

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>info.bmjopen@bmj.com</u>

BMJ Open

BMJ Open

Electronic Health Records, Interoperability, and Patient Safety in Health Systems of High-Income Countries: A Systematic Review Protocol

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-044941
Article Type:	Protocol
Date Submitted by the Author:	19-Sep-2020
Complete List of Authors:	Li, Edmond; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; London School of Hygiene and Tropical Medicine Faculty of Infectious and Tropical Diseases, Clinical Research Department Neves, Ana Luisa; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; University of Porto, Center for Health Technology and Services Research / Department of Community Medicine, Health Information and Decision Clarke, Jonathan; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; Imperial College London, Centre for Mathematics of Precision Healthcare Ashrafian, Hutan; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer Darzi, Ara; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, Information technology < BIOTECHNOLOGY & BIOINFORMATICS, Information management < BIOTECHNOLOGY & BIOINFORMATICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

Electronic Health Records, Interoperability, and Patient Safety in Health Systems of High-Income Countries: A Systematic Review Protocol

Edmond Li^[1], Ana Luisa Neves^[1,2], Jonathan Clarke^[1,3], Hutan Ashrafian^[1], Ara Darzi^[1] ^[1] Imperial NIHR Patient Safety Translational Research Centre (PSTRC), Institute of Global Health Innovation (IGHI), Imperial College London, London, United Kingdom ^[2] Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS) / Center for Health Technology and Services Research (CINTESIS), University of Porto, Porto,

Portugal.

unde. Tics of Precision . ^[3] Centre for Mathematics of Precision Healthcare, Imperial College London, London, United Kingdom

Corresponding author

Name: Edmond Li

Email: edmond.li19@imperial.ac.uk

Address: Institute of Global Health Innovation, Room 1035/7, QEQM Wing, St Mary's Campus, London W2 1NY

Keywords [MeSH terms]: electronic health records, electronic medical records, computerised patient records, health information technology, health information exchanges, interoperability, patient safety, patient harm, adverse events, health outcomes

Word count: 1821

Target journal: BMJ Open

Abstract

Introduction

The availability and routine use of electronic health records (EHRs) have become commonplace in healthcare systems of many high-income countries. While there is an ever-growing body of literature pertaining to EHR use, evidence surrounding the importance of EHR interoperability and its impact on patient safety remains less clear. There is therefore a need and opportunity to evaluate the evidence available regarding this relationship so as to better inform health informatics development and policies in the years to come.

Objective

This systematic review aims to evaluate the impact of EHR interoperability on patient safety in health systems of high-income countries.

Methods and analysis

A systematic literature review will be conducted via a computerised search through three databases: PubMed, Embase, and HMIC for relevant articles published between March 2010 and March 2020. Outcomes of interest will include: impact on patient safety, and the broader effects on health systems. Quality of the randomised quantitative studies will be assessed using Cochrane Risk of Bias Tool. Non-randomised papers will be evaluated with the Risk of Bias In Non-Randomised Studies - of Interventions (ROBINS-I) tool. Drummond's Checklist will be utilised for publications pertaining to economic evaluation. The National Institute for Health and Care Excellence (NICE) quality appraisal checklist will be used to assess qualitative studies. A narrative synthesis will be conducted for included studies, and the body of evidence will be summarised in a summary of findings table.

Ethics and dissemination

This review will summarise published studies with non-identifiable data and therefore does not require ethical approval. This protocol complies with the Preferred Reporting Items for Systematic Review and Meta-Analyses Protocols guidelines. Findings will be disseminated through preprints, open access peer-reviewed publication, and conference presentations. Patients or members of the public were not involved in the design of this study.

Strengths and limitations of this study

Strengths	Limitations
 Comprehensive characterisation of interventions using interoperable EHRs Summary and quality appraisal of existing evidence on the potential impact on patient safety Inclusion of both quantitative and qualitative methods can provide a comprehensive overview of the multitude of ways in which interoperable EHRs may affect patient safety and health systems. 	 The heterogeneity of methods and outcomes assessed may obscure the true effect interoperable EHRs have had on patient safety in the clinical setting Potential small sample size in subgroup analyses, may negatively impact the statistical power in quantitative data synthesis.

	pragmatic question which is integral to influencing future health informatics
--	----------------------------------------------------------------------------------

PROSPERO registration number [CRD42020209285]

This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the licence is given, and indication of whether changes were made. See: https://creativecommons.org/licenses/by/4.0/.

to perteries only

Introduction

Electronic health records (EHRs) have become an integral part of modern healthcare since their initial mainstream implementation in the mid-late 2000s through the passing of the Health Information Technology for Economic and Clinical Health Act (HITECH) in the United States and the NHS National Programme for IT initiative (NPfIT) in England (1–4). From the documentation & retrieval of patient records and the prescription of medications, to coordinating complex care plans between different healthcare providers and electronic billing, EHRs fulfil a multitude of roles for both clinicians and patients alike (5–9).

In order to achieve EHR's full potential, it is critical to improve interoperability - i.e. "*the ability of health information systems to work together within and across organisation boundaries in order to advance effective delivery of healthcare for individuals and communities*" (10). The lack of universal interoperability is often cited as one of the many significant shortcomings of EHRs currently in use, resulting in duplication in healthcare costs, increased clinician workload fatigue, and poses a potential risk to patient safety (2). This is especially problematic for patient populations with chronic conditions, polypharmacy, and multiple comorbidities who are reliant upon effective patient information sharing via EHRs to facilitate their care (11).

In the fragmented EHR landscape of the United Kingdom, understanding this poor interoperability and accurately measuring its cost both to patient safety and the health system as a whole, remain challenging (12). Although there is a growing body of literature investigating areas such as the facilitators and barriers to EHR greater adoption, technical capabilities, and usability (13,14), no systematic review has been conducted exploring specifically the problem of interoperability amongst the assortment of EHRs in use, how it affects patient safety, and ultimately the financial cost savings lost to health systems.

In a recent systematic review by Dobrow *et al.* assessing the effects of EHR and HIT interoperability on health systems, 130 publications were included, with the majority being studies conducted in the United States, utilised quantitative methods, and focussed primarily in acute healthcare settings. The authors noted the use of interoperable EHRs had a positive impact on outcomes measures such as quality of care and productivity (13). However, in domains such as stakeholder engagement, performance & reliability, security & privacy, information quality, and ease of use, the benefits of interoperable EHRs was less clear (13). Amongst the 130 publications, 17 were reviews with the majority directed at exploring facilitators & barriers to EHR implementation, and the general benefits and impact of EHR use. While this review did focus on studies pertaining to the topic of interoperable EHRs, this was done so only from a broad perspective and included studies exploring a wide range of outcomes related to the effects of EHR on healthcare rather than specifically on their implications to patient safety.

In another review by Hersh *et al.*, the authors explored how health information exchange (HIE) affected health systems on a variety of domains, including costs, healthcare utilisation, health outcomes, healthcare worker attitudes, and sustainability. Despite the widespread routinely use of HIE, the authors described a general lack of robust evidence on the quality, costs, efficiency, usage, and sustainability (15). However, there was some evidence demonstrating HIEs being

associated with reduced utilisation and costs in emergency care settings despite methodological issues being present in many of the included publications (15). Although this review was ambitious in the wide scope of interest regarding the effects of HIE use, patient safety was not a primary topic of focus. Another limitation of this study was that it only contained US-based publications, and thus findings lack generalisability internationally to other health systems in high-income countries (HIC) which are both organised, financed differently.

Research aim

The overall aim of this literature review is to explore how EHR interoperability impacts patient safety, in the context of health systems in HICs. The results generated will aim to inform healthcare policymakers and help shape more effective EHR system implementation and modernisation efforts in the coming years.

Methods and analysis

Search strategy

A computerised search of the literature published in the last 10 years (March 2010 to March 2020) search will be performed on PubMed, Embase and Health Management Information Consortium (HMIC). The list of search strings used will include both free text and controlled terms, whenever supported (Table 1) and will be iteratively refined in consultation with the Imperial College St. Mary's campus medical librarian.

Grey literature sources will also be searched, including registrations in the International Prospective Register of Systematic Reviews, reports of relevant stakeholder organisations (NHS England, American Medical Informatics Association (AMIA), eHealth at WHO, and conference proceedings (last 5 years) of several related conferences (AMIA, MedInfo, Medicine 2.0, Medicine X)), in order to identify possible additional studies that meet the inclusion criteria.

The search has also been restricted to HIC and articles published in English only.

