyp] OR Case Reports[ptyp] OR Dictionary[ptyp])

AND

Search 5: Limit to year. Searches were run by year from 1980 to 2013

Appendix 2: Detailed summary of impact analysis studies of CPRs relevant to primary care

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
Musculoskeletal							
Auleley, 1997, France (14)	Ottawa ankle rule Sensitivity 100% (95-100%), Specificity 50% (46-55%), LR+=2.0 (1.8-2.2) Cluster RCT	4980, ≥ 18 years, emergency departments of 5 Paris university teaching hospitals Preintervention:2218, (male 620, female 1086), mean age 35 (18-92) Intervention: 1911, (male 546, female 463), mean age 34 (18-94) Post-intervention: 851,	**Intervention:** educational intervention to encourage CPR use (i.e. posters, pocket cards, and data forms) **Post-intervention:** only posters alone used to sustain the intervention effect. **Comparison:** Usual care	**Physician behaviour:** Referral for radiography (ankle/foot)	Relative reduction intervention site: 22.4% (95% CI 19.8-24.9), control group increase of 0.5% (95% CI 0-1.4). Post-intervention x-ray requests (83.1% vs. 98%). Fracture prevalence rate: 12.4% control, 12.3%	1. Missed fractures 2. Patient satisfaction	1. More missed fractures in intervention (n=3) than control (n=0) 2. Greater patient satisfaction in control (98%) than intervention (96%)

		other demographics not presented			intervention		
Cameron, 1999, Canada, (18)	Ottawa Ankle Rule Sensitivity 100% (95-100), Specificity 50% (46-55%), LR=2.0 (1.8-2.2) Controlled before-after	1648, ≥18 years, Male 885, Female 763, Mean age 38 (18-91), emergency departments in 10 hospitals Group A: 516 Group B: 567 Group C: 565	**Group A:** little or no prior use of the CPR and educational intervention (educational meeting, posters, pocket cards and patient information leaflets) **Group B:** some prior use of the CPR and educational intervention **Group C:** active local implementation of the CPR and no educational intervention.	**Physician behaviour:** Referral for ankle X-ray	No reduction referral for ankle X-rays: intervention before 73%, after 78%, p=0.11, control: before 75%, after 65%, p=0.022 Fracture prevalence rate 11.7%	NA	NA
Stiell, 1994, Canada, ER(15)	Ottawa ankle rule Controlled before-after Sensitivity 100% (95-100), Specificity 50% (46-55%), LR=2.0 (1.8-2.2)	2342, ≥ 18 years, emergency departments of 2 hospitals Intervention Before: 657 After: 551 Male 51% Mean age 37 (18-92) Control	**Intervention:** educational intervention to encourage CPR use (i.e. lecture, pocket cards, and posters) **Post-intervention:** posters remained in ER **Comparison:** Usual care	**Physician behaviour:** Referral for radiography (ankle/foot)	*Ankle x-ray:* Relative reduction 28% in intervention group, increase of 2% in control group (p<0.001). *Foot X-ray:* Relative reduction of 14 % intervention	Difference in intervention between patients with X-ray vs non X-ray 1. Time spent in ER (minutes) 2. Subsequent physician visits 3. Subsequent ankle x-ray 4. Mean days off work	1. Less time in ED for non-X-ray: 80 vs. 116 minutes. 2. More subsequent visits for X-ray: 20% vs 7%, p<0.001 3. Subsequent X-ray: same 5% 4. More days off in X-ray group: 5 vs 3, p<0.001 5. Lower costs for

		Before:541 After:593 Male 54% Mean age 36 (18-86)			group, increase of 13% in control group (p<0.05). Fracture prevalence: Before 14.7% After: 17.1%	5. Mean cost ($) 6. Patient satisfaction	non-X-ray: $62 vs. $173. p<0.0001 6. Satisfaction similar: 95% vs. 96%.
Boutis, 2013, Canada, ER(19)	Low Risk Ankle Rule Sensitivity 100% [93.3-100) Specificity NR ITS	2151, children aged 3-16, emergency departments of six hospitals Intervention: 1055, Male 46%, Mean age 12.3 Control: 1096, Male 49%, Mean age 13.4	**Phase 1:** no intervention **Phase 2:** educational interventions to encourage CPR use (i.e. physician education, pocket cards, posters) and CDSS **Phase 3:** CDSS only **Comparison:** Usual care	**Physician behaviour:** Referral for ankle X-ray	Relative reduction in ankle x-rays in intervention sites compared to control sites. RR: 21.9% (95% CI 15.2-28.6) Fracture prevalence rate: NR	1. Significant missed fractures 2. Length of stay (hours) 3. Physician satisfaction 4. Patient satisfaction	1. RR: 0.008 (-0.004 – 0.02) 2. RR: 0.4 (-0.2 – 0.9) 3. RR: 8.3 (-16.9 – 0.4) 4. RR: -11.5 (-23.4 – 0.5)
Stiell, 1997, Canada, ER(16)	Ottawa Knee Rule Sensitivity 100% (94-100), Specificity 49% (46-	3907, ≥ 18 years, emergency departments of 4 hospitals (2 community and 2 teaching) Intervention	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters). **Comparison:** Usual care	**Physician behaviour:** Referral for knee radiography	Relative reduction of 26.4% of patients referred for knee x-ray in intervention group (77.6% vs.	Difference in intervention between patients with X-ray vs non X-ray 1. Time spent in ER (minutes) 2. Subsequent	1. Less time in ED for non-X-ray: 86 vs. 119 minutes. 2. More subsequent visits for X-ray: 52.4% vs. 38.3% 3. More subsequent X-ray in non X-ray

	52%), LR+=2.0 (1.7-2.1) Controlled before-after	before: 982 after: 1063 Male: 54% Mean age: 39 (18-101) Control before:962 after: 900 Male: 54% Mean age: 41 (18-97)			57.1% (p<0.001), vs. relative reduction of 1.3% in control group (76.9% vs. 75.9%, p=0.6) Fracture prevalence rate: Intervention: 5.8% Control: 10.3%	physician visits 3. Subsequent ankle x-ray 4. Mean days off work 5. Mean cost ($) 6. Patient satisfaction	group: 6.9% vs. 1.7% 4. More days off in X-ray group: 6 vs. 3 5. Lower costs for non-X-ray: $80 vs. $183 6. Satisfaction similar: 96% vs. 98%.
Stiell, 2009, Canada, ER(17)	Canadian C-spine Rule Sensitivity 99% (96-100%), Specificity 45% (44-46%), LR+=1.8 (1.7-1.9) Cluster RCT	11824, ≥ 16 years, emergency departments of 6 hospitals Intervention Before: 3267 After: 3628 Male: 50%, Mean age 39 (16-100) Control Before: 2413 After: 2516 Male: 48% Mean age: 38 (16-102)	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters) and CDSS at point of requesting imaging **Comparison:** Usual care	**Physician behaviour:** Diagnostic imaging rate of cervical spine	Relative reduction of 12.8% for cervical spine imaging (95% CI 9-16%) intervention group. Control group showed a relative increase of 12.5% (95% CI 7-18%) Prevalence rate clinically important cervical spine	1. Serious adverse outcomes 2. Physician accuracy in using the rule 3. Sensitivity of rule	1. No serious adverse outcomes 2. 82.9% accurate interpretation rule 3. Se: 100% [85-100]

		Postintervention: 5800			injury (fracture/dislocation/ligamentous instability): Before: 1.6% After: 0.8%		
Respiratory							
McIsaac, 2002, Canada, Primary care(28)	McIsaac Sensitivity 83% (no CIs), Specificity 94% (no CIs) LR+=13.8 RCT	621, ≥ 3 years, general practice, 97 participating GPs, Intervention: 304 Mean age: 27.5 Female: 65.4% Control: 317 Mean age: 28.1, Female: 69.1%	**Intervention:** mailed educational intervention (published score with summary explanation with pocket card). Physicians were provided with a sticker to apply to the encounter form that listed the score and management approach. **Comparison:** Physicians only received the education material.	**Physician behaviour:** Unnecessary antibiotic prescriptions (negative throat swab)	Non-significant difference intervention vs. control groups in unnecessary antibiotic prescription (20.4% vs. 16.1%, p=0.29) Prevalence of swab confirmed diagnosis streptococcal throat infection: Control 12.6%, Intervention: 7.9%	Overall antibiotic use	No difference between groups in overall antibiotic use (28.1% vs. 27.9%, p=0.97)
McIsaac, 1998, Canada, Primary	Centor score Sensitivity 90% (no CIs),	396, ≥ 15 years, general practice, 450 participating GPs	**Intervention:** mailed educational intervention (published score	**Physician behaviour**: Antibiotic prescription	Non-significant reduction in antibiotic prescription in	Antibiotic prescribing per estimated Group A streptococcal	In score category 1 the antibiotic prescription rates were statistically significant. 16.2% in

care(27)	Specificity 92% (no CIs) LR+=11.3 RCT	Intervention: 184 Mean age: 31.6 Male: 41.2% Control: 212 Mean age: 31.5 Male 40.1%	with summary explanation and patient information). Physicians asked to complete an encounter form with symptom check list, CPR score and management actions. **Comparison:** mailed educational intervention and a control form with no score or management actions.		intervention group (27.8%) vs. control (35.7%) (p=0.09)	prevalence calculation	control vs. 3.6% in intervention.
McGinn, 2013, USA, (31)	1) Walsh rule for streptococcal pharyngitis 2) Heckerling rule for pneumonia Walsh rule: c-statistic: 0.71 [95% CI, 0.67-0.74)	168 Primary care providers, 2 large academic ambulatory care centres in New York 984 Patients **Intervention**:586 Mean age: 43 Female: 24% **Control:**398	**Intervention:** education session and computerised CDSS with CPRs embedded promoting physician to calculate scores of both CPRs and receive management recommendations. **Comparison:** Usual	**Physician behaviour**: Change in antibiotic prescription	Intervention group significantly less likely to order antibiotics than control (age-adjusted RR, 0.74; 95% CI, 0.60-0.92). Absolute risk difference 9.2%.	1. Rate of chest radiographs 2. Rate of rapid streptococcal tests 3. Number throat cultures ordered	1. Intervention less likely to order chest radiographs (RR 0.89; 95% CI, 0.55-1.46) 2. Intervention significantly less likely to order rapid streptococcal test (RR 0.75; 95% CI, 0.58-0.97) 3. Intervention significantly less

	Heckerling rule: c-statistic 0.82 (0.74-0.9) RCT	Mean age: 49 Female: 23%	care with background information on CPRs				likely to do throat cultures (RR 0.55; 95% CI, 0.35-0.86)
Worrall, 2007, Canada, (29)	Modified Centor score Sensitivity 90% (no CIs), Specificity 92% (no CIs), LR+=11.3 RCT	533, ≥ 19 years, 37 practices in eastern Newfoundland CPR:170 RADT: 120 RADT+CPR:102 Control:141 Gender and age patient demographics NR	**CPR group**: decision rules only **RADT group**: rapid antigen test only **RADT+CPR group**: decision rules and antigen test combined **Comparison:** Usual care	**Physician behaviour**: Prescribing rate of antibiotics	Prescription rates: CPR alone - 55% RADT - 27% (NS) RADT+CPR -38% (p<0.001) Control: 58%	Types of antibiotics prescribed	Amoxicillin most commonly prescribed (47%), followed by penicillin (20%)
Little, 2013, UK (30)	FeverPAIN c-statistic: 0.71 RCT	631, ≥ 3 years, general practice (48 UK practices) CPR group:211 Female: 60% Mean age: NR	**CPR group:** CPR was applied and antibiotic prescribed according to the score. **CPR+RADT group:** CPR was applied and	**Patient behaviour:** Patient reported symptom severity days 2-4 after consultation on a 7-point Likert scale	Greater improvements in symptom severity for CPR group compared to control (−0.33, 95% CI −0.64 to −0.02)	1. Antibiotic prescribing 2. Symptom duration 3. Medicalising beliefs 4. Return consultations	1. Lower use of antibiotics in CPR group than control (RR 0.71, 0.50 to 0.95) 2. Symptom resolution was significantly faster in