Table 1: Concepts and database search terms	Table	1:	Concepts	and	database	search	terms
---------------------------------------------	-------	----	----------	-----	----------	--------	-------

Electronic health		Interoperability	5	Patient safety
 Electronic health record* / EHR Electronic medical record* / EMR Health information exchange / HIE Health information technology / HIT EHR-based interventions 	AND	 Interoperabl* Interoperability Standards of information 	AND	 Patient safety Patient adj1 incident* Adverse adj1 event* Patient adj1 outcome* Patient adj1 harm Risk management

• Computerised		
patient record* /		
CPR		

Study selection criteria

A summary of the population, intervention, comparison, outcomes, and type of studies being considered is provided in **Table 2**. This systematic review will focus on studies performed in high-income countries and published in English only. Studies assessing the impact of EHR interoperability will be included. Interventions will include EHR systems interoperable with other health information technology systems both within and across healthcare facilities, as well as those used in tertiary and community settings. The primary outcomes to be considered in this review will be safety outcomes, including adverse events/incidents, safety-related patient experiences, and health outcomes. In addition, secondary outcomes would include studies exploring the broader impact of interoperable EHRs on health systems such as cost effectiveness and clinical culture amongst healthcare providers on the topic. Both qualitative and quantitative studies will be included. Reference lists of the selected articles will also be screened for papers which may have been missed by the initial database search but still meet the eligibility criteria.

Table 2: PICO inclusion criteria

Population	High-income countries utilising electronic health records
Intervention	EHRs with interoperability
Comparison	Usual care (i.e. existing baseline of interoperability)
Outcome	Impact on patient safety and quality of care

Screening

Articles to be included will be screened by two independent reviewers, following the process described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (16). The initial screening will be done by the first reviewer based on the publication titles, followed by a second screening based on the abstracts. Included abstracts will then be fully reviewed by two independent researchers to produce a unified selection of articles to be included in this review. Cohen's kappa will be calculated to ensure inter-rater agreement and consistency in the selection of studies to be included (17,18). Any disagreements will be resolved by consensus; if a Cohen's kappa value of less than 0.6 is reported, the discrepancies will be addressed through discussions with a more experienced third investigator.

Data extraction & analysis

Data extraction will be performed using a standardised extraction table for each of the two investigators to summarise the characteristics and findings of each included study, including name of the first author, year of publication, study design, number of participants, retention rates, setting characteristics, outcome measures, and main results. The content of the two summary tables will then be aggregated and reviewed once more by both investigators, with any disagreements being solved by the third senior investigator.

Quality assessment

The quality of randomised controlled trials and cluster randomised trials will be assessed using the Cochrane Risk of Bias Tool (19), and the quality of non-randomised intervention studies (i.e., case control, cohort, quasi-experimental) will be appraised using the 'Risk of Bias In Non-

Randomised Studies - of Interventions' (ROBINS-I) tool (20). For cost-effectiveness studies, the Drummond's checklist for assessing economic evaluations will be used (21). The National Institute for Health and Care Excellence (NICE) quality appraisal checklist will be utilised to assess the selected qualitative studies (22). Two independent reviewers will score the selected studies and any disagreements will be resolved by a third person. A risk of bias table along with an overall, collective bias narrative will be produced to summarise the biases of outcomes observed amongst the evaluated studies.

Descriptive analysis

A narrative synthesis will be conducted for all the included studies.

Quantitative studies with comparable outcome measures will be aggregated to allow for comparative analyses whenever possible. However, no meta-analysis will be done for this systematic review as the likely heterogeneity of the outcomes would make this impractical. Qualitative studies will be thematically analysed. Those that demonstrate related, prominent themes in their findings will be grouped together and collectively summarised via a thematic narrative. The body of evidence will be summarised in two separate Summary of Findings tables (for both qualitative and quantitative studies) in accordance to the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE) criteria where possible (23). Patient and public involvement

This systematic literature review saw no direct participation by patients or the public during the design of this study. However, this study was designed following a series of structured interviews with patients regarding their experience of attending multiple institutions for hospital care (24). As this literature review will be used to form the basis for subsequent studies exploring the topic including ones involving patients, findings from this review will be shared with patient research groups to gain feedback and encourage further discourse surrounding the topic of EHR interoperability and patient safety.

Amendments

Any amendments to this protocol will be documented with reference to saved searches and analysis methods, which will be recorded in bibliographic databases, Mendeley and Excel templates for data collection and synthesis.

Discussion

One of the primary strengths stemming from the almost exploratory nature of this systematic review is the ability to generate a succinct, comprehensive appraisal of the best evidence currently available regarding how EHR interoperability impacts patient care and safety. By publishing this review protocol beforehand, we demonstrate a clear, robust, and transparent approach to aggregating the anticipated assortment of literature on the subject in question. There are also some potential limitations to be acknowledged. A potential challenge would be the likely anticipated heterogeneity in methodology of the included articles. With such diverse means of measuring and assessing the effects of EHR interoperability, this will likely make comparisons between studies difficult and may obscure the true measure of effect EHR interoperability has had in the clinical setting. To mitigate this risk, outcomes will be grouped whenever possible, and summarised as a narrative synthesis. However, this can also represent a strength as it will provide a comprehensive overview on the subject, capitalising on various research methodologies, and providing novel insights on the impact of interoperable EHR systems on patient safety.

Acknowledgments

We would like to thank Michael Gainsford (Library Manager and Liaison Librarian at Imperial College London) for his support and guidance provided to improve the composition of the search terms and procedural aspects of the overall search strategy. JC acknowledges support from the Wellcome Trust [215938/Z/19/Z].

Funding

This research was supported through the Imperial College National Institute for Health Research (NIHR) Patient Safety Translational Research Centre (PSTRC) and the Imperial College Biomedical Research Centre (BRC). However, the funder/sponsor has had no role in development and drafting of this protocol.

or occience i en ont

References

- Colicchio TK, Cimino JJ, Del Fiol G. Unintended consequences of nationwide electronic health record adoption: Challenges and opportunities in the post-meaningful use era. *Journal of Medical Internet Research*. [Online] 2019;21(6): 1–9. Available from: doi:10.2196/13313
- Roman LC, Ancker JS, Johnson SB, Senathirajah Y. Navigation in the electronic health record: A review of the safety and usability literature. *Journal of Biomedical Informatics*. [Online] Elsevier Inc.; 2017;67: 69–79. Available from: doi:10.1016/j.jbi.2017.01.005
- 3. Justinia T. The UK's National Programme for IT: Why was it dismantled? *Health Services Management Research*. [Online] 2017;30(1): 2–9. Available from: doi:10.1177/0951484816662492
- 4. Wachter RM. Making IT work : harnessing the power of health IT to improve care in England. *National Advisory Group on Health Information Technology in England*. [Online] 2016; 71. Available from:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/550866/Wa chter_Review_Accessible.pdf%0Ahttps://assets.publishing.service.gov.uk/government/upl oads/system/uploads/attachment_data/file/550866/Wachter_Review_Accessible.pdf

- Kruse CS, Kristof C, Jones B, Mitchell E, Martinez A. Barriers to Electronic Health Record Adoption: a Systematic Literature Review. *Journal of Medical Systems*. [Online] Journal of Medical Systems; 2016;40(12). Available from: doi:10.1007/s10916-016-0628-
- Ayaad O, Alloubani A, ALhajaa EA, Farhan M, Abuseif S, Al Hroub A, et al. The role of electronic medical records in improving the quality of health care services: Comparative study. *International Journal of Medical Informatics*. [Online] Elsevier; 2019;127(April): 63–67. Available from: doi:10.1016/j.ijmedinf.2019.04.014
- Evans RS. Electronic Health Records: Then, Now, and in the Future. *Yearbook of Medical Informatics*. [Online] 2016;25(S 01): S48–S61. Available from: doi:10.15265/IYS-2016-s006
- 8. Gagnon MP, Payne-Gagnon J, Breton E, Fortin JP, Khoury L, Dolovich L, et al. Adoption of electronic personal health records in Canada: Perceptions of stakeholders. *International Journal of Health Policy and Management*. [Online] 2016;5(7): 425–433. Available from: doi:10.15171/ijhpm.2016.36
- 9. Campanella P, Lovato E, Marone C, Fallacara L, Mancuso A, Ricciardi W, et al. The impact of electronic health records on healthcare quality: a systematic review and metaanalysis. *The European Journal of Public Health*. [Online] 2016;26(1): 60–64. Available from: doi:10.1093/eurpub/ckv122
- Reis ZSN, Maia TA, Marcolino MS, Becerra-Posada F, Novillo-Ortiz D, Ribeiro ALP. Is There Evidence of Cost Benefits of Electronic Medical Records, Standards, or Interoperability in Hospital Information Systems? Overview of Systematic Reviews. *JMIR Medical Informatics*. [Online] 2017;5(3): e26. Available from: doi:10.2196/medinform.7400
- 11. World Health Organization (WHO). *eHealth in the Region of the Americas: breaking down the barriers to implementation*. [Online] 2016. Available from: http://iris.paho.org/xmlui/bitstream/handle/123456789/31286/9789275119259-eng.pdf?sequence=6&isAllowed=y
- 12. McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory

1		
2		
3		Electronic Health Record System Implementation: Evidence from a Qualitative Study.
4 E		BioMed Research International. [Online] 2013;2013: 1–9. Available from:
5		doi:10.1155/2013/629574
7	13.	Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health
, 8		Records and Health Information Exchanges. Systematic Review JMIR Medical
9		Informatics [Online] 2019:7(2): e12607 Available from: doi:10.2196/12607
10	14	Zahabi M Kaber DB Swangnetr M Usability and Safety in Electronic Medical Records
11	17,	Interface Design: A Review of Recent Literature and Guideline Formulation. Human
12		Easters [Online] 2015:57(5): 805-824 Available from: doi:10.1177/0018720815576827
13	15	Lagh WD Tatter AM Edge KD Daving D Corresp D Kagashige SZ at al Outcomes
14	13.	Freisi WK, Totten AM, Eden KB, Devine B, Golman P, Kassakian SZ, et al. Outcomes
15		From Health Information Exchange: Systematic Review and Future Research Needs.
16		JMIR Medical Informatics. [Online] 2015;3(4): e39. Available from:
1/ 10		doi:10.2196/medinform.5215
10	16.	Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred
20		reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS
21		Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097
22	17.	Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.
23		<i>Biometrics</i> . [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310
24	18.	McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i> . 2012;22(3):
25		276–282.
26	19.	Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A
27		revised tool for assessing risk of bias in randomised trials. <i>The BMJ</i> . [Online]
28		2019:366(August), Available from: doi:10.1136/bmi.14898
29	20	Sterne IA Hernán MA Reeves BC Savović I Berkman ND Viswanathan M et al
30	-0.	ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions
32		RMI(Opling) [Opline] 2016:355: 4–10. Available from: doi:10.1136/bmi.i4919
33	21	Drummond ME Brian BL Torrance GW Stoddart GL Methods for the Economic
34	21.	Evaluation of Health Care Programmes, 2nd od Oxford University Press: 1007
35	22	Liver and the development of NICE multic health wideway [Online] 2nd n National
36	22.	Methods for the development of NICE public health guidance. [Online]. Std n. National
37		Institute for Clinical Excellence (NICE); 2018. Available from:
38		https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice-
39		public-health-guidance-third-edition-pdf-2007967445701
40	23.	Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al.
41 42		GRADE: an emerging consensus on rating quality of evidence and strength of
42		recommendations. BMJ. [Online] 2008;336(7650): 924–926. Available from:
44		doi:10.1136/bmj.39489.470347.AD
45	24.	Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design
46		an electronic health record interface: A qualitative mixed-methods study. BMC Medical
47		Informatics and Decision Making. [Online] BMC Medical Informatics and Decision
48		Making; 2019;19(1): 1-8. Available from: doi:10.1186/s12911-019-0993-7
49		
50		
51 52		
52		
53 54		
55		
56		
57		
58		10
59		
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Section and topic	Item No.	Checklist item	Reported on Page No.
ADMINISTRATIV	E INFO	ORMATION	
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

 BMJ Open

Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6-7
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	-
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6-7
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6-7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6-7
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6-7

clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the

PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

BMJ Open

BMJ Open

Electronic Health Records, Interoperability, and Patient Safety in Health Systems of High-Income Countries: A Systematic Review Protocol

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-044941.R1
Article Type:	Protocol
Date Submitted by the Author:	04-Feb-2021
Complete List of Authors:	Li, Edmond; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; London School of Hygiene and Tropical Medicine Faculty of Infectious and Tropical Diseases, Clinical Research Department Neves, Ana Luisa; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; University of Porto, Center for Health Technology and Services Research / Department of Community Medicine, Health Information and Decision Clarke, Jonathan; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; Imperial College London, Centre for Mathematics of Precision Healthcare Ashrafian, Hutan; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer Darzi, Ara; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer
Primary Subject Heading :	Health informatics
Secondary Subject Heading:	Health policy, Public health, Health services research
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, Information technology < BIOTECHNOLOGY & BIOINFORMATICS, Information management < BIOTECHNOLOGY & BIOINFORMATICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT
	1

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

2		
3	1	Electronic Health Records, Interoperability, and Patient Safety in
4 5	-	
6	2	Health Systems of High-Income Countries: A Systematic Review
7	3	Protocol
8	4	Edmond Li ^[1] Ana Luisa Neves ^[1,2] Jonathan Clarke ^[1,3] Hutan Ashrafian ^[1] Ara Darzi ^[1]
9	- -	[]] Imporial NIHD Datiant Safaty Translational Dasaarah Contra (DSTDC). Instituta of Clabal
10 11	5	In the second control of the second control
12	6	Health Innovation (IGHI), Imperial College London, London, United Kingdom
13	7	^[2] Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS)
14	8	/ Center for Health Technology and Services Research (CINTESIS), University of Porto, Porto,
15	9	Portugal.
16	10	^[3] Centre for Mathematics of Precision Healthcare, Imperial College London, London, United
17 18	11	Kingdom
19	12	
20	13	
21	14	
22	15	
23	16	
24 25	10	
26	1/	
27	18	
28	19	
29	20	
30 21	21	
32	22	
33	23	
34	23	
35	24	
36	25	
37 38	26	
39	27	
40	28	
41	29	
42	30	
43 44	31	Corresponding author
45	32	Name ⁻ Edmond Li
46	33	Fmail: edmond li19@imperial ac.uk
47	24	Address: Institute of Clobal Health Inneviation, Deem 1025/7, OEOM Wing, St Marrie Commun.
48	54 25	Address. Institute of Global Health Innovation, Room 1055/7, QEQM wing, St Mary's Campus,
49 50	35	London W2 INY
51	36	Keywords [MeSH terms]: electronic health records, electronic medical records, computerised
52	37	patient records, health information technology, health information exchanges, interoperability,
53	38	patient safety, patient harm, adverse events, health outcomes
54	39	Word count: 2723
55 56	40	
50		
58		1
59		· · · · · · · · · · · · · · · · · · ·
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1		
2		
3	41	Abstract
4 5	12	Introduction
6	42	The availability and routing use of electronic health records (EUDs) have become commonpless
7	45 44	in healthcare systems of many high income countries. While there is an ever growing hedy of
8	44 15	literature pertaining to EHR use evidence surrounding the importance of EHR interoperability
9 10	45	and its impact on notions safety remains less clear. There is therefore a need and opportunity to
10	40	evaluate the evidence available regarding this relationship so as to better inform health
12	47	informatics development and policies in the years to come
13	40 49	information development and ponetes in the years to come.
14	50	Objective
15	50	
10 17	51	I his systematic review aims to evaluate the impact of EHR interoperability on patient safety in
18	52	nealth systems of high-income countries.
19	55	
20	54	Methods and analysis
21	55	A systematic literature review will be conducted via a computerised search through four
22	56	databases: PubMed, Embase, HMIC, and PsycInfo for relevant articles published between 2010
25 24	57	and 2020. Outcomes of interest will include: impact on patient safety, and the broader effects on
25	58	health systems. Quality of the randomised quantitative studies will be assessed using Cochrane
26	59	Risk of Bias Tool. Non-randomised papers will be evaluated with the Risk of Bias In Non-
27	60	Randomised Studies - of Interventions (ROBINS-I) tool. Drummond's Checklist will be utilised
28	61	for publications pertaining to economic evaluation. The National Institute for Health and Care
29	62	Excellence (NICE) quality appraisal checklist will be used to assess qualitative studies. A
30	63	narrative synthesis will be conducted for included studies, and the body of evidence will be
32	64	summarised in a summary of findings table.
33	65	
34	66	Ethics and dissemination
35	6/	This review will summarise published studies with non-identifiable data and therefore does not
30 37	68	require ethical approval. This protocol complies with the Preferred Reporting Items for
38	09 70	systematic Review and Meta-Analyses Protocols guidennes. Findings will be disseminated
39	70	ar members of the public were not involved in the design of this study
40	71	of members of the public were not involved in the design of this study.
41	12	
42 43	72	Article Summary
44	75	Strength and Limitation of the start
45	/4	Strengths and limitations of this study
46	15	Strengths
47	/0 77	• Inclusion of quantitative, qualitative, and mixed-methods studies can provide a
48 70	70	comprehensive overview of the multitude of ways in which interoperable EHRs may
50	/8 70	The proposed review attempts to answer a progratic question which is integral to
51	/9 00	• The proposed review altempts to answer a pragmatic question which is integral to influencing future health informatics development and policies.
52	0U Q 1	influencing future nearth informatics development and policies.
53	01 87	Limitations
54 55	82	• The beterogeneity of methods and outcomes assessed may obscure the true effect
56	84	interoperable EHRs have had on patient safety in the clinical setting
57	Т	incoroporable Errics have had on patient safety in the enhear setting.
58		2
59		For peer review only - http://bmionen.hmi.com/site/about/quidelines.yhtml
60		For peer review only inter, / binjopen.onj.com/site/about/guidelines.xhtml

- Potential small sample size in subgroup analyses, may negatively impact the statistical
 power in quantitative data synthesis.
 - Limiting the search strategy to English-only publications may not capture studies
 exploring the EHR interoperability experiences of health systems in non-English
 speaking countries.