		CPR+RADT group: 213 Female: 65% Mean age: NR Delayed prescribing: 207 Female:67% Mean age: NR	antibiotic prescribed or RADT carried out according to the score. **Comparison:** Delayed prescribing			5. Suppurative complications	the CPR group (hazard ratio 1.30, 95% CI 1.03 to 1.63) 3. No significant difference in beliefs 4. No significant difference in return to GP 5. No suppurative complications.
Cardiovascular							
Pozen, 1984, USA, ER(20)	Pozen score for chest pain Sensitivity 94% (no CIs), Specificity 78% (no CIs) LR+=4.3 ITS	2320, aged ≥30 male and ≥40 female, emergency departments of 6 US hospitals Intervention: 1288 Control: 1032 Overall mean age 62 Male: 62%	**Intervention:** Research assistant presented physicians with the CPR probability score. **Comparison:** Usual care, the CPR probability was calculated but not presented to the physicians.	**Physician behaviour:** Appropriate admission/discharge	30% relative reduction in patients admitted to CCU who did not have acute coronary syndrome Overall prevalence of cardiac ischaemia 32% intervention, 29% control	Diagnostic accuracy of acute myocardial infarction	Overall diagnostic accuracy significantly higher in intervention group. Intervention: 83.4%, control 79.6% (p=0.002) There was no significant difference in sensitivity. (intervention: 94.5%, control 95.3, NS)
Kline, 2009, USA, ER(21)	Kline chest pain CPR c-statistic	369 adults presenting with chest pain, one emergency room	**Intervention:** Clinicians and patients received a printout of CPR	**Physician behaviour**: Hospital admission with no significant cardiovascular	No significant decrease for patients admitted with	Delayed/missed diagnosis of ACS, thoracic imaging with a negative	Significant decrease in thoracic imaging: 16/184 intervention vs. 36/185 control, (95% CI 3.8%-

	0.74 (0.65-0.82) RCT	in an academic urban US hospital Intervention: 185 Female: 64% Mean age: 46 Control 184 Female: 61% Mean age: 46	result displayed numerically and graphically. **Comparison:** Usual care, no printout was provided to clinicians or patients.	diagnosis	no CVD diagnosis: 11% vs. 5% (95% CI -0.2%-11%), p=0.059 Prevalence of acute coronary syndrome (ACS): 2.1%	result, median length of stay, patient satisfaction, readmission	18%, p=0.004), higher patient satisfaction: (90/184 intervention rate vs. 70/185 control 'very satisfied' (95% CI 0.9%-21%), p=0.01, decreased readmission rate/return to ER: 4% intervention vs. 11% controls (95% CI 2.5%-13.2%), p=0.001, no difference in length of hospital stay: 11.4 hours control vs. 9.2 hours intervention, p=0.36.
Persell, 2012, primary care(26)	Framingham risk estimate and global cardiovascular risk score Cluster RCT	N=14 physicians, n=218 adult patients randomised to intervention, n=15 physicians, n=217 adults patients randomised to control, US primary care	**Intervention**: Individualised CVD risk estimate posted to high-risk patients and their physicians alerted by secure email Control: usual care	**Patient:** Reduction in LDL-cholesterol level by 30mg/dl	No difference in the primary outcome (11% vs. 11.1% OR 0.99, 95% CI 0.56, 1.74, p=0.96)	Receipt of a statin prescription	Intervention patients were more likely to receive a prescription for a statin (11.9% vs. 6%, OR 2.13, 95% CI 1.05, 4.32, p=0.038)
Grover 2007 and 2008, primary	Framingham risk score RCT	N=3,053 adults mean age 56.4, male 66.9%, n=230 primary	**Intervention:** Patients identified as high risk and randomised to	**Patient outcomes:** 1. Reduction in LDL-cholesterol level	Statistically significant reduction in LDL and total	Reduction in BP	Patients in intervention group were more likely to receive appropriate antihypertensive

care(24, 25)		care physicians, 10 provinces in Canada primary care	intervention had their individualised coronary risk profile discussed **Control:** usual care, coronary risk profile withheld		cholesterol-HDL ratio in intervention vs. control and patients were more likely to reach lipid targets		treatment and more likely to start or modify treatment
Hall, 2003, UK, (22)	New Zealand cardiovascular risk score NR Pilot RCT	323, aged 35-75 years, patients with no history of cardiovascular or renal disease, one UK hospital outpatient department (OPD) clinic Experimental: 162 Control:161 Age and gender demographics: NR	**Intervention:** Risk scores were clearly documented at the front of the notes of patients. **Comparison:** Usual care	**Physician behaviour:** 3. Prescription of risk modifying drugs 4. Management of CVD risk factors	5. No significant between group differences: change in diabetes treatment 42% (95% CI 34-50) vs. 58 (95 CI 29-45%), change in antihypertensive drugs 26 (95% CI 10-22%) vs. 10% (95% CI 5-16%), change in lipid lowering	Time to next OPD appointment	No difference in time to next OPD (24% in each group received OPD appointment in <6 months).

					drugs: 12% (7-17%) vs. 9% (95% CI 4-14%) 6. Referral to dietician 10% (95% CI 6-15%) vs. 13% (95% CI 7-19%)		
Hanon, 2000, France (23)	Framingham risk score NR RCT	1243, aged 18 -75 years with hypertension attending a general physician Mean age: 60 Male: 54%	**Intervention:** Physicians knowledge of the calculated risk score. **Comparison:** Usual care	**Patient and Physician behaviour:** Change in BP, patients prescribed dual therapy	No difference in BP (patients with BP <140/90 mmHg intervention: 64%, control 62%) or % patients on dual therapy (41% intervention vs. 46% control)	Physician estimation vs. Framingham risk equation calculated 10 year CVD risk	General physicians' calculation of CVD risk at 10 years has poor concordance with the Framingham risk model (35%).
Neurological							
Stiell, 2010, Canada, ER(32)	CT head rule Sensitivity 100% (96-100%), Specificity 51% (48-53%),	4531, alert and stable adults with minor head injury aged ≥ 16 years, 12 emergency departments in three provinces of Canada (6	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters) and real-time reminder at point of	**Physician behaviour:** Proportion of patients referred for CT imaging	Increased proportion of patients referred for CT imaging intervention: before: 62.8%, after: 76.2%	1. Accuracy CPR 2. Number of clinically important brain injuries not identified at ER 3. Adverse	1. Sensitivity 100% [96-100%] 2. No missed brain injuries or adverse outcomes. 3. Deaths from brain injury: intervention: before: 0.1%, after:

	LR+=2.0 (1.8-2.3) Cluster RCT	teaching sites, 6 community sites) Intervention: Before: 1049 After:1531 Mean age: 37 (16-99) Male: 70% Control: Before: 876, After:1075 Mean age: 39 (16-97) Male: 71%	requesting imaging **Comparison:** Usual care		(difference: 13.3% (95% CI 9.7%-17.0%) Control: before: 67.5%, after: 74.1% (difference: 6.7% (95% CI 2.6-10.8)	outcomes	0.1%, control: before 0.3%, after: 0.1%

***NR=Not reported, **NA=Non-applicable, ***NS=Non-significant, $ CPR predictive accuracy as referenced in the impact analysis study**

Appendix 3: Uncontrolled before-after impact analysis CPR studies excluded from data analysis due to study design

Author, Year	CPR name	Type of study	Implementation	Predictive accuracy (reported), level of evidence	Type of outcome
Bessen, 2009 (35)	Ottawa ankle rule	Before-after	CPR only	Sensitivity 100% (95-100%), Specificity 50% (46-55%), LR=2.0 (1.8-2.2)	Physician behaviour
Stiell, 1995 (34)	Ottawa ankle rule	Before-after	CPR only	Sensitivity 100% (95-100%), Specificity 50% (46-55%), LR=2.0 (1.8-2.2)	Physician behaviour
Kerr, 2005 (36)	Canadian C-spine rule	Before-after	CPR only	Sensitivity 99% (96-100%), Specificity 45% (44-46%), LR+=1.8 (1.7-1.9)	Physician behaviour
Stanley, 2009 (37)	Glasgow Blatchford bleeding score	Before-after	CPR only	Sensitivity 99% (no CIs), Specificity 32% (no CIs), LR+-1.5	Physician behaviour + patient
Sultan, 2004 (38)	CT head rule	Before-after	CPR only	Sensitivity 100% (96-100%), Specificity 51% (48-53%), LR+=2.0 (1.8-2.3)	Physician behaviour

PRISMA 2009 Checklist

1Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	na
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5, 6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5,6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5,6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5,6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6, 7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	na
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1 and Appendix 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figure 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 1 and Appendix 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Figure 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	na
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12,13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

BMJ Open

Impact analysis studies of clinical prediction rules relevant to primary care: a systematic review

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2015-009957.R1
Article Type:	Research
Date Submitted by the Author:	13-Nov-2015
Complete List of Authors:	Wallace, Emma; Royal College of Surgeons in Ireland Medical School, HRB Centre for Primary Care Research Uijen, Maike; Radboud University, Medical school Clyne, Barbara; RCSI, HRB Centre for Primary Care Research Zarabzadeh, Atieh; RCSI, HRB Centre for Primary Care Research Keogh, Claire; RCSI, HRB Centre for Primary Care Research Galvin, Rose; University of Limerick, Department of Clinical Therapies Smith, Susan; RCSI, HRB Centre for Primary Care Research Fahey, Tom; RCSI, HRB Centre for Primary Care Research
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	General practice / Family practice, Epidemiology, Evidence based practice
Keywords:	risk prediction, clinical prediction rule, impact analysis

Title:

Impact analysis studies of clinical prediction rules relevant to primary care: a systematic review

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Abstract

Objectives: Following appropriate validation, clinical prediction rules (CPRs) should undergo impact analysis to evaluate their effect on patient care. The aim of this systematic review is to narratively review and critically appraise CPR impact analysis studies relevant to primary care.

Setting: Primary care

Participants: Adults and children

Intervention: Studies that implemented the CPR compared to usual care were included. Study design: randomised controlled trial (RCT), controlled before-after and interrupted time-series

Primary outcome: Physician behaviour and/or patient outcomes.

Results: A total of 18 studies, incorporating 14 unique CPRs, were included. The main study design was RCT (n=13). Overall, 10 studies reported an improvement in primary outcome with CPR implementation. Of six musculoskeletal studies, five were effective in altering targeted physician behaviour in ordering imaging for patients presenting with ankle, knee and neck musculoskeletal injuries. Of six cardiovascular studies, four implemented cardiovascular risk scores and three reported no impact on physician behaviour outcomes such as prescribing and referral or patient outcomes such as reduction in serum lipid levels. Two studies examined CPRs in decision-making for patients presenting with chest pain and reduced inappropriate admissions. Of five respiratory studies, two were effective in reducing antibiotic prescribing for sore throat following CPR implementation. Overall, study methodological quality was often unclear due to incomplete reporting.

Conclusions: Despite increasing interest in developing and validating CPRs relevant to primary care, relatively few have gone through impact analysis. To date research has focused on a small number of CPRs across few clinical domains only.

Keywords: Clinical prediction rule, Impact analysis, Risk prediction, Primary care

Strengths and limitations of this study

- Clinical prediction rules (CPRs) are increasingly developed and advocated for use in clinical practice. However, little is known regarding the effectiveness of these tools versus usual care for relevant clinical outcomes.
- This is the first systematic review of CPRs relevant to primary care that have gone through impact analysis.
- The main limitation of this review is that the electronic search was limited to 30 pre-specified journals which may mean that some relevant studies were not retrieved. This search was supplemented with key author searches and reviewing other resources known to publish CPRs.
- Nevertheless, this is the first study to examine in detail impact analysis studies of CPRs relevant to primary care.