91 PROSPERO registration number [CRD42020209285]

- 92 This is an open access article distributed in accordance with the Creative Commons Attribution
- 93 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform
- 94 and build upon this work for any purpose, provided the original work is properly cited, a link to
- 95 the licence is given, and indication of whether changes were made. See:
- 96 https://creativecommons.org/licenses/by/4.0/.

2	
3	97
4	00
5 6	90
7	100
8	100
9	101
10	102
11	103
12	104
14	105
15	106
16	107
17	108
18	109
20	110
21	111
22	112
23	113
24	114
25 26	115
20	116
28	117
29	118
30	110
31	119
32 33	120
34	121
35	122
36	123
37	124
38 20	125
40	126
41	12/
42	128
43	129
44 45	130
45 46	121
47	132
48	133
49	134
50	136
51 52	130
52 53	138
54	130
55	140
56	110
57	
58	

Introduction 97 98 Electronic health records (EHRs) have become an integral part of modern healthcare since their 99

initial mainstream implementation in the mid-late 2000s through the passing of the Health

00 Information Technology for Economic and Clinical Health Act (HITECH) in the United States

- 01 and the NHS National Programme for IT initiative (NPfIT) in England (1-4). From the 02 documentation & retrieval of patient records and the prescription of medications, to coordinating
- 03 complex care plans between different healthcare providers and electronic billing. EHRs fulfil a
- 04 multitude of roles for both clinicians and patients alike (5–9).

06 In order to achieve EHR's full potential, it is critical to improve interoperability - i.e., "the ability 07 of health information systems to work together within and across organisation boundaries in 08 order to advance effective delivery of healthcare for individuals and communities" (10). The lack 09 of universal interoperability is often cited as one of the many significant shortcomings of EHRs 10 currently in use, resulting in duplication in healthcare costs, increased clinician workload fatigue, 11 and poses a potential risk to patient safety (2). This is especially problematic for patient 12 populations with chronic conditions, polypharmacy, and multiple comorbidities who are reliant

13 upon effective patient information sharing via EHRs to facilitate their care (11).

14 15 Poor EHR interoperability is detrimental to patient safety and costly for health systems. Its consequences range from increased risks of medication errors, fragmentation of patient data, to 16 17 iatrogenic harm resulting from redundant testing, and additional healthcare expenditure (12–17). 18 In the fragmented EHR landscape of the United Kingdom, measuring the effect poor EHR 19 interoperability has in the National Health Service (NHS), remain challenging (18). Although there is a growing body of literature investigating areas such as the facilitators and barriers to 20 21 EHR greater adoption, technical capabilities, and usability (19,20), no systematic review has been conducted exploring specifically the problem of interoperability amongst the assortment of 22 23 EHRs in use, how it affects patient safety, and ultimately the financial cost savings lost to health 24 systems.

26 In a recent systematic review by Dobrow et al. assessing the effects of EHR and HIT 27 interoperability on health systems, 130 publications were included, with the majority being

28 studies conducted in the United States, utilised quantitative methods, and focussed primarily in 29 acute healthcare settings. The authors noted the use of interoperable EHRs had a positive impact 30 on outcomes measures such as quality of care and productivity (19). However, in domains such 31 as stakeholder engagement, performance & reliability, security & privacy, information quality, 32 and ease of use, the benefits of interoperable EHRs was less clear (19). Amongst the 130 33 publications, 17 were reviews with the majority directed at exploring facilitators & barriers to 34 EHR implementation, and the general benefits and impact of EHR use. While this review did 35 focus on studies pertaining to the topic of interoperable EHRs, this was done so only from a broad perspective and included studies exploring a wide range of outcomes related to the effects 36 37 of EHR on healthcare rather than specifically on their implications to patient safety.

38 39 In another review by Hersh *et al.*, the authors explored how health information exchange (HIE) 40 affected health systems on a variety of domains, including costs, healthcare utilisation, health

- $\frac{3}{4}$ 141 outcomes, healthcare worker attitudes, and sustainability. Despite the widespread routinely use
- $\frac{4}{5}$ 142 of HIE, the authors described a general lack of robust evidence on the quality, costs, efficiency,
- usage, and sustainability (21). However, there was some evidence demonstrating HIEs being
 associated with reduced utilisation and costs in emergency care settings despite methodological
- associated with reduced utilisation and costs in emergency care settings despite methodological
 issues being present in many of the included publications (21). Although this review was
- ambitious in the wide scope of interest regarding the effects of HIE use, patient safety was not a
- ¹⁰ 147 primary topic of focus. Another limitation of this study was that it only contained US-based
- ¹¹ 148 publications, and thus findings lack generalisability internationally to other health systems in
- $\frac{12}{13}$ 149 high-income countries (HIC) which are both organised, financed differently.

14 15 150 Research aim

1 2

16
 151 The overall aim of this literature review is to explore how EHR interoperability impacts patient
 152 safety, in the context of health systems in HICs. The results generated will aim to inform
 153 healthcare policymakers and help shape more effective EHR system implementation and

²⁰ 154 modernisation efforts in the coming years.

²¹ ²² 155 Methods and analysis

²³ 156 Search strategy

- A computerised search of the literature published in the last 10 years (2010 to 2020) search will
 be performed on PubMed/Medline, Embase, Cumulative Index to Nursing and Allied Health
 Literature (CINAHL), Health Management Information Consortium (HMIC), and PsycInfo. This
- ²⁸ 160 publication timeframe was chosen as it coincides with the mainstream implementation of EHRs
- ²⁹ 100 publication timenane was closen as it coincides with the mainstream implementation of Erros
 ³⁰ 161 in several HIC healthcare systems such as Kaiser Permanente in the US, and thus would select
- 162 for the most up to date, relevant evidence concerning EHR interoperability and patient safety
- 163 challenges faced by healthcare systems today to be included (22,23). The list of search strings
- ³³ 164 used will include both free text and controlled terms, whenever supported (Table 1) and will be
- ³⁴ 165 iteratively refined in consultation with the Imperial College St. Mary's campus medical librarian.
- ³⁶ 166 Grey literature sources will also be searched, including registrations in the International
- ³⁷ 167 Prospective Register of Systematic Reviews, reports of relevant stakeholder organisations (NHS
- 168 England, American Medical Informatics Association (AMIA), eHealth at WHO, and conference
- 169 proceedings (last 5 years) of several related conferences (AMIA, MedInfo, Medicine 2.0,
- 41 170 Medicine X)), in order to identify possible additional studies that meet the inclusion criteria.
 42
- 171 The search has also been restricted to HIC and articles published in English only.
- 44
45172Table 1: Concepts and database search terms

Electronic health records		Interoperability		Patient safety
 Electronic health records Electronic medical records Computerised medical records systems 	AND	 Interoperability Health information interoperability Systems integration 	AND	 Patient safety Patient adj1 incident* Adverse adj1 event* Patient adj1 outcome*

 Health information exchange / HIE Health 	 Patient adj1 harm Risk management
information	
technology /	
HIT	
• Hospital	
information	
systems	
Medical informatics	
Medical records	
linkage	

²¹ 174 Study selection criteria

A summary of the population, intervention, comparison, outcomes, and type of studies being considered is provided in Table 2. This systematic review will focus on studies performed in high-income countries and published in English only. Studies assessing the impact of EHR interoperability will be included. Interventions will include EHR systems interoperable with other health information technology systems both within and across healthcare facilities, as well as those used in tertiary and community settings. The primary outcomes to be considered in this review will be safety outcomes, including adverse events/incidents, safety-related patient experiences, and health outcomes. In addition, secondary outcomes would include studies exploring the broader impact of interoperable EHRs on health systems such as cost effectiveness and clinical culture amongst healthcare providers on the topic Quantitative, qualitative, and mixed methods studies will be included. Reference lists of the selected articles will also be screened for papers which may have been missed by the initial database search but still meet the eligibility criteria.