Introduction

Clinical prediction rules (CPRs) are clinical tools that quantify the individual contributions that various components of the history, physical examination and investigations contribute towards diagnosis, prognosis, or likely response to treatment in a patient.(1) These tools simplify, standardise, and attempt to increase the accuracy and consistency of clinicians' diagnostic and prognostic assessments and management decisions.(1, 2) Well recognized examples of CPRs include the Framingham cardiovascular risk score, the Ottawa ankle rule and the Centor score for sore throat.

Developing and validating a CPR requires reference to specific methodological standards.(1, 3, 4) Conventionally, these tools go through three distinct stages prior to full implementation in a clinical setting.(1, 3, 4) The first stage is derivation, where the independent and combined effects of explanatory variables such as symptoms, signs and/or investigations, is established. The next stage is validation, where the final derived CPR is evaluated first in a similar clinical setting (internal validation), followed by different clinical settings (external validation). If following these stages predictive accuracy is established, then the final stage of evaluation is to test the impact of using the CPR in clinical practice, ideally in a randomized controlled trial (RCT) for relevant clinical outcomes.(1, 5, 6) Impact analysis aims to investigate if the implementation of a CPR in clinical practice is better than usual care for patient, process of care and/or cost outcomes.(7, 8)

Our research group recently published two studies detailing the development and content of an international register of CPRs relevant to primary care.(2, 9) With increasing interest in CPRs, large numbers have been derived but fewer have been validated or tested in an impact analysis study.(2) If CPRs are to truly improve the quality of patient care then evaluation of these tools is crucial.

The aim of this systematic review is to present a narrative and critical analysis of CPRs relevant to primary care which have gone through impact analysis.

Methods

The methods used for identifying CPRs from the literature and in developing a register of these tools relevant to primary care have been published in detail previously.(2, 9) These methods are summarised below.

Search strategy

An electronic search string for PubMed was developed to retrieve CPRs relevant to primary care from 30 pre-selected medical journals (See Appendix 1 for search string and journals included).(9) No restriction was placed on language. Original electronic searches were conducted from 1980-2009 and for the purposes of this review were updated to the end of 2013.(2) In addition, secondary sources of CPRs were searched including the Journal of the American Medical Association (JAMA) Rational Clinical Examination series, a handbook of CPRs and personal resources. (2, 9, 10) Author searches for key experts in the field were also conducted for additional relevant articles. Furthermore, reference lists of each relevant impact analysis study were searched to identify possible additional studies.

Inclusion criteria

Studies were eligible for inclusion if they met following criteria;

1) Population: Relevant to primary care defined as "normally the point of first medical contact within the health care system, providing open and unlimited access to its users, dealing with all health problems regardless of the age, sex, or any characteristic of the person concerned. (11) Although studies may not have been conducted in a primary care setting, they were eligible for inclusion providing they were relevant to primary care (e.g. implementation of the Canadian head CT rule with the aim of reducing imaging for patient presenting with minor head injury). This inclusion criterion was designed to be broad to acknowledge variation in the same-day diagnostic tests that are available across different countries and the international variation in the role of primary care clinicians. Studies set in the emergency department were considered relevant to primary care if following application of the CPR the patient could be discharged home following application of the CPR.

2) Intervention: CPR defined as "a clinical tool that quantifies the individual contributions that various components of the history, physical examination, and investigations make toward the diagnosis, prognosis, or likely response to treatment in a patient."(1) Diagnostic,

prognostic and management CPRs were included and screening questionnaires (i.e. applied to apparently healthy people who may be at increased risk of a disease or condition) were excluded. A requirement for inclusion was that the CPR comprised the entire intervention. Studies where the CPR was implemented as part of a broader guideline, protocol or decision aid were excluded. Studies that used a CPR to determine eligibility for trial inclusion but were not part of the intervention were also excluded.

The following study designs were included: (cluster) RCT, controlled before-after or interrupted time series studies. Uncontrolled study designs were excluded as the aim of this review was to examine the effectiveness of CPR implementation, rather than the performance of the CPR which would be captured in validation studies using observational study designs.

3) Comparison: Usual care.

4) Primary Outcome: Physician behaviour e.g. ordering of diagnostic tests, process of care e.g. number of inpatient bed days and/or patient outcomes e.g. duration of symptoms.(1)

Data extraction

All articles were initially screened for inclusion according to title and abstract by one reviewer. Potentially relevant articles were then reviewed by a second reviewer with any disagreements resolved by a third independent reviewer. For each relevant article the following data was extracted: i) Name of CPR (ii) Type of CPR: prediction rule, decision rule or both; (iii) Clinical domain: using International Classification of Primary Care – second edition (ICPC-2)(12); (iv) Clinical setting; (v) Study population; (vi) Primary outcome of interest; (vii) Predictive accuracy of the CPR (measured by sensitivity/specificity (95% confidence intervals) where reported, otherwise the model's c-statistic was recorded); and (viii) Impact on primary outcome of interest.

Data analysis

i) Critical analysis of CPR impact analysis

Each article was critically appraised utilising a published framework for impact analysis of CPRs.(7) Developed in 2011 by an expert panel, this four-phase framework provides guidance for impact analysis studies (See Figure 1). The phases are as follows; 1) *Exploratory*

phase; evaluate the level of evidence and predictive accuracy of the CPR; 2) *Preparation for impact analysis*; consider potential barriers, assess acceptability of the CPR to clinicians and local stakeholders and conduct a pilot study; 3) *Experimental phase*; evaluation of the CPR with monitoring of the use of the CPR in a clinical setting; 4) *Long-term implementation phase*; examine if a CPR with reported positive impact on relevant clinical outcomes is implemented long-term and how this was achieved.(7)

ii) Summary of effect on process and outcome of care

Meta-analysis was not possible due to heterogeneity in CPRs and outcomes of interest, so a narrative analysis was conducted. In this section, where appropriate and where data was available, crude odds ratios and absolute risk reductions (ARR) were calculated.

Methodological quality assessment

The methodological quality of each impact analysis study was independently evaluated by two reviewers (MU, BC) and by a third reviewer if consensus was not reached (EW). For each study design, an appropriate quality assessment check list was used. RCTs and cluster RCTs were assessed through the Cochrane risk of bias tool.(13) Controlled before-after studies and interrupted time series studies were evaluated through Cochrane criteria for these study designs.(14)

Results

Overview of studies

Study identification

A flow diagram of the search strategy is presented in Figure 2. The PubMed search (1980-2013) and supplementary sources searches retrieved a total of 86,158 studies of which 1,111 CPR studies were identified following review of title and abstract. A total of 18 studies met the inclusion criteria for the systematic review.

Description of included impact analysis studies

A total of 14 unique CPRs were tested in 18 impact analysis studies (See Table 1 and Appendix 2). According to ICPC-2, these studies were classified into four broad clinical domains namely; musculoskeletal, most commonly the Ottawa ankle rule (15-20) (n=6); cardiovascular (21-27) (n=6) respiratory (28-32) (n=5), and neurological (33) (n=1). The majority of studies were conducted in North America (Canada n=10, United States n=4) with the remainder in the United Kingdom (n=2) and France (n=2). Most studies were set in the emergency department (ER) (n=9) and primary care (n=7). The remainder were carried out in the outpatient department (n=2).

Regarding study design, there were four cluster RCTs (15, 18, 27, 33), eight RCTs (22, 24-26, 28-32), one pilot RCT (23), three controlled before-after studies (16, 17, 19) and two interrupted time series. (20, 21) In a total of 16 studies, the intervention was the impact of the CPR alone (15-29, 32, 33), and two studies utilised different trial arms to test the CPR alone versus CPR and protocol versus usual care.(30, 31) Two studies integrated the CPR into a computerised clinical decision support system (CDSS). (20, 32) Two studies used real-time CPR reminders at the point of test ordering.(18, 33)

i) Critical analysis of CPR impact analysis studies

i) Preparation for impact analysis: level of evidence of CPR, consideration of potential barriers and assessment of CPR acceptability

Fifteen of 18 studies implemented a CPR that was externally validated, while three studies tested a CPR that had been derived or internally validated only.(21, 30, 31) Ten studies reported the CPR's sensitivity from validation studies in identifying the target outcome which ranged from 85%-100%.(15-20, 28, 29, 31, 33) Five studies identified and addressed

potential barriers for implementation before impact analysis, most frequently through barriers analysis.(18, 20, 22, 32, 33) Six studies assessed the acceptability of the CPR to clinicians prior to the implementation phase of the study, usually through training sessions and engagement with local stakeholders. (15, 19, 22, 27, 32, 33) Seven studies reported that a pilot or simulation phase was conducted or there was a previous impact analysis on the same CPR by the same authors. (16-19, 21, 32, 33)

ii) Impact analysis phase: adherence with CPR use and reasons for non-adherence

Twelve studies tracked the use of the CPR during implementation, usually with standardised data collection forms or computerised tools.(15-18, 20, 22, 25, 26, 29, 31-34) Overall, adherence with CPR use varied between studies ranging from 57.5% to 100%, with reported reasons for non-adherence including fear of missing the diagnosis, preference for own clinical judgment and patient request.(20, 33) Of the 12 studies that tracked CPR adherence, seven reported adherence of ≥80%, four reported adherence of 60-80% and one study reported adherence of ≤60%. Nine of 12 studies reported a positive impact on primary study outcome following CPR intervention but there was no clear link between level of adherence and successful CPR implementation. Clinicians' acceptability of CPR use during the intervention phase was evaluated in four studies (16, 17, 20, 33), of which two assessed the reported rate of comfort using a five-point likert scale.(16, 17)

iii) Post implementation phase: maintaining use of CPR

Of 10 studies with a positive impact on primary outcome, four evaluated the effect of the CPR in a post intervention phase ranging from 5 to 12 months. (15, 16, 18, 20) To maintain CPR use, two studies used a passive strategy of posters, one retained computerized clinical decision support and one did not employ any particular strategy. In all four studies the effect of CPR use was maintained.

Importance of study design in assessing the impact of CPRs

There were five uncontrolled before-after studies retrieved during the initial search, which were excluded from data analysis based on their uncontrolled study design (See Appendix 3).(35-39) These studies tested the impact of the Ottawa ankle rule (n=2), the Canadian C-spine rule (n=1), the CT head rule (n=1) and the Glasgow Blatchford bleeding score (n=1). All five studies demonstrated a positive impact on primary outcome, usually physician behaviour in ordering imaging.

ii) Effect on the process and outcome of care

Overall, ten studies reported that CPR implementation resulted in a positive impact on primary outcome while eight studies reported no impact versus usual care. There were no clinically important adverse outcomes reported. Studies are presented according to clinical domain. Table 2 presents a summary of the estimated effect sizes for the impact analysis studies.

Musculoskeletal (cluster RCTs n=2, Controlled before-after studies n=3, interrupted time-series n=1)

All six musculoskeletal studies focused on the implementation of CPRs for deciding upon further imaging for patients presenting with ankle, knee or neck injury.(15-20) All included musculoskeletal CPRs had reported sensitivities of 100% in their validation studies and all focused on physician behaviour in deciding to order imaging. Of these six studies, five reported a positive effect on reducing imaging with crude ORs ranging from 0.03 to 0.96.(15-18, 20) (See Table 2) All studies adopted an educational approach to encourage CPR use amongst clinicians, through use of educational meetings, posters and pocket cards. Of note three studies tested the impact of the Ottawa ankle rule; two controlled before-after trials in Canada and one cluster RCT in France.(15, 16, 19)

Cardiovascular (cluster RCT n=1, RCTs n=4, Interrupted time series n=1)

Of six cardiovascular studies, two implemented chest pain CPRs to assess the impact on physician decision-making regarding emergency admission for patients with suspected myocardial infarction.(21, 22) One of these studies reported a 30% relative reduction in patients admitted inappropriately.(21) The remaining four studies implemented cardiovascular risk scores in general practice. Three of these studies reported no impact on physician behaviour such as prescribing and referral to dieticians or on patient outcomes such as reduction in lipid levels.(23, 24, 27) However, in one large scale RCT (n=3,053), that published its findings in two separate articles; both patient lipid levels and physician antihypertensive prescribing were improved.(25, 26)

Respiratory (RCTs n=5)

Of five respiratory studies, four focused on physician behaviour in terms of antibiotic prescribing for sore throat in general practice.(28-30, 32) Of these four studies, only one

reported significantly reduced antibiotic prescription rates in the intervention group (age-adjusted relative risk 0.74, 95% CIs 0.60-0.92) versus usual care.(32) The primary outcome in the fifth study was reported symptom severity in patients presenting with sore throat and antibiotic prescribing was included as a secondary outcome.(31) This study found that use of the CPR alone or CPR in combination with a rapid antigen detection test (RADT) improved patient reported symptom severity and duration, and reduced antibiotic use by 29% (adjusted risk ratio 0.71, 95% CI 0.50-0.95).(31)

Neurological (cluster RCT n=1)

One study implemented the Canadian CT head rule, which guides the ordering of brain imaging in patients presenting following minor head injury.(33) Despite this CPR having 100% sensitivity in validation studies, it did not reduce imaging rates. In process evaluation, clinicians' reported unease with certain components of the rule and fear of missing a high-stakes diagnosis as reasons for not adopting the CPR.(33)

Methodological quality assessment of included studies

Studies were heterogeneous with regard to risk of bias. For the RCT designs (n=13), five studies were considered low risk of bias for random sequence generation and five were considered low risk in relation to allocation concealment (See Figure 3i). The remaining RCT studies had an unclear risk in these domains. Due to the nature of many of the interventions, it was not always possible to blind participants and research personnel, therefore, performance bias was judged to be unclear or high in over half of these studies. In the non-randomised study designs, the risk of selection bias was high in all studies while the risk of blinding and contamination was low in all studies (See Figure 3ii). Overall, six studies tested the impact of a CPR in which the authors were involved in developing. (17, 18, 22, 29, 31, 33) The impact that this may have in terms of bias is unclear.

Discussion

Summary of main findings

This review indicates that despite the increasing research interest in developing and validating CPRs, relatively few of these tools relevant to primary care have gone through impact analysis. Implementation has been restricted to a few clinical domains mainly musculoskeletal, cardiovascular and respiratory and certain CPRs have undergone multiple evaluations, for example, the Ottawa ankle rule. Of 18 studies meeting inclusion criteria, 10 demonstrated an improvement in primary outcome with CPR use when compared to usual care. Approximately half of these successful studies focused on changing physician behaviour in ordering imaging for patients presenting with ankle, knee and neck musculoskeletal injuries.(15-18, 20) Four studies with a positive impact on the study's primary outcome successfully implemented post RCT measures to maintain the impact through both passive (posters) and active strategies (retention of computerised CDSS).(15, 16, 18, 20)

Studies which aimed to alter physician behaviour regarding prescribing were less successful with three of six such studies successful in reducing prescription rates.(23, 31, 32) Studies that reduced antibiotic prescription rates invested significant time before CPR implementation in assessing acceptability to clinicians' and also integrated the CPR into the clinical work flow through computerised clinical decision support or point of care reminders.(31, 32) The importance of this type of impact analysis preparation in adequately addressing barriers to implementation and in integrating the CPR into the clinical workflow has been highlighted.(5, 7, 40) In this review, 12 studies considered barriers to implementation and/or gauged the acceptability of the CPR to clinicians' prior to impact analysis. However, only four studies integrated the CPR into clinical work flow using either computerised CDSS or point of care reminders.(18, 20, 32, 33)

The perceived seriousness of the target condition may also affect CPR implementation. For instance, the impact of the Canadian CT head rule was evaluated in the diagnostic pathway of intracranial bleeding following minor head injury.(33) This CPR has 100% sensitivity and though implemented by an experienced CPR research group, this CPR did not impact on CT imaging rates.(33) In a parallel process evaluation, clinicians' reported unease with certain

components of the rule and fear of missing a high-stakes diagnosis as reasons for not adopting the CPR.(33)

Overall, adherence with CPR use during implementation varied considerably between studies ranging from 57% to 100%. Reasons for non-adherence, established through process evaluation, related to fear of missing the diagnosis, preference for own clinical judgment and patient request for further investigation or management.

Comparison with existing literature

Previous CPR reviews relevant to inpatient and paediatric settings reported issues around the variability of methodological quality in conducting CPR studies and a paucity of impact analysis studies.(3, 6, 41) The issue of methodological quality has recently been addressed with the publication of two standardized reporting guidelines for CPR derivation and validation studies and systematic reviews of CPRs.(42, 43) These publications will have an important role to play in standardising CPR research and in promoting robust validation of CPRs which should then be prioritised for evaluation in future impact analysis studies.

CPRs, which demonstrate improvements in the process of care and/or patient outcomes, should then be considered for inclusion in relevant clinical guidelines to facilitate dissemination into clinical practice. A recent survey which examined the use of CPRs in clinical practice by GPs in the United Kingdom reported that GPs most often used cardiovascular, depression, fracture and atrial fibrillation CPRs.(44) CPR use was dictated by perceived clinical utility, familiarity and local policy requirements. In a supplementary review of clinical guidelines very little inter-guideline consistency was found to guide clinicians in terms of which, if any, of these tools to use in practice.(44) Prioritising the evaluation of a few adequately validated CPRs with proven predictive accuracy in relevant clinical settings would add significantly to this evidence base and facilitate, if appropriate, the inclusion of certain CPRs into future clinical guidelines.

Implications for clinical practice and research

CPR research is a relatively new methodological discipline and a challenging area of research.(2) In the conduct of this review several uncontrolled before-after impact analysis studies were retrieved. While these studies have a role in contributing to the overall evidence base, they are not a substitute for carefully conducted RCTs in determining the

effectiveness of CPRs on clinically relevant outcomes.(6) In this review the majority of included RCTs focused on physician behaviour or process of care as the primary outcome. This is not surprising considering how challenging it is to demonstrate differences in patient outcomes, requiring much larger sample sizes which significantly increase running costs.(10) In addition, contextual issues which exist between countries, due to differences in healthcare delivery, healthcare systems and incentives, render process of care outcomes difficult to generalise.(5, 6)

Certainly CPR impact needs to be considered early in the development phase of any new CPR. For instance, Irish research shows high levels of GP referrals to symptomatic breast units.(45) Recent research efforts have focused on the development of a breast cancer CPR for use in primary care to aid these referral decisions.(42) However, although this CPR underwent methodologically robust development and demonstrates good predictive accuracy it is unlikely its use will impact on referral rates. This is due largely to the existence of a low risk threshold for referral driven by a combination of factors including patient expectation, media interest and fears of medico-legal ramifications for clinicians if a diagnosis is missed. So when considering an impact analysis RCT in this clinical domain, these contextual issues would need to be addressed in tandem with validation and impact analysis studies.

Certain clinical domains have seen a proliferation of CPR research, particularly musculoskeletal and cardiovascular conditions. The publication of several carefully conducted impact analysis trials for CPRs relating to knee, ankle and neck injuries is largely due to one Canadian research group while historically the availability of large UK population datasets facilitated the development of cardiovascular prognostic CPRs.(15-18, 46, 47) In this review five impact analysis studies (two were uncontrolled before-after studies detailed in Appendix 3) focused on the impact of the Ottawa ankle rule in emergency room settings, three of which were conducted in the same country.(15, 16, 19, 35, 36) Ideally CPR development and impact analysis should be aligned with clinical need rather than developing or testing the effectiveness of CPRs when accurate tools already exist.(44)

The relatively small number of impact analysis studies retrieved means it is not possible to make firm conclusions about the overall effectiveness of these tools in primary care.

However, certain CPRs such as the Ottawa ankle and knee rules are appropriate for use in clinical practice and have a role in reducing unnecessary imaging rates. Future research should focus on conducting RCTs of broadly validated CPRs with consideration of contextual and local implementation factors.(7) Pertinent issues include how best to integrate the CPR into clinical workflow and the potential benefits of embedding CPRs as part of computerised clinical decision support.

Study limitations

Although this review was conducted systematically and multiple resources searched to retrieve relevant articles, electronic searches were limited to 30 pre-selected journals and as a result it is possible relevant studies were not retrieved. In addition, this search was last updated in December 2013. However, to the best of our knowledge, this review is the first to analyse in detail CPR impact analysis studies relevant to primary care. The broad definition of primary care used for this review led to the inclusion of impact analysis studies conducted in the emergency room setting. This was necessary to account for the variation in primary care services and access internationally. Studies that implemented CPRs as part of a broader guideline, protocol or decision aid were excluded. Finally, due to the heterogeneous nature of the included studies, meta-analysis was not possible.

Conclusion

Impact analysis of CPRs in primary care has to date focused on a small number of CPRs in a limited number of clinical domains. Future research should focus on prioritising well-validated and accurate CPRs for impact analysis to determine if these tools impact on the process of clinical care and patient outcomes.

Contributorship statement

Emma Wallace wrote the manuscript, acted as a reviewer during the systematic review and contributed to the results. Maike Ujen contributed to writing the manuscript, acted as a reviewer for the systematic review, contributed to the results and did methodological quality assessment. Barbara Clyne acted as a reviewer for the systematic review, contributed to the results and completed the methodological quality assessment of included articles. Atieh Zarabzadeh acted as a reviewer for the systematic review and contributed to the results. Claire Keogh ran the original electronic searches, acted as a reviewer and contributed to the results and discussion. Rose Galvin acted as a reviewer and contributed to the results and discussion. Susan M Smith acted as a reviewer and contributed to the results and discussion. Tom Fahey conceived the idea, oversaw the project and acted as a reviewer. All authors read and approved the final manuscript.

Declaration of competing interests

We have read and understood BMJ policy on declaration of interests and declare that we have no competing interests.

Funding sources

This research was funded by the Health Research Board (HRB) of Ireland through the HRB Centre for Primary Care Research, Grant No. HRC/2007/1.

Data sharing

No additional data available.