189 Table 2: PICO inclusion criteria

Population	High-income countries utilising electronic health records
Intervention	EHRs with interoperability
Comparison	Usual care (i.e., existing baseline of interoperability)
Outcome	Impact on patient safety and quality of care

46 190 Screening

47	191	Articles to be included will be screened by two independent reviewers, following the process
48	192	described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses
49	193	(PRISMA) flow diagram (24). The initial screening will be done by the first reviewer based on
50	194	the publication titles, followed by a second screening based on the abstracts. Included abstracts
51	195	will then be fully reviewed by two independent researchers to produce a unified selection of
52 53	196	articles to be included in this review. Cohen's kappa will be calculated to ensure inter-rater
55 54	197	agreement and consistency in the selection of studies to be included (25,26). Any disagreements
55	198	will be resolved by consensus; if a Cohen's kappa value of less than 0.6 is reported, the
56	199	discrepancies will be addressed through discussions with a more experienced third investigator.
57		
58		
59		

³ 200 Data extraction

201 Data extraction will be performed using a standardised extraction table for each of the two

202 investigators to summarise the characteristics and findings of each included study, including

203 name of the first author, year of publication, study design, number of participants, retention rates,

204 setting characteristics, outcome measures, and main results. The content of the two summary 205 tables will then be aggregated and reviewed once more by both investigators with any

- 205 tables will then be aggregated and reviewed once more by both investigators, with any 206 diag are among a plug d by the third conier investigator.
- $\begin{array}{c} 0 \\ 1 \\ 206 \\ 207 \end{array}$ disagreements being solved by the third senior investigator.

208 Quality assessment

The quality of randomised controlled trials and cluster randomised trials will be assessed using the Cochrane Risk of Bias Tool (27), and the quality of non-randomised intervention studies (i.e., case control, cohort, quasi-experimental) will be appraised using the 'Risk of Bias In Non-Randomised Studies - of Interventions' (ROBINS-I) tool (28). For cost-effectiveness studies, the Drummond's checklist for assessing economic evaluations will be used (29). The National Institute for Health and Care Excellence (NICE) quality appraisal checklist will be utilised to assess the selected qualitative studies (30). Two independent reviewers will score the selected studies and any disagreements will be resolved by a third person. A risk of bias table along with

²³ 217 an overall, collective bias narrative will be produced to summarise the biases of outcomes

- $\frac{4}{5}$ 218 observed amongst the evaluated studies.
- 26 219

220 Narrative synthesis, subgroup analysis, and meta-analysis

A narrative synthesis will be performed for all studies included in this systematic review to summarise any salient findings observed (31).

In quantitative studies with homogenous or comparable outcome measures, whenever possible, continuous and dichotomous outcomes will be pooled together in a meta-analysis. If possible, effect sizes will be transformed in a common metric (Hedges' g – the bias-corrected standardised difference in means) and classified as positive when in favour of the intervention. Heterogeneity will be assessed using I² and the presence of publication bias will be evaluated using a funnel plot and the Duval and Tweedie's trim and fill method (32).

For both qualitative and quantitative studies that report comparable outcomes, a subgroup analysis based on clinical settings (e.g., primary vs. secondary healthcare settings) will be conducted to explore any patterns or relationships ascertained from the data. Through a standardised spreadsheet shared amongst the reviewers, the body of evidence will be organised in two separate Summary of Findings tables (for both qualitative and quantitative studies) in accordance to the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE) criteria (33).

47 237 48 238

⁴⁹ 239 Patient and public involvement

This systematic literature review saw no direct participation by patients or the public during the design of this study. However, this study was designed following a series of structured interviews with patients regarding their experience of attending multiple institutions for hospital care (34). As this literature review will be used to form the basis for subsequent studies exploring the topic including ones involving patients, findings from this review will be shared with patient

research groups to gain feedback and encourage further discourse surrounding the topic of EHR
interoperability and patient safety.

6 247 7 248 Amendments

Any amendments to this protocol will be documented with reference to saved searches and analysis methods, which will be recorded in bibliographic databases, Mendeley and Excel templates for data collection and synthesis.

13 252 Discussion

One of the primary strengths stemming from the almost exploratory nature of this systematic review is the ability to generate a succinct, comprehensive appraisal of the best evidence currently available regarding how EHR interoperability impacts patient care and safety. By publishing this review protocol beforehand, we demonstrate a clear, robust, and transparent approach to aggregating the anticipated assortment of literature on the subject in question.

There are also some limitations to be acknowledged. By restricting the inclusion criteria to publications made English only, this could potentially exclude relevant papers pertaining to interoperable EHR systems in non-English healthcare settings. However, this is expected to be minimal as the majority of the papers concerning this topic published from the United States and European countries and are primarily done so in English journals. It must also be noted that both the heterogeneity of measures and outcomes evaluated, as well as the potentially reduced number of studies in subgroup analyses, may negatively influence the statistical power in data synthesis, and may preclude pooling of data as a meta-analysis. With such diverse means of measuring and assessing the effects of EHR interoperability, this will likely make comparisons between studies difficult and may obscure the true measure of effect EHR interoperability has had in the clinical setting. To mitigate this risk, outcomes will be grouped whenever possible, and summarised as a narrative synthesis. However, this can also represent a strength, as it will provide a comprehensive overview on the subject, capitalising on various research methodologies and

³⁶ 272 providing novel insights on the impact of interoperable EHR systems on patient safety.

³⁸₃₉ 273 Acknowledgments

We would like to thank Michael Gainsford (Library Manager and Liaison Librarian at Imperial
 College London) for his support and guidance provided to improve the composition of the search
 terms and procedural aspects of the overall search strategy.

45 277 Authors' contributions

Conception and design of the work: ECL, ALN, and JC wrote the manuscript. HA, and AD
provided critical revision of drafts for important intellectual content. All authors provided input into drafts of the manuscript and agree on the contents of the final version.

51 281 Funding statement

This research was supported through the Imperial College National Institute for Health Research (NIHR) Patient Safety Translational Research Centre (PSTRC) and the Imperial College Biomedical Research Centre (BRC). JC acknowledges support from the Wellcome Trust

BMJ Open

[215938/Z/19/Z]. However, the funder/sponsor has had no role in development and drafting of
 this protocol.

287 Competing Interests

288 The authors declare that there are no competing interests.

to peer terien only

1 2			
3	200	Dof	oronoos
4	289	Rei	
5	290	1.	Colicchio TK, Cimino JJ, Del Fiol G. Unintended consequences of nationwide electronic
6 7	291		health record adoption: Challenges and opportunities in the post-meaningful use era.
/ 8	292		Journal of Medical Internet Research. [Online] 2019;21(6): 1–9. Available from:
9	293		doi:10.2196/13313
10	294	2.	Roman LC, Ancker JS, Johnson SB, Senathirajah Y. Navigation in the electronic health
11	295		record: A review of the safety and usability literature. Journal of Biomedical Informatics.
12	296		[Online] Elsevier Inc.; 2017;67: 69–79. Available from: doi:10.1016/j.jbi.2017.01.005
13	297	3.	Justinia T. The UK's National Programme for IT: Why was it dismantled? Health Services
14	298		Management Research. [Online] 2017;30(1): 2–9. Available from:
15	299		doi:10.1177/0951484816662492
10 17	300	4.	Wachter RM. Making IT work : harnessing the power of health IT to improve care in
18	301		England. National Advisory Group on Health Information Technology in England.
19	302		[Online] 2016; 71. Available from:
20	303		https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/550866/Wa
21	304		chter Review Accessible.pdf%0Ahttps://assets.publishing.service.gov.uk/government/upl
22	305		oads/system/uploads/attachment data/file/550866/Wachter Review Accessible.pdf
23	306	5.	Kruse CS, Kristof C, Jones B, Mitchell E, Martinez A. Barriers to Electronic Health
24	307		Record Adoption: a Systematic Literature Review. Journal of Medical Systems. [Online]
25	308		Journal of Medical Systems: 2016:40(12). Available from: doi:10.1007/s10916-016-0628-
20	309		9
28	310	6.	Avaad O. Alloubani A. ALhajaa EA. Farhan M. Abuseif S. Al Hroub A. et al. The role of
29	311	0.	electronic medical records in improving the quality of health care services: Comparative
30	312		study International Journal of Medical Informatics [Online] Elsevier: 2019.127(April).
31	313		63–67 Available from doi:10.1016/i jimedinf 2019.04.014
32	314	7	Evans RS Electronic Health Records: Then Now and in the Future <i>Yearbook of Medical</i>
33 24	315		<i>Informatics</i> [Online] 2016:25(S 01): S48–S61 Available from: doi:10.15265/IVS-2016-
54 35	316		s006
36	317	8	Gagnon MP Payne-Gagnon I Breton E Fortin IP Khoury L Dolovich L et al Adoption
37	318	0.	of electronic personal health records in Canada: Perceptions of stakeholders <i>International</i>
38	319		<i>Journal of Health Policy and Management</i> [Online] 2016:5(7): 425–433 Available from:
39	320		doi:10.15171/iihnm 2016.36
40	321	0	Campanella P. Lovato F. Marone C. Fallacara I. Mancuso A. Ricciardi W. et al. The
41	321).	impact of electronic health records on healthcare quality: a systematic review and meta
42	222		analysis The European Journal of Public Health [Online] 2016;26(1): 60, 64 Available
43 11	222		from: doi:10.1002/ourpub/olg/122
45	224	10	Dois 75N Mais TA Marcalina MS Decorre Decode E Neville Ortiz D Dibeiro ALD Ia
46	523 226	10.	There Exidence of Cast Denefits of Electronic Medical Decords, Standards, er
47	520 227		Incle Evidence of Cost Benefits of Electronic Medical Records, Standards, of Internet and hility in Hagmital Information Systems? Overview of Systematic Deviews - D(ID
48	327		Medical Information [Online] 2017;5(2): -2(Assilette formation Systematic Reviews. JMIR
49	328		Medical Informatics. [Online] $2017;5(3)$: e26. Available from:
50	329	11	doi:10.2196/medinform./400
51 52	330	11.	world Health Organization (WHO). <i>eHealth in the Region of the Americas: breaking</i>
52 52	331		down the barriers to implementation. [Online] 2016. Available from:
54	332		http://iris.paho.org/xmlui/bitstream/handle/123456/89/31286/9/892/5119259-
55	333		eng.pdf?sequence=6&isAllowed=y
56	334	12.	Zaheer S, Pimentel SD, Simmons KD, Kuo LE, Datta J, Williams N, et al. Comparing
57			
58			10
59 60			For peer review only - http://bmiopen.bmi.com/site/about/quidelines.xhtml
00			. of peer retrett only inteps/bill/bill/bell/bill/bell/bill/bout/guidelines/httml