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Table 1: Summary of impact analysis studies of CPRs relevant to primary care

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)
Auleley, 1997, France (15)	Ottawa ankle rule Sensitivity 100% (95-100%), Specificity 50% (46-55%) Cluster RCT	4980, ≥ 18 years, emergency departments of 5 Paris university teaching hospitals	**Intervention:** educational intervention to encourage CPR use (i.e. posters, pocket cards, and data forms) **Post-intervention:** only posters alone used to sustain the intervention effect. **Comparison:** Usual care	**Physician behaviour:** Referral for radiography (ankle/foot)	Relative reduction intervention site: 22.4% (95% CI 19.8-24.9), control group increase of 0.5% (95% CI 0-1.4).
Cameron, 1999, Canada, (19)	Ottawa Ankle Rule Sensitivity 100% (95-100), Specificity 50% (46-55%) Controlled before-after	1648, ≥18 years, Male 885, Female 763, Mean age 38 (18-91), emergency departments in 10 hospitals	**Group A:** little or no prior use of the CPR and educational intervention (educational meeting, posters, pocket cards and patient information leaflets) **Group B:** some prior use of the CPR and educational intervention **Group C:** active local implementation of the CPR and no educational intervention.	**Physician behaviour:** Referral for ankle X-ray	No reduction referral for ankle X-rays: intervention before 73%, after 78%, p=0.11, control: before 75%, after 65%, p=0.022

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)
Stiell, 1994, Canada, ER(16)	Ottawa ankle rule Controlled before-after Sensitivity 100% (95-100), Specificity 50% (46-55%),	2342, ≥ 18 years, emergency departments of 2 hospitals	**Intervention:** educational intervention to encourage CPR use (i.e. lecture, pocket cards, and posters) **Post-intervention:** posters remained in ER **Comparison:** Usual care	**Physician behaviour:** Referral for radiography (ankle/foot)	*Ankle x-ray:* Relative reduction 28% in intervention group, increase of 2% in control group (p<0.001). *Foot X-ray:* Relative reduction of 14 % intervention group, increase of 13% in control group (p<0.05).
Boutis, 2013, Canada, ER(20)	Low Risk Ankle Rule Sensitivity 100% [93.3-100) Specificity NR ITS	2151, children aged 3-16, emergency departments of six hospitals	**Phase 1:** no intervention **Phase 2:** educational interventions to encourage CPR use (i.e. physician education, pocket cards, posters) and CDSS **Phase 3:** CDSS only **Comparison:** Usual care	**Physician behaviour:** Referral for ankle X-ray	Relative reduction in ankle x-rays in intervention sites compared to control sites. RR: 21.9% (95% CI 15.2-28.6)
Stiell, 1997, Canada, ER(17)	Ottawa Knee Rule Sensitivity 100% (94-100), Specificity 49% (46-52%), Controlled before-after	3907, ≥ 18 years, emergency departments of 4 hospitals (2 community and 2 teaching)	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters). **Comparison:** Usual care	**Physician behaviour:** Referral for knee radiography	Relative reduction of 26.4% of patients referred for knee x-ray in intervention group (77.6% vs. 57.1% (p<0.001), vs. relative reduction of 1.3% in control group (76.9% vs. 75.9%, p=0.6)

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)
Stiell, 2009, Canada, ER(18)	Canadian C-spine Rule Sensitivity 99% (96-100%), Specificity 45% (44-46%) Cluster RCT	11824, ≥ 16 years, emergency departments of 6 hospitals	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters) and CDSS at point of requesting imaging **Comparison:** Usual care	**Physician behaviour:** Diagnostic imaging rate of cervical spine	Relative reduction of 12.8% for cervical spine imaging (95% CI 9-16%) intervention group. Control group showed a relative increase of 12.5% (95% CI 7-18%)
McIsaac, 2002, Canada, Primary care(29)	McIsaac Sensitivity 83% (no CIs), Specificity 94% (no CIs) RCT	621, ≥ 3 years, general practice, 97 participating GPs,	**Intervention:** mailed educational intervention (published score with summary explanation with pocket card). Physicians were provided with a sticker to apply to the encounter form that listed the score and management approach. **Comparison:** Physicians only received the education material.	**Physician behaviour:** Unnecessary antibiotic prescriptions (negative throat swab)	Non-significant difference intervention vs. control groups in unnecessary antibiotic prescription (20.4% vs. 16.1%, p=0.29)
McIsaac, 1998, Canada, Primary	Centor score Sensitivity 90% (no CIs), Specificity 92%	396, ≥ 15 years, general practice, 450 participating GPs	**Intervention:** mailed CPR with summary explanation and patient information. Physicians asked to	**Physician behaviour**: Antibiotic prescription	Non-significant reduction in antibiotic prescription in intervention group (27.8%) vs. control (35.7%) (p=0.09)

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)
care(28)	(no CIs) RCT		complete an encounter form. **Comparison:** mailed educational intervention and a control form with no score or management actions.		
McGinn, 2013, USA, (32)	1) Walsh rule for streptococcal pharyngitis 2) Heckerling rule for pneumonia Walsh rule: c-statistic: 0.71 [95% CI, 0.67-0.74) Heckerling rule: c-statistic 0.82 (0.74-0.9) RCT	168 Primary care providers, 2 large academic ambulatory care centres in New York	**Intervention:** education session and computerised CDSS with CPRs embedded promoting physician to calculate scores of both CPRs and receive management recommendations. **Comparison:** Usual care with background information on CPRs	**Physician behaviour**: Change in antibiotic prescription	Intervention group significantly less likely to order antibiotics than control (age-adjusted RR, 0.74; 95% CI, 0.60-0.92). Absolute risk difference 9.2%.
Worrall, 2007, Canada, (30)	Modified Centor score Sensitivity 90% (no CIs), Specificity 92% (no CIs)	533, ≥ 19 years, 37 practices in eastern Newfoundland CPR:170 RADT: 120	**CPR group**: decision rules only **RADT group**: rapid antigen test only **RADT+CPR group**: decision rules and antigen test	**Physician behaviour**: Prescribing rate of antibiotics	Prescription rates: CPR alone - 55% RADT - 27% (NS) RADT+CPR -38% (p<0.001) Control: 58%

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)
	RCT	RADT+CPR:102 Control:141	combined **Comparison:** Usual care		
Little, 2013, UK (31)	FeverPAIN c-statistic: 0.71 RCT	631, ≥ 3 years, general practice (48 UK practices)	**CPR group:** CPR was applied and antibiotic prescribed according to the score. **CPR+RADT group:** CPR was applied and antibiotic prescribed or RADT carried out according to the score. **Comparison:** Delayed prescribing	**Patient behaviour:** Patient reported symptom severity days 2-4 after consultation on a 7-point Likert scale	Greater improvements in symptom severity for CPR group compared to control (−0.33, 95% CI −0.64 to −0.02)
Pozen, 1984, USA, ER(21)	Pozen score for chest pain Sensitivity 94% (no CIs), Specificity 78% (no CIs) ITS	2320, aged ≥30 male and ≥40 female, emergency departments of 6 US hospitals	**Intervention:** Research assistant presented physicians with the CPR probability score. **Comparison:** Usual care, the CPR probability was calculated but not presented to the physicians.	**Physician behaviour:** Appropriate admission/discharge	30% relative reduction in patients admitted to CCU who did not have acute coronary syndrome
Kline, 2009, USA, ER(22)	Kline chest pain CPR c-statistic 0.74 (0.65-0.82)	369 adults presenting with chest pain, one emergency room in	**Intervention:** Clinicians and patients received a printout of CPR result displayed numerically and graphically.	**Physician behaviour**: Hospital admission with no significant cardiovascular	No significant decrease for patients admitted with no CVD diagnosis: 11% vs. 5% (95% CI -0.2%-11%), p=0.059

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)
	RCT	an academic urban US hospital	**Comparison:** Usual care, no printout was provided to clinicians or patients.	diagnosis	
Persell, 2012, primary care(27)	Framingham risk estimate and global cardiovascular risk score Cluster RCT	N=14 physicians, n=218 adult patients randomised to intervention, n=15 physicians, n=217 adults patients randomised to control, US primary care	**Intervention**: Individualised CVD risk estimate posted to high-risk patients and their physicians alerted by secure email Control: usual care	**Patient:** Reduction in LDL-cholesterol level by 30mg/dl	No difference in the primary outcome (11% vs. 11.1% OR 0.99, 95% CI 0.56, 1.74, p=0.96) but intervention patients were more likely to receive a prescription for a statin (11.9% vs. 6%, OR 2.13, 95% CI 1.05, 4.32, p=0.038)
Grover 2007 and 2008, primary care(25, 26)	Framingham risk score RCT	N=3,053 adults mean age 56.4, male 66.9%, n=230 primary care physicians, 10 provinces in Canada primary care	**Intervention:** Patients identified as high risk and randomised to intervention had their individualised coronary risk profile discussed **Control:** usual care, coronary risk profile withheld	**Patient outcomes:** 1. Reduction in LDL-cholesterol level 2. Reduction in BP	1. Statistically significant reduction in LDL and total cholesterol-HDL ratio in intervention vs. control and patients were more likely to reach lipid targets 2. Patients in intervention group were more likely to receive appropriate antihypertensive treatment and more likely to start or modify treatment
Hall, 2003, UK, (23)	New Zealand cardiovascular risk	323, aged 35-75 years, patients	**Intervention:** Risk scores were clearly documented at	**Physician behaviour:** 1. Prescription of risk	3. No significant between group differences: change in diabetes

Author, Year, Country	CPR name, CPR predictive accuracy (95% CI), Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)
	score NR Pilot RCT	with no history of cardiovascular or renal disease, one UK hospital outpatient department (OPD) clinic	the front of the notes of patients. **Comparison:** Usual care	modifying drugs 2. Management of CVD risk factors	treatment 42% (95% CI 34-50) vs. 58 (95 CI 29-45%), change in antihypertensive drugs 26 (95% CI 10-22%) vs. 10% (95% CI 5-16%), change in lipid lowering drugs: 12% (7-17%) vs. 9% (95% CI 4-14%) 4. Referral to dietician 10% (95% CI 6-15%) vs. 13% (95% CI 7-19%)
Hanon, 2000, France (24)	Framingham risk score NR RCT	1243, aged 18 -75 years with hypertension attending a general physician	**Intervention:** Physicians knowledge of the calculated risk score. **Comparison:** Usual care	**Patient and Physician behaviour:** Change in BP, patients prescribed dual therapy	No difference in BP (patients with BP <140/90 mmHg intervention: 64%, control 62%) or % patients on dual therapy (41% intervention vs. 46% control)
Stiell, 2010, Canada, ER(33)	CT head rule Sensitivity 100% (96-100%), Specificity 51% (48-53%) Cluster RCT	4531, alert and stable adults with minor head injury aged ≥ 16 years, 12 emergency departments in three provinces of Canada (6 teaching sites, 6 community sites)	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters) and real-time reminder at point of requesting imaging **Comparison:** Usual care	**Physician behaviour:** Proportion of patients referred for CT imaging	Increased proportion of patients referred for CT imaging intervention: before: 62.8%, after: 76.2% (difference: 13.3% (95% CI 9.7%-17.0%) Control: before: 67.5%, after: 74.1% (difference: 6.7% (95% CI 2.6-10.8)

***NR=Not reported, **NA=Non-applicable, ***NS=Non-significant, $ CPR predictive accuracy as referenced in the impact analysis study**

Table 2: Table of estimated effect sizes for impact analysis studies

Author, Year CPR name	Study design (n)	Sample size calculation reported (n)	Primary outcome	Effect size: Crude odds ratio (OR) of improvement in primary outcome in intervention versus control (95% CI)	Absolute risk reductions (95% CI)
Auleley, 1997(15) Ottawa ankle rule	Cluster RCT (4980)	Yes (900)	**Physician behaviour:** Referral for radiography (ankle/foot)	Crude OR 0.03 (0.01-0.06)	22.8% (20.0-25.7)
Stiell, 1994(16) Ottawa ankle rule	Controlled before-after (2342)	NA	**Physician behaviour:** Referral for radiography (ankle/foot)	*Ankle X-ray:* Crude OR 0.11 (0.08-0.16) *Foot X-ray:* Crude OR 0.73 (0.57-0.94)	33.4% (28.9-37.9) 6.6% (1.1-11.7)
Cameron, 1999(19) Ottawa Ankle Rule	Controlled before-after (1648)	NA	**Physician behaviour:** Referral for ankle X-ray	Crude OR 0.96 (0.60-1.55)	0.8% (-8.5 – 9.8)
Boutis, 2013(20) Low Risk Ankle Rule	ITS (2151)	NA	**Physician behaviour:** Referral for ankle X-ray	[#]NA	[#]NA
Stiell, 1997(17) Ottawa Knee Rule	Controlled before-after (3907)	NA	**Physician behaviour:** Referral for knee radiography	Crude OR 0.42 (0.35-0.51)	18.8% (14.7-22.9)
Stiell, 2009(18) Canadian C-spine Rule	Cluster RCT (11824)	Yes (9600)	**Physician behaviour:** Diagnostic imaging rate of cervical spine	Crude OR 0.82 (0.74-0.90)	5% (2.5-7.5)
Pozen, 1984(21) Pozen score for	ITS (2320)	NA	**Physician behaviour:** Appropriate admission	[#]NA	[#]NA

Author, Year CPR name	Study design (n)	Sample size calculation reported (n)	Primary outcome	Effect size: Crude odds ratio (OR) of improvement in primary outcome in intervention versus control (95% CI)	Absolute risk reductions (95% CI)
chest pain					
Kline, 2009(22) Kline chest pain CPR	RCT (369)	Yes (400)	**Physician behaviour**: Admission with no significant cardiovascular diagnosis	Crude OR 0.47 (0.22-1.04)	5.4% (-0.2 – 10.9)
Persell, 2012(27) Framingham risk score	Cluster RCT (425)	Yes (406)	**Patient:** Proportion of patients with a reduction in LDL-cholesterol level by 30mg/dl	Crude OR 0.99 (0.55-1.81)	0.1% (-0.0 – 0.0)
Grover, 2007 and 2008 (25, 26) Framingham risk score	RCT (3053)	Yes (3000)	**Patient:** 1. Reduction in LDL-cholesterol level	*Reduction in LDL-cholesterol level: mean difference −0.33mg/dl (−0.5.4 to −1.1; P=0.02)*	NA
Hall, 2003(23) New Zealand cardiovascular risk score	Pilot RCT (323)	NA	**Physician behaviour:** Prescription of risk modifying drugs, management of CVD risk factors	*Diabetes treatment:* Crude OR 1.28 (0.82-2.01) *Antihypertensive drugs:* Crude OR 1.62 (0.84-3.12) *Lipid lowering drugs:* Crude OR 1.48 (0.72-3.04) *Referral to dietician:* Crude OR 0.78 (0.40-1.54)	-6.0% (-16.6-4.7) -5.5% (-12.9-1.9) -3.7% (-10.3-3.0) 2.5% (-4.47-9.57)
Hanon, 2000(24) Framingham risk score	RCT (1243)	No	**Patient and Physician behaviour:** BP, patients prescribed dual therapy	*Normal BP:* Crude OR 1.09 (0.87-1.38) *Dual therapy:* Crude OR 0.82 (0.65-1.02)	- 2.1% (-7.4-3.3) 4.9% (-0.6-10.4)

Author, Year CPR name	Study design (n)	Sample size calculation reported (n)	Primary outcome	Effect size: Crude odds ratio (OR) of improvement in primary outcome in intervention versus control (95% CI)	Absolute risk reductions (95% CI)
McIsaac, 2002(29) McIsaac	RCT (621 patients, 97 physicians)	Yes (850 patients, 85 physicians)	**Physician behaviour:** Unnecessary antibiotic prescriptions (negative throat swab)	Crude OR 0.71 (0.47-1.08)	4.9% (-1.1 – 10.9)
McIsaac, 1998(28) Centor	RCT (396)	Yes (800)	**Physician behaviour**: Antibiotic prescription	Crude OR 0.69 (0.45-1.05)	8.1% (-1.0-17.3)
McGinn, 2013(32) 1) Walsh rule (streptococcal pharyngitis) 2) Heckerling rule (pneumonia)	RCT (168)	No	**Physician behaviour**: Change in antibiotic prescription	Crude OR 0.66 (0.50-0.86)	9.3% (3.2 – 15.3)
Worrall, 2007(30) Modified Centor score	RCT (533)	Yes (196)	**Physician behaviour**: Prescribing rate of antibiotics	Crude OR 0.89 (0.57-1.40)	2.9% (-8.2 – 13.9)
Little, 2013(31) FeverPAIN	RCT (6131)	Yes (909)	**Patient behaviour:** Patient reported symptom severity	Adjusted mean difference−0.33 (−0.64 to −0.02; P=0.04)	NA
Stiell, 2010(33) CT head rule	Cluster RCT (4531)	Yes (4800)	**Physician behaviour:** Proportion of patients referred for CT imaging	Crude OR 0.81 (0.69-0.96)	4.7% (1.0-8.4)

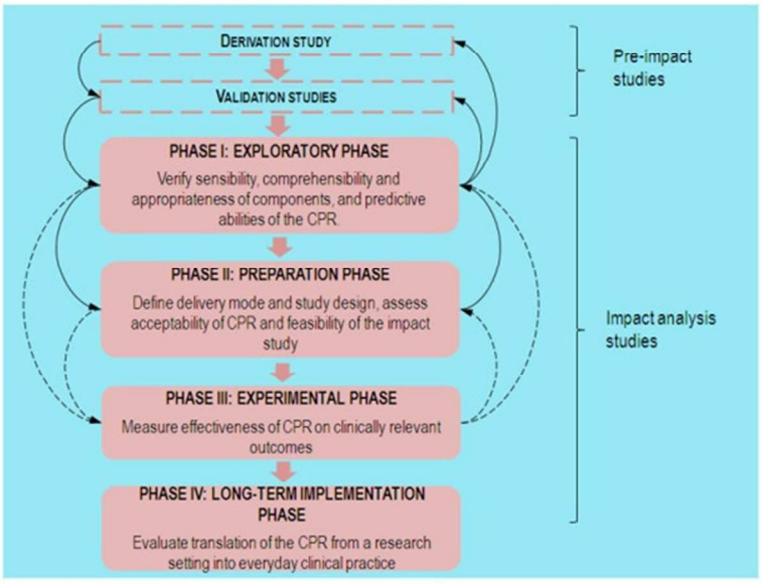

Figure 1: Framework for the impact analysis and implementation of CPRs (7)
67x50mm (300 x 300 DPI)

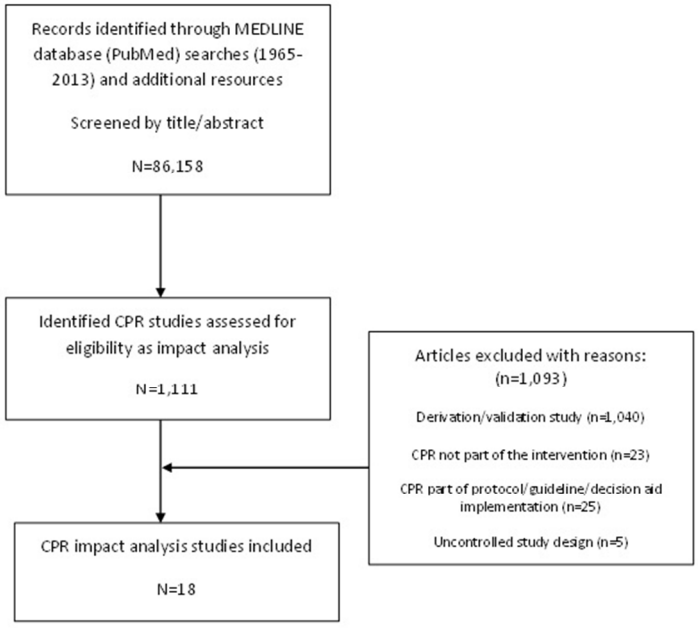

Figure 2: Flow diagram of search strategy
67x50mm (300 x 300 DPI)

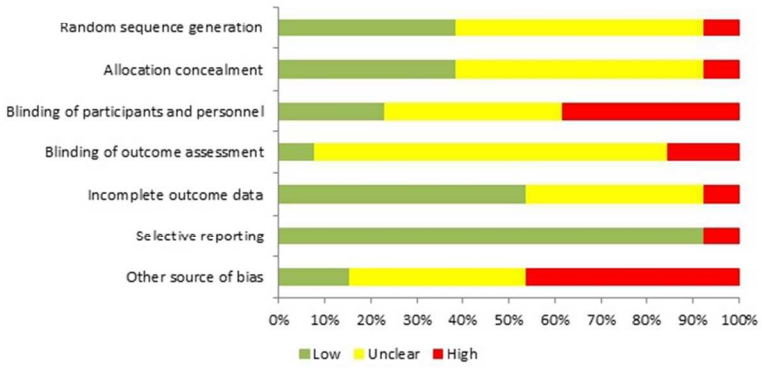

Figure 3i): Methodological quality assessment of impact analysis studies with RCT study design
67x50mm (300 x 300 DPI)

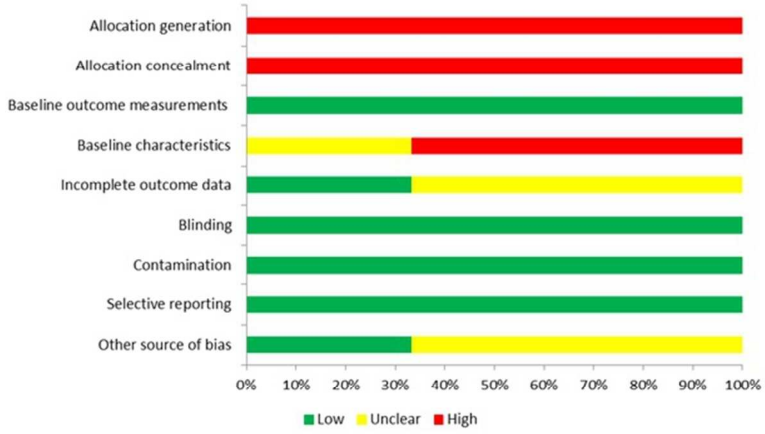

Figure 3ii) Methodological quality assessment of impact analysis studies with controlled before-after study design
67x50mm (300 x 300 DPI)

Appendix 1: Journal selection criteria and search strategy

Thirty journals relevant to primary care listed below were purposively chosen through various methods, including:

(1) The ISI Web of Knowledge Journal Citation Reports, listed under the category ''medicine, general, and internal'' and mentioned primary care, family medicine, or family practice in their title

(2) The 15 highest-ranked journals according to impact factor ratings in this same category

(3) Specialist journals that are known to publish CPRs (based on type of journal/expert opinion)

(4) A list of recommendations generated by an information specialist

(5) An expert consensus meeting attended by primary care clinicians, academics, and information specialists. (T.F., B.D.D., S.M.S., K.K.O.B., P.J.M., and B.Mc.G.)