 335 International and United States Undergraduate Medical Education and Surgical Outcomes Using a Refined Balance Matching Methodology. Anals of Surgery: [Online] 2017; Available from: doi:10.1097/SLA.0000000000001878 338 [3]. Everson J, Adler-Milstein J, Gaps in health information exchange between hospitals that treat many shared patients. Journal of the American Medical Informatics Association. [Online] 2018;25(9): 1114–1121. Available from: doi:10.1093/jamia/ocy089 341 [4]. Thompson MP, Graetz I. Hospital adoption of interoperability functions. Healthcare. [Online] Elsevier Inc; 2019;7(3): 100347. Available from: doi:10.1016/j.hjdsi.2018.12.001 344 [5]. Tapuria A, Kalra D, Kobayashi S, Contribution of elinical archetypes, and the challenges, towards achieving semantic interoperability for EHRs. Healthcare Informatics Research. [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286 347 [6]. Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. BMJ Open. [Online] 2019;9(12): c031637. Available from: doi:10.1036/bmjopen-2019-031637 351 [7]. Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health record strongh patient-sharing networks. npj Digital Medicine. [Online] 2019;9(12): c031637. Available from: doi:10.1038/s41746-018-0072-y 354 [8]. McAlcarney AS, Sice C, Efford J, Robbins J, Huerta TR, Faciliating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. BioMed Research International. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 355 [9]. Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. JMIR Medical Informatics. [Online] 2015	2			
 Using a Refined Balance Matching Methodology. Annals of Surgery: [Online] 2017; Available from: doi:10.1097/SLA.00000000000001878 Everson J, Adler-Milstein J. Gaps in health information exchange between hospitals that treat many shared patients. Journal of the American Medical Informatics Association. [Online] 2018;25(9): 1114–1121. Available from: doi:10.1093/jamia/ocy089 Thompson MP, Graetz I. Hospital adoption of interoperability functions. Healthcare. [Online] Elsevier Inc. 2019;7(3): 100347. Available from: doi:10.1016/j.hjdsi.2018.12.001 Tapuria A, Kafa D, Kobayashi S. Contribution of clinical archetypes, and the challenges, towards achieving semantic interoperability for EHRS. Healthcare Informatics Research. [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): c031637. Available from: doi:10.1038/a1746-018-0072. Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable clectronic health records through patient-sharing networks. <i>npj Digtal Medicine</i>. [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/a1746-018-0072. McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical Informatics</i>. [Online] 2019;7(2): e12607. Available from: doi:10.1177/018720815576827 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Elec	3	335		International and United States Undergraduate Medical Education and Surgical Outcomes
 Available from: doi:10.1097/SLA.00000000001878 Everson J, Adler-Milstein J. Gaps in health information exchange between hospitals that treat many shared patients. <i>Journal of the American Medical Informatics Association</i>. [Online] 2018;25(9): 1114–1121. Available from: doi:10.1093/jamia/ocy089 Thompson MP, Gractz I. Hospital adoption of interoperability functions. <i>Healthcare</i>. [Online] Elsevier Inc.; 2019;7(3): 100347. Available from: doi:10.1016/j.hjdsi.2018.12.001 Tapuria A, Kaira D, Kobayashi S. Contribution of clinical archetypes, and the challenges, towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research</i>. [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir;2013.19.4.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): c031637. Available from: doi:10.1036/mjopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health record shrough patient-sharing networks. <i>npJ Digital Medicine</i>. [Online] 353 springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y McAlearney AS, Sieck C, Heffer J, Robbins J, Huerta TR, Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/2029574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical Informatics</i>. [Online] 2019;7(3): 12607. Available from: doi:10.12196/12607 Zahabi M, Kaber DB, Swangnert M. Usability and Safety in Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR M</i>	4	336		Using a Refined Balance Matching Methodology <i>Annals of Surgery</i> [Online] 2017
 Everson J, Adler-Milstein J, Gaps in health information exchange between hospitals that treat many shared patients. <i>Journal of the American Medical Informatics Association</i>. [Online] 2018;25(9): 1114-1121. Available from: doi:10.1039/amaiocy089 Thompson MP, Graetz I. Hospital adoption of interoperability functions. <i>Healthcare</i>. [Online] Elsevier Inc. 2019;7(3): 100347. Available from: doi:10.1016/j.hjdsi.2018.12.001 Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges. towards achieving semantic interoperability for EHRs. <i>HealthCare Informatics Research</i>. [Online] 2013;19(4): 286–292. Available from: doi:10.14258/hir 2013.19.4.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): e031637. Available from: doi:10.1136/bmjopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. <i>npj Digital Medicine</i>. [Online] 817 Koklearney AS, Sicek C, Heffner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical Informatics</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1107/1018720815576827 Zahabi M, Kaber DB, Swangnert M. Usability and Safety in Electronic Health Records and Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Information</i>: Evidenge: Systematic Review and Future Research Needs. <i>JMIR Medical Informa</i>	5	337		Available from: doi:10.1097/SLA.00000000001878
 Develson J, Auder-Mistein J. Odps in Indentication Exchange Overent InSpirals that treat many shared patients. Journal of the American Medical Informatics Association. [Online] 2018;25(9): 1114–1121. Available from: doi:10.1093/jamia/ocy089 Thompson MP, Grazt I. Hospital adoption of Interoperability functions. <i>Healthcare</i>. [Online] Elsevier Inc.; 2019;7(3): 100347. Available from: doi:10.1016/j.hjdsi.2018.12.001 Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges. towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research</i>. [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England; an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): e031637. Available from: doi:10.1136/bmjopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. <i>mpl Digital Medicine</i>. [Online] 535 McAlcarney AS, Sicek C, Hefner J, Robbins J, Huctra TR, Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. BioMed Research International. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. JMIR Medical Informatics. [Online] 2019;7(2): c12607. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Health Records and Health Information Exchange: Systematic Review. JMIR Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors</i>. [Online] 2019;5(7): 805–834. Available fr	6	220	12	Everson L Adler Milstein I Cons in health information eveloped between hespitals that
 Barting Shared patients. Journal of the American Medical Information: Association. [Online] 2018;25(9):1114–1121. Available from: doi:10.103/jamia/ocy089 Jati La, Thompson MP, Graetz L. Hospital adoption of interoperability functions. Healthcare. [Online] Elsevier Inc.; 2019;7(3): 100347. Available from: doi:10.1016/j.hjdsi.2018.12.001 Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges, towards achieving semantic interoperability for FHRs. Healthcare Informatics Research. [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute bospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. BMJ Open. [Online] 2019;9(12): e031637. Available from: doi:10.1136/bmjopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. npj Digital Medicine. [Online] Springer US: 2018;1(1): 1–6. Available from: doi:10.1038/41746-018-0072-y McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. JMIR Medical Informatics. [Online] 2019;7(2): c12607. Available from: doi:10.1177/1018720815576827 Zahabi M, Kaber DB, Swangnetr M, Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. Human Factors. [Online] 2019;7(2): c12607. Available from: doi:10.11377/1018720815576827 Hersh WR, Totten AM, Eden KB,	7	220	13.	treast many shared notionts. Leave al of the American Medical Information Association
 Marce J. Continel 2018;25(9): 1114–1121. Available from: doi:10.1093/jama/cov089 Thompson MP, Gratz L. Hospital adoption of interoperability functions. <i>Healthcare</i>. [Online] Elsevier Inc.; 2019;7(3): 100347. Available from: doi:10.1016/j.hjdsi.2018.12.001 Tapuria A, Kaira D, Kobayashi S. Contribution of clinical archetypes, and the challenges, towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research</i>. [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England; an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): e031637. Available from: doi:10.136/bnijopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health record styneugh patient-sharing networks. <i>npJ Digital Medicine</i>. [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical Informatics.</i> [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent I. Lerature and Guideline Formulation. <i>Human Factors.</i> [Online] 2015;57(5): 805–834. Available from: doi:10.1377/bithaf728.2323 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kasakian SZ, et al. Outcomes From Health Information Exchange	8	339		treat many shared patients. <i>Journal of the American Medical Informatics Association</i> .
 Jal I., Thompson MP, Graetz I. Hospital adoption of interoperability functions. <i>Healthcare</i>. [Online] Elscvier Inc.; 2019;7(3): 100347. Available from: doi:10.1016/j.hjdsi.2018.12.001 Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges, towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research</i>. [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.194.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): c031637. Available from: doi:10.1136/bmijopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. <i>npj Digital Medicine</i>. [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y McAlearney AS, Sieck C, Heftier J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMR Medical Informatics</i>. [Online] 2015;7(5): 805–834. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M, Usability and Safty in Electronic Mediael Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors</i>. [Online] 2015;7(5): 805–834. Available from: doi:10.1177/1018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kasakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics</i>. [Online] 2	9	340		[Online] 2018;25(9): 1114–1121. Available from: doi:10.1093/jamia/ocy089
 [Online] Elsevier Inc.; 2019;7(3): 100347. Available from: doi:10.1016/j.hjdai.2018.12.001 343 Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges, towards achieving semantic interoperability for FIRs. <i>Healthcare Informatics Research</i>. [Online] 2013;19(4): 286–292. Available from: doi:10.458/khr.2013.19.4.286 347 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England; an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): c031637. Available from: doi:10.1136/bmjopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guigin interoperable electronic health records through patient-sharing networks. <i>npj Digital Medicine</i>. [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y BM CAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges. Systematic Review. <i>JMIR Medical Informatics</i>. [Online] 2019;7(2): c12607. Available from: doi:10.2196/12607 Zahabi M, Kabor DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 Zuhabi M, Kabor DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1377/htta7208	10	341	14.	Thompson MP, Graetz I. Hospital adoption of interoperability functions. <i>Healthcare</i> .
 433 doi:10.1016/j.hjdsi.2018.12.001 545 Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges, towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research.</i> [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286 647 16 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open.</i> [Online] 2019;9(12): c031637. Available from: doi:10.1136/bnijopen-2019-031637 751 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health record sthrough patient-sharing networks. <i>njj Digulal Medicine.</i> [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y 754 18. McAlearney AS, Sieck C, Heffier J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 765 19. Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Record System Implementation: Evidence from: Addical Informatics. [Online] 2019;7(2): c12607. Available from: doi:10.2196/12607 706 20. Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Encords Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1197/0018720815576827 707 42 718 420. Wheatley B. Transforming care delivery through health information technology. <i>The Permanente Journal</i>. [Online] 2015;37(4): c39. Available from: doi:10.1371/journal. 719 720. Chen C, Permanent K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalitie	17	342		[Online] Elsevier Inc.; 2019;7(3): 100347. Available from:
 Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges, towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research</i>. [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): e031637. Available from: doi:10.1136/bmijopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. <i>njj Digital Medicine</i>. [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y McAlcarney AS, Sicek C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Record system miter and Guideline Formulation. <i>Human Factors.</i> [Online] 2015;7(5): 805–834. Available from: doi:10.1177/0018720815576827 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electrone Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors.</i> [Online] 2015;7(5): 805–834. Available from: doi:10.1177/0018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics.</i> [Online] 2015;3(4): c39. Available from: doi:10.1377/hlthaff:28.2.323 [Accessed: 22nd January 2021] Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And StreamInning Modalit	12	343		doi:10.1016/j.hjdsi.2018.12.001
 towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research.</i> [Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir 2013.19.4.286 Warren LR, Clark JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open.</i> [Online] 2019;9(12): c031637. Available from: doi:10.136/bmjoen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. <i>npJ Digital Medicine.</i> [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.038/s41746-018-0072-y McAlcarney AS, Sicek C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Record Sand Health Information Exchanges. Systematic Review. <i>JMIR Medical Informatics.</i> [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors.</i> [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information. Exchanges: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics.</i> [Online] 2015;57(5): 805–834. Available from: doi:10.1377/hithaff.28.2.323 [Accessed: 22nd January 2021] Wheatley B. Transforming care delivery through health information technology. <i>The Permanente Journal.</i> [Online] 2015;37(4): e39. Available from: doi:10.1377/hithaff.28.2.323 [Acce	14	344	15.	Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges,
 ie Goninej 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): e031637. Available from: doi:10.1136/bmjopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. <i>npJ Digital Medicine</i>. [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y McAlearney AS, Sicek C, Hefner J, Robbins J, Huerta TR, Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical Informatics</i>. [Online] 2019;7(2): e12607. Available from: doi:10.1177/0018720815576827 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics</i>. [Online] 2015;3(4): e39. Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalitics Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] Chen C, Permanente K. The Kaiser Permanente El	15	345		towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research</i> .
 Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute hospitals in England: an overview of health record system distribution and retrospective observational analysis of inter-hospital transitions of care. <i>BMJ Open</i>. [Online] 2019;9(12): e031637. Available from: doi:10.1136/bmjopen-2019-031637 Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. <i>npj Digital Medicine</i>. [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Bobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical</i> <i>Informatics</i>. [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guident Formulation. <i>Human</i> <i>Factors</i>. [Online] 2015;7(5): 805–834. Available from: doi:10.1197/0018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information: Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics</i>. [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal</i>. [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalitics Of Care. 2009; Available from: doi:10.1377/hlthaff 28.2.	16	346		[Online] 2013:19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286
 ¹⁸ ¹⁰ ¹⁰ ¹⁰ ¹⁰ ¹⁰ ¹⁰ ¹⁰ ¹⁰	17	347	16	Warren LR Clarke IM Arora S Darzi AW Improving data sharing between acute
 and the probability of the probability	18	348	10.	hospitals in England: an overview of health record system distribution and retrospective
20347Sobset valiable of mit anisolus of care. Jobs Open. 2019-031637213502019;9(12): c031637. Available from: doi:10.1136/bmiopen-2019-0316372135117.Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable22electronic health records through patient-sharing networks. <i>mp Digital Medicine</i> . [Online]23Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y2418.McAlearney AS, Sieck C, Heffer J, Robbins J, Huerta TR. Facilitating Ambulatory25Electronic Health Record System Implementation: Evidence from a Qualitative Study.26 <i>BioMed Research International</i> . [Online] 2013;2013: 1–9. Available from:27doi:10.1155/2013/c025742819.29Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health2936120.Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records29101155/2013/c0257420Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records20Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human</i> 20 <i>Factors</i> . [Online] 2015;57(5): 805–834. Available from: doi:10.1177/01872081557682721Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes23From Health Information Exchange: Systematic Review and Future Research Needs.24JMIR Medical Informatics. [Online] 2015;3(4): c39. Available from:25doi:10.2196/medinform.521526Wheatley B. Transforming care Gliver	19	240		observational analysis of inter hospital transitions of care <i>BMLOnan</i> [Online]
 2019, 9(12), e051657, Available from: doi:10.1136/07010j0e1/2019-0131637 351 17. Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable electronic health records through patient-sharing networks. <i>npj Digital Medicine</i>. [Online] 353 354 18. McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 19. Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical Informatics</i>. [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 20. Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1197/0018720815576827 21. Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kasakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics</i>. [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 22. Wheatley B. Transforming care delivery through health information technology. <i>The Permanente journal</i>. [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 23. Chen C, Permanente K. The Kaiser Permanente Electronic dealth Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS Medicine</i>. [Online] 2009;6(7).	20	250		2010.0(12): a021627 Available from dai:10.1126/hmianar 2010.021627
 Si 17. Clarke JM, Warren LK, Arora S, Barahona M, Darzi AW, Guiding interoperable electronic health records through patient-sharing networks. <i>npj Digital Medicine</i>. [Online] Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International</i>. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical</i> <i>Informatics</i>. [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human</i> <i>Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics</i>. [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 Ste Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal</i>. [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/htthaff.28.2.323 [Accessed: 22nd January 2021] Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS Medicine</i>. [Online] 1907;33(1): 159. Available from: doi:10.2307/2529310 Medical	21	33U 251	17	2019,9(12): e031037. Available from: doi:10.1130/bmjopen-2019-031037
 352 electronic health records through patient-sharing networks. npl Digital Medicine. [Online] 353 Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y 354 18. McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR, Facilitating Ambulatory 355 Electronic Health Record System Implementation: Evidence from a Qualitative Study. 356 <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: 357 doi:10.1155/2013/629574 358 19. Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health 359 Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical Informatics.</i> [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 361 20. Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records 361 Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors.</i> [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 364 21. Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes 365 From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics.</i> [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 368 22. Wheatley B. Transforming care delivery through health information technology. <i>The Permanente journal.</i> [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyse	22	351	17.	Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable
 Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical</i> <i>Informatics.</i> [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human</i> <i>Factors.</i> [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics.</i> [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.3215 Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal.</i> [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine.</i> [Online] 2009;6(7). Available from: doi:10.371/journal.pmed.1000	23	352		electronic health records through patient-sharing networks. <i>npj Digital Medicine</i> . [Online]
 354 18. McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 358 19. Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical Informatics.</i> [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 361 20. Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human Factors.</i> [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 363 <i>Factors.</i> [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 364 21. Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Informatics. [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 366 <i>JMIR Medical Informatics.</i> [Online] 2015;3(4): e39. Available from: doi:10.196/medinform.5215 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] 372 373 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS Medicine.</i> [Online] 1907;33(1): 159. Available from: doi:10.2307/2529310 376 40. Hugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica.</i> 2012;22(3): 276–282. 	24	353		Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y
 Electronic Health Record System Implementation: Evidence from a Qualitative Study. <i>BioMed Research International.</i> [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical</i> <i>Informatics.</i> [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human</i> <i>Factors.</i> [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics.</i> [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal.</i> [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] Tans for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine.</i> [Online] 2009;6(7). Available from: doi:10.1377/hlthaff.28.2.323 Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine.</i> [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 Stock GG. The Measurement of Observer Agreement for Categorical Data. <i>Biometrics.</i> [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 McHugh ML. Interrater reliability: the kappa statistic. <i>Bi</i>	25	354	18.	McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory
 BioMed Research International. [Online] 2013;2013: 1–9. Available from: doi:10.1155/2013/629574 Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. JMIR Medical Informatics. [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. Human Factors. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. JMIR Medical Informatics. [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 Wheatley B. Transforming care delivery through health information technology. The Permanente journal. [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] The Quitage from: doi:10.1371/journal.pmed.1000097 Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3): 276–282. 	26	355		Electronic Health Record System Implementation: Evidence from a Qualitative Study.
 doi:10.1155/2013/629574 357 doi:10.1155/2013/629574 358 19. Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical</i> <i>Informatics</i>. [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 361 20. Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human</i> <i>Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 364 21. Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics</i>. [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 368 22. Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal</i>. [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 377 25. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. <i>Biometrics</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 378 <i>Biometrics</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 276–282. 	27	356		BioMed Research International. [Online] 2013;2013: 1–9. Available from:
 358 19. Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health Records and Health Information Exchanges: Systematic Review. <i>JMIR Medical</i> <i>Informatics</i>. [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607 20. Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human</i> <i>Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 21. Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics</i>. [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 22. Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal</i>. [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.371/journal.pmed.1000097 25. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. <i>Biometrics</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 276–282. 	28	357		doi:10.1155/2013/629574
359Records and Health Information Exchanges: Systematic Review. JMIR Medical360Informatics. [Online] 2019;7(2): e12607. Available from: doi:10.2196/1260736120.Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records362Interface Design: A Review of Recent Literature and Guideline Formulation. Human363Factors. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/001872081557682736421.Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes365From Health Information Exchange: Systematic Review and Future Research Needs.366JMIR Medical Informatics. [Online] 2015;3(4): e39. Available from:40doi:10.2196/medinform.5215373doi:10.2196/medinform.521537422.23.Wheatley B. Transforming care delivery through health information technology. The379doi:10.7812/TPP/12-030 [Accessed: 20th January 2021]37123.372Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming373[Accessed: 22nd January 2021]37424.375Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred376reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS37425.Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.37637725.378Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/252931037926.McHugh ML. Interrater reliability: the kappa statistic. Bioc	29	358	19.	Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S, Interoperable Electronic Health
13731373111360Informatics. [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607137320.Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records137420.Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records137510.Interface Design: A Review of Recent Literature and Guideline Formulation. Human137611.Factors. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827137621.Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes138711.From Health Information Exchange: Systematic Review and Future Research Needs.138811.11.138922.Wheatley B. Transforming care delivery through health information technology. The139912.Permanente journal. [Online] Winter; 2013;17(1): 81–86. Available from:1301doi:10.7812/TPP/12-030 [Accessed: 20th January 2021]131123.Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming137123.Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming1372And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.3231437424.Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred1375reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS1376Medicine. [Online] 2009;6(7). Available from: doi:10.2307/2529310137725.Landis JR, Koch GG. The Measurement of Ob	30	359	- / ·	Records and Health Information Exchanges: Systematic Review IMIR Medical
 300 <i>Informatics</i>. [Online] 2017, 7(2): C12007: Available from: doi:10.1107/10012003 20. Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records Interface Design: A Review of Recent Literature and Guideline Formulation. <i>Human</i> <i>Factors</i>. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 364 21. Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes From Health Information Exchange: Systematic Review and Future Research Needs. <i>JMIR Medical Informatics</i>. [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 368 22. Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal</i>. [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 377 25. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. <i>Biometrics</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 276–282. 	32	360		Informatics [Online] 2010:7(2): e12607 Available from: doi:10.2106/12607
 John Z. Zahabi M, Kaber DB, Swalghen M. Osadniy and safety in Electronic Medical Revolution in the formation in	33	261	20	Zahahi M. Kabar DP. Swangnatr M. Usahility and Safaty in Elastronia Madical Pasards
362363Factors. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827363363Factors. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/001872081557682736421.Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes385From Health Information Exchange: Systematic Review and Future Research Needs.39366JMIR Medical Informatics. [Online] 2015;3(4): e39. Available from:40doi:10.2196/medinform.52154136822.42Wheatley B. Transforming care delivery through health information technology. The43Permanente journal. [Online] Winter; 2013;17(1): 81–86. Available from:44370doi:10.7812/TPP/12-030 [Accessed: 20th January 2021]4537123.46Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming47And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.32348[Accessed: 22nd January 2021]4837424.49Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred49376Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.100009743378Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/25293104437926.45McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3):4637926.473764837926.4937940370 <td>34</td> <td>262</td> <td>20.</td> <td>Landol W, Kabel DD, Swalighen W. Osability and Safety in Electronic Medical Records</td>	34	262	20.	Landol W, Kabel DD, Swalighen W. Osability and Safety in Electronic Medical Records
 365 Factors. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827 364 21. Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes 365 From Health Information Exchange: Systematic Review and Future Research Needs. 366 JMIR Medical Informatics. [