Journal titles

Academic Emergency Medicine

Family Medicine

American Family Physician

Family Practice

American Journal of Medicine

Journal of American Medical Association

Annals of Emergency Medicine

Journal of the American Board of Family Medicine

Annals of Family Medicine

Journal of Clinical Epidemiology

Annals of Internal Medicine

Journal of Family Practice

Annals of Medicine

Journal of Internal Medicine

Annual Review of Medicine

Lancet

Archives of Internal Medicine

Medical Care

BMC Family Practice

Medical Decision Making

British Medical Journal

Medicine

British Journal of General Practice

New England Journal of Medicine

Canadian Family Physician

Public Library of Science Medicine

Canadian Medical Association Journal

Primary Care

Cochrane Database Systematic Reviews

Scandinavian Journal of Primary Health Care

Search on MEDLINE (PubMed)

Search 1: 30 journals, no limits

("American family physician"[Jour] OR "Annals of family medicine"[Jour] OR "The British journal of general practice : the journal of the Royal College of General Practitioners"[Jour] OR "Canadian family physician Medecin de famille canadien"[Jour] OR "Family medicine"[Jour] OR "Family practice"[Jour] OR "Journal of the American Board of Family Medicine : JABFM"[Jour] OR "The Journal of family practice"[Jour] OR "Primary care"[Jour] OR "Scandinavian journal of primary health care"[Jour] OR "BMC family practice"[Jour] OR "The New England journal of medicine"[Jour] OR "Lancet"[Jour] OR "JAMA : the journal of the American Medical Association"[Jour] OR "Annals of internal medicine"[Jour] OR "Annual review of medicine"[Jour] OR "PLoS medicine"[Jour] OR "British medical journal"[Jour] OR "Archives of internal medicine"[Jour] OR "Canadian Medical Association journal"[Jour] OR "Annals of medicine"[Jour] OR "The American journal of medicine"[Jour] OR "Medicine (Baltimore)"[Journal] OR "Cochrane database of systematic reviews (Online)"[Jour] OR "Journal of clinical epidemiology"[Jour] OR "Medical decision making : an international journal of the Society for Medical Decision Making"[Jour] OR "Medical care"[Jour] OR

"Academic emergency medicine : official journal of the Society for Academic Emergency Medicine"[Jour] OR "Annals of emergency medicine"[Jour] OR "Journal of Internal Medicine"[Jour]) OR ("Br Med J"[Journal] OR "Br Med J (Clin Res Ed)"[Journal] OR "BMJ"[Journal] OR ("british"[All Fields] AND "medical"[All Fields] AND "journal"[All Fields]) OR "british medical journal"[All Fields]) OR ("Can Med Assoc J"[Journal] OR "CMAJ"[Journal] OR ("canadian"[All Fields] AND "medical"[All Fields] AND "association"[All Fields] AND "journal"[All Fields]) OR "canadian medical association journal"[All Fields])

AND

Search 2: CPR search terms

"clinical prediction"[All Fields] OR "clinical model*"[All Fields] OR "clinical score*"[All Fields] OR "decision rule*"[All Fields] OR "diagnostic accuracy"[All Fields] OR "diagnostic rule*"[All Fields] OR "diagnostic score*"[All Fields] OR "diagnostic value"[All Fields] OR "predictive outcome*"[All Fields] OR "predictive rule*"[All Fields] OR "predictive score*"[All Fields] OR "predictive value"[All Fields] OR "predictive risk*"[All Fields] OR "prediction outcome*"[All Fields] OR "prediction rule*"[All Fields] OR "prediction score*"[All Fields] OR "prediction value*"[All Fields] OR "prediction risk*"[All Fields] OR "risk assessment"[All Fields] OR "risk score*"[All Fields] OR (validation[All Fields] AND decision[All Fields]) OR (validation[All Fields] AND rule[All Fields]) OR "validation score*"[All Fields] OR (derivation[All Fields] AND validation[All Fields]) OR (("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) AND ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields])) OR (("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "symptoms"[All Fields] OR "diagnosis"[MeSH Terms] OR "symptoms"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "signs"[All Fields] OR "diagnosis"[MeSH Terms] OR "signs"[All Fields]))

AND

Search 3: limit to humans

NOT

Search 4: Publication type

(News[ptyp] OR Comment[ptyp] OR Editorial[ptyp] OR Case Reports[ptyp] OR Dictionary[ptyp])

AND

Search 5: Limit to year. Searches were run by year from 1980 to 2013

Appendix 2: Detailed summary of impact analysis studies of CPRs relevant to primary care

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
Musculoskeletal							
Auleley, 1997, France (15)	Ottawa ankle rule Sensitivity 100% (95-100%), Specificity 50% (46-55%), LR+=2.0 (1.8-2.2) Cluster RCT	4980, ≥ 18 years, emergency departments of 5 Paris university teaching hospitals Preintervention:2218, (male 620, female 1086), mean age 35 (18-92) Intervention: 1911, (male 546, female 463), mean age 34 (18-94) Post-intervention: 851, other	**Intervention:** educational intervention to encourage CPR use (i.e. posters, pocket cards, and data forms) **Post-intervention:** only posters alone used to sustain the intervention effect. **Comparison:** Usual care	**Physician behaviour:** Referral for radiography (ankle/foot)	Relative reduction intervention site: 22.4% (95% CI 19.8-24.9), control group increase of 0.5% (95% CI 0-1.4). Post-intervention x-ray requests (83.1% vs. 98%). Fracture prevalence rate: 12.4% control, 12.3% intervention	Missed fractures Patient satisfaction	1. More missed fractures in intervention (n=3) than control (n=0) 2. Greater patient satisfaction in control (98%) than intervention (96%)

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
		demographics not presented					
Cameron, 1999, Canada, (19)	Ottawa Ankle Rule Sensitivity 100% (95-100), Specificity 50% (46-55%), LR=2.0 (1.8-2.2) Controlled before-after	1648, ≥18 years, Male 885, Female 763, Mean age 38 (18-91), emergency departments in 10 hospitals Group A: 516 Group B: 567 Group C: 565	**Group A:** little or no prior use of the CPR and educational intervention (educational meeting, posters, pocket cards and patient information leaflets) **Group B:** some prior use of the CPR and educational intervention **Group C:** active local implementation of the CPR and no educational intervention.	**Physician behaviour:** Referral for ankle X-ray	No reduction referral for ankle X-rays: intervention before 73%, after 78%, p=0.11, control before 75%, after 65%, p=0.022 Fracture prevalence rate 11.7%	NA	NA
Stiell, 1994, Canada, ER(16)	Ottawa ankle rule Controlled before-after	2342, ≥ 18 years, emergency departments of 2 hospitals Intervention	**Intervention:** educational intervention to encourage CPR use (i.e. lecture, pocket cards, and posters)	**Physician behaviour:** Referral for radiography (ankle/foot)	*Ankle x-ray:* Relative reduction 28% in intervention group, increase of 2% in control	No difference in intervention between patients with X-ray vs non X-ray 1. Time spent in ER	1. Less time in ED for non-X-ray: 80 vs. 116 minutes. 2. More subsequent visits for X-ray: 20% vs 7%,

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
	Sensitivity 100% (95-100), Specificity 50% (46-55%), LR=2.0 (1.8-2.2)	Before: 657 After: 551 Male 51% Mean age 37 (18-92) Control Before:541 After:593 Male 54% Mean age 36 (18-86)	**Post-intervention:** posters remained in ER **Comparison:** Usual care		group (p<0.001). *Foot X-ray:* Relative reduction of 14% intervention group, increase of 13% in control group (p<0.05). Fracture prevalence: Before 14.7% After: 17.1%	(minutes) 2. Subsequent physician visits 3. Subsequent ankle x-ray 4. Mean days off work 5. Mean cost ($) 6. Patient satisfaction	p<0.001 3. Subsequent X-ray: same 5% 4. More days off in X-ray group: 5 vs 3, p<0.001 5. Lower costs for non-X-ray: $62 vs. $173. p<0.0001 6. Satisfaction similar: 95% vs. 96%.
Boutis, 2013, Canada, ER(20)	Low Risk Ankle Rule Sensitivity 100% [93.3-100)	2151, children aged 3-16, emergency departments of six hospitals	**Phase 1:** no intervention **Phase 2:** educational interventions to encourage CPR use (i.e. physician education, pocket cards, posters)	**Physician behaviour:** Referral for ankle X-ray	Relative reduction in ankle x-rays in intervention sites compared to control sites.	Significant missed fractures 2. Length of stay (hours) 3. Physician satisfaction	1. RR: 0.008 (-0.004 – 0.02) 2. RR: 0.4 (-0.2 – 0.9) 3. RR: 8.3 (-16.9 –

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
	Specificity NR ITS	Intervention: 1055, Male 46%, Mean age 12.3 Control: 1096, Male 49%, Mean age 13.4	and CDSS **Phase 3:** CDSS only **Comparison:** Usual care		RR: 21.9% (95% CI 15.2-28.6) Fracture prevalence rate: NR	4. Patient satisfaction	0.4) 4. RR: -11.5 (-23.4 – 0.5)
Stiell, 1997, Canada, ER(17)	Ottawa Knee Rule Sensitivity 100% (94-100), Specificity 49% (46-52%), LR+=2.0 (1.7-2.1) Controlled before-after	3907, ≥ 18 years, emergency departments of 4 hospitals (2 community and 2 teaching) Intervention before: 982 after: 1063 Male: 54% Mean age: 39 (18-101) Control	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters). **Comparison:** Usual care	**Physician behaviour:** Referral for knee radiography	Relative reduction of 26.4% of patients referred for knee x-ray in intervention group (77.6% vs. 57.1% (p<0.001), vs. relative reduction of 1.3% in control group (76.9% vs. 75.9%, p=0.6)	1. Difference in intervention between patients with X-ray vs non X-ray 2. Time spent in ER (minutes) 3. Subsequent physician visits 4. Subsequent ankle x-ray 5. Mean days off work 6. Mean cost ($) 7. Patient	1. Less time in ED for non-X-ray: 86 vs. 119 minutes. 2. More subsequent visits for X-ray: 52.4% vs. 38.3% 3. More subsequent X-ray in non X-ray group: 6.9% vs. 1.7% 4. More days off in X-ray group: 6 vs. 3 5. Lower costs for non-X-ray: $80 vs.

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
		before:962 after: 900 Male: 54% Mean age: 41 (18-97)			Fracture prevalence rate Intervention: 5.8% Control: 10.3%,	satisfaction	$183 6. Satisfaction similar: 96% vs. 98%.
Stiell, 2009, Canada, ER(18)	Canadian C-spine Rule Sensitivity 99% (96-100%), Specificity 45% (44-46%), LR+=1.8 (1.7-1.9) Cluster RCT	11824, ≥ 16 years, emergency departments of 6 hospitals Intervention Before: 3267 After: 3628 Male: 50%, Mean age 39 (16-100) Control Before: 2413 After: 2516 Male: 48% Mean age: 38	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters) and CDSS at point of requesting imaging **Comparison:** Usual care	**Physician behaviour:** Diagnostic imaging rate of cervical spine	Relative reduction of 12.8% for cervical spine imaging (95% CI 9-16%) intervention group. Control group showed a relative increase of 12.5% (95% CI 7-18%) Prevalence rate clinically important	1. Serious adverse outcomes 2. Physician accuracy in using the rule 3. Sensitivity of rule	1. No serious adverse outcomes 2. 82.9% accurate interpretation rule 3. Se: 100% [85-100]

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
		(16-102) Postintervention: 5800			cervical spine injury (fracture/dislocation/ligamentous instability): Before: 1.6% After: 0.8%		
Respiratory							
McIsaac, 2002, Canada, Primary care(29)	McIsaac Sensitivity 83% (no CIs), Specificity 94% (no CIs) LR+=13.8 RCT	621, ≥ 3 years, general practice, 97 participating GPs, Intervention: 304 Mean age: 27.5 Female: 65.4% Control: 317 Mean age: 28.1, Female: 69.1%	**Intervention:** mailed educational intervention (published score with summary explanation with pocket card). Physicians were provided with a sticker to apply to the encounter form that listed the score and management approach.	**Physician behaviour:** Unnecessary antibiotic prescriptions (negative throat swab)	Non-significant difference intervention vs control groups in unnecessary antibiotic prescription (20.4% vs. 16.1%, p=0.29). Prevalence of swab confirmed diagnosis streptococcal	Overall antibiotic use	No difference between groups in overall antibiotic use (28.1% vs. 27.9%, p=0.97)

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
			Comparison: Physicians only received the education material.		throat infection: Control 12.6%, Intervention: 7.9%		
McIsaac, 1998, Canada, Primary care(28)	Centor score Sensitivity 90% (no CIs), Specificity 92% (no CIs) LR+=11.3 RCT	396, ≥ 15 years, general practice, 450 participating GPs Intervention: 184 Mean age: 31.6 Male: 41.2% Control: 212 Mean age: 31.5 Male 40.1%	**Intervention:** mailed educational intervention (published score with summary explanation and patient information). Physicians asked to complete an encounter form with symptom check list, CPR score and management actions. **Comparison:** mailed educational	**Physician behaviour**: Antibiotic prescription	Non-significant reduction in antibiotic prescription in intervention group (27.8%) vs. control (35.7%) (p=0.09)	Antibiotic prescribing per estimated Group A streptococcal prevalence calculation	In score category 1 the antibiotic prescription rates were statistically significant. 16.2% in control vs. 3.6% in intervention.

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
			intervention and a control form with no score or management actions.				
McGinn, 2013, USA, (32)	1) Walsh rule for streptococcal pharyngitis 2) Heckerling rule for pneumonia Walsh rule: c-statistic: 0.71 [95% CI, 0.67-0.74) Heckerling rule: c-statistic 0.82 (0.74-	168 Primary care providers, 2 large academic ambulatory care centres in New York 984 Patients **Intervention**:586 Mean age: 43 Female: 24% **Control:**398 Mean age: 49 Female: 23%	**Intervention:** education session and computerised CDSS with CPRs embedded promoting physician to calculate scores of both CPRs and receive management recommendations. **Comparison:** Usual care with background information on CPRs	**Physician behaviour**: Change in antibiotic prescription	Intervention group significantly less likely to order antibiotics than control (age-adjusted RR, 0.74; 95% CI, 0.60-0.92). Absolute risk difference 9.2%.	Rate of chest radiographs Rate of rapid streptococcal tests Number throat cultures ordered	1. Intervention less likely to order chest radiographs (RR 0.89; 95% CI, 0.55-1.46) 2. Intervention significantly less likely to order rapid streptococcal test (RR 0.75; 95% CI, 0.58-0.97) 3. Intervention significantly less likely to do throat cultures (RR 0.55; 95% CI, 0.35-0.86)

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
	0.9) RCT						
Worrall, 2007, Canada, (30)	Modified Centor score Sensitivity 90% (no CIs), Specificity 92% (no CIs), LR+=11.3 RCT	533, ≥ 19 years, 37 practices in eastern Newfoundland CPR:170 RADT: 120 RADT+CPR:102 Control:141 Gender and age patient demographics NR	**CPR group**: decision rules only **RADT group**: rapid antigen test only **RADT+CPR group**: decision rules and antigen test combined **Comparison:** Usual care	**Physician behaviour**: Prescribing rate of antibiotics	Prescription rates: CPR alone - 55% RADT - 27% (NS) RADT+CPR -38% (p<0.001) Control: 58%	Types of antibiotics prescribed	Amoxicillin most commonly prescribed (47%), followed by penicillin (20%)
Little, 2013, UK (31)	FeverPAIN c-statistic: 0.71	631, ≥ 3 years, general practice (48 UK practices)	**CPR group:** CPR was applied and antibiotic prescribed according to the score.	**Patient behaviour:** Patient reported symptom severity days 2-4 after consultation on a 7-	Greater improvements in symptom severity for CPR group compared	1. Antibiotic prescribing 2. Symptom duration 3. Medicalising	1. Lower use of antibiotics in CPR group than control (RR 0.71, 0.50 to 0.95)

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Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
	RCT	CPR group:211 Female: 60% Mean age: NR CPR+RADT group: 213 Female: 65% Mean age: NR Delayed prescribing: 207 Female:67% Mean age: NR	**CPR+RADT group:** CPR was applied and antibiotic prescribed or RADT carried out according to the score. **Comparison:** Delayed prescribing	point Likert scale	to control (−0.33, 95% CI −0.64 to −0.02)	beliefs 4. Return consultations 5. Suppurative complications	2. Symptom resolution was significantly faster in the CPR group (hazard ratio 1.30, 95% CI 1.03 to 1.63) 3. No significant difference in beliefs 4. No significant difference in return to GP 5. No suppurative complications.
Cardiovascular							
Pozen, 1984, USA, ER(21)	Pozen score for chest pain Sensitivity 94% (no CIs), Specificity 78% (no CIs) LR+=4.3	2320, aged ≥30 male and ≥40 female, emergency departments of 6 US hospitals Intervention:	**Intervention:** Research assistant presented physicians with the CPR probability score. **Comparison:** Usual care, the CPR	**Physician behaviour:** Appropriate admission/discharge	30% relative reduction in patients admitted to CCU who did not have acute coronary syndrome	diagnostic accuracy of acute myocardial infarction	Overall diagnostic accuracy significantly higher in intervention group. Intervention: 83.4%, control 79.6% (p=0.002) There was no significant

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
	ITS	1288 Control: 1032 Overall mean age 62 Male: 62%	probability was calculated but not presented to the physicians.		Overall prevalence of cardiac ischaemia 32% intervention, 29% control		difference in sensitivity. (intervention: 94.5%, control 95.3, NS)
Kline, 2009, USA, ER(22)	Kline chest pain CPR c-statistic 0.74 (0.65-0.82) RCT	369 adults presenting with chest pain, one emergency room in an academic urban US hospital Intervention: 185 Female: 64% Mean age: 46 Control 184 Female: 61% Mean age: 46	**Intervention:** Clinicians and patients received a printout of CPR result displayed numerically and graphically. **Comparison:** Usual care, no printout was provided to clinicians or patients.	**Physician behaviour**: Hospital admission with no significant cardiovascular diagnosis	No significant decrease for patients admitted with no CVD diagnosis: 11% vs. 5% (95% CI 0.2%-11%), p=0.059 Prevalence of acute coronary syndrome (ACS): 2.1%	Delayed/missed diagnosis of ACS, thoracic imaging with a negative result, median length of stay, patient satisfaction, readmission	Significant decrease in thoracic imaging: 16/184 intervention vs. 36/185 control, (95% CI 3.8%-18%, p=0.004), higher patient satisfaction: (90/184 intervention rate vs. 70/185 control 'very satisfied' (95% CI 0.9%-21%), p=0.01, decreased readmission rate/return to ER: 4% intervention vs. 11% controls (95% CI 2.5%-13.2%), p=0.001, no

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
							difference in length of hospital stay: 11.4 hours control vs. 9.2 hours intervention, p=0.36.
Persell, 2012, primary care(27)	Framingham risk estimate and global cardiovascular risk score Cluster RCT	N=14 physicians, n=218 adult patients randomised to intervention, n=15 physicians, n=217 adults patients randomised to control, US primary care	**Intervention**: Individualised CVD risk estimate posted to high-risk patients and their physicians alerted by secure email Control: usual care	**Patient:** Reduction in LDL-cholesterol level by 30mg/dl	No difference in the primary outcome (11% vs. 11.1% OR 0.99, 95% CI 0.56, 1.74, p=0.96)	Receipt of a statin prescription	Intervention patients were more likely to receive a prescription for a statin (11.9% vs. 6%, OR 2.13, 95% CI 1.05, 4.32, p=0.038)
Grover 2007 and 2008, primary care(25, 26)	Framingham risk score RCT	N=3,053 adults mean age 56.4, male 66.9%, n=230 primary care physicians, 10 provinces in Canada primary	**Intervention:** Patients identified as high risk and randomised to intervention had their individualised coronary risk profile	**Patient outcomes:** 1. Reduction in LDL-cholesterol level	Statistically significant reduction in LDL and total cholesterol-HDL ratio in intervention vs.	Reduction in BP	Patients in intervention group were more likely to receive appropriate antihypertensive treatment and more likely to start or modify treatment

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
		care	discussed **Control:** usual care, coronary risk profile withheld		control and patients were more likely to reach lipid targets		
Hall, 2003, UK, (23)	New Zealand cardiovascular risk score NR Pilot RCT	323, aged 35-75 years, patients with no history of cardiovascular or renal disease, one UK hospital outpatient department (OPD) clinic Experimental: 162 Control:161 Age and gender demographics: NR	**Intervention:** Risk scores were clearly documented at the front of the notes of patients. **Comparison:** Usual care	**Physician behaviour:** 1. Prescription of risk modifying drugs 2. Management of CVD risk factors	1. No significant between group differences, change in diabetes treatment 42% (95% CI 34-50) vs. 52 (95 CI 29-45%), change in antihypertensive drugs 26 (95% CI 10-22%) vs.	time to next OPD appointment	No difference in time to next OPD (24% in each group received OPD appointment in <6 months).

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
					10% (95% CI 5-16%), change in lipid lowering drugs: 12% (7-17%) vs. 9% (95% CI 4-14%) 2. Referral to dietician 10% (95% CI 6-15%) vs. 13% (95% CI 7-19%)		
Hanon, 2000, France (24)	Framingham risk score NR RCT	1243, aged 18 -75 years with hypertension attending a general physician Mean age: 60	**Intervention:** Physicians knowledge of the calculated risk score. **Comparison:** Usual care	**Patient and Physician behaviour:** Change in BP, patients prescribed dual therapy	No difference in BP (patients with BP <140/90 mmHg intervention: 64%, control 62%) or %	Physician estimation vs. Framingham risk equation calculated 10 year CVD risk	General physicians' calculation of CVD risk at 10 years has poor concordance with the Framingham risk model (35%).

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
		Male: 54%			patients on dual therapy (41% intervention vs 46% control)		
Neurological							
Stiell, 2010, Canada, ER(33)	CT head rule Sensitivity 100% (96-100%), Specificity 51% (48-53%), LR+=2.0 (1.8-2.3) Cluster RCT	4531, alert and stable adults with minor head injury aged ≥ 16 years, 12 emergency departments in three provinces of Canada (6 teaching sites, 6 community sites) Intervention: Before: 1049 After:1531 Mean age: 37 (16-99) Male: 70%	**Intervention:** educational interventions to encourage CPR use (i.e. lecture, pocket cards and posters) and real-time reminder at point of requesting imaging **Comparison:** Usual care	**Physician behaviour:** Proportion of patients referred for CT imaging	Increased proportion of patients referred for CT imaging intervention: before: 62.8%, after: 76.2% (difference: 13.3% (95% CI 9.7%-17.0%) Control: before: 67.5%, after: 74.1% (difference: 6.7% (95% CI	1. Accuracy CPR 2. Number of clinically important brain injuries not identified at ER 3. Adverse outcomes	1. Sensitivity 100% [96-100%] 2. No missed brain injuries or adverse outcomes. 3. Deaths from brain injury: intervention: before: 0.1%, after: 0.1%, control: before 0.3%, after: 0.1%

Author, Year, Country	CPR name, predictive accuracy (95% CI), Positive likelihood ratio (LR+)[$], Study design	Population and study setting	Intervention and comparison	Primary outcome(s)	Results: primary outcome (CI)	Secondary outcome(s)	Results: secondary outcomes
		Control: Before: 876, After:1075 Mean age: 39 (16-97) Male: 71%			2.6-10.8)		

*NR=Not reported, **NA=Non-applicable, ***NS=Non-significant, [$] CPR predictive accuracy as referenced in the impact analysis study

Appendix 3: Uncontrolled before-after impact analysis CPR studies excluded from data analysis due to study design

Author, Year	CPR name	Type of study	Implementation	Predictive accuracy (reported), level of evidence	Type of outcome
Bessen, 2009 (36)	Ottawa ankle rule	Before-after	CPR only	Sensitivity 100% (95-100%), Specificity 50% (46-55%), LR=2.0 (1.8-2.2)	Physician behaviour
Stiell, 1995 (35)	Ottawa ankle rule	Before-after	CPR only	Sensitivity 100% (95-100%), Specificity 50% (46-55%), LR=2.0 (1.8-2.2)	Physician behaviour
Kerr, 2005 (37)	Canadian C-spine rule	Before-after	CPR only	Sensitivity 99% (96-100%), Specificity 45% (44-46%), LR+=1.8 (1.7-1.9)	Physician behaviour
Stanley, 2009 (38)	Glasgow Blatchford bleeding score	Before-after	CPR only	Sensitivity 99% (no CIs), Specificity 32% (no CIs), LR+=1.5	Physician behaviour + patient
Sultan, 2004 (39)	CT head rule	Before-after	CPR only	Sensitivity 100% (96-100%), Specificity 51% (48-53%), LR+=2.0 (1.8-2.3)	Physician behaviour

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PRISMA 2009 Checklist

1Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	na
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5, 6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5,6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5,6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5,6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6, 7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	na
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1 and Appendix 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figure 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 1 and Appendix 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Figure 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	na
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12,13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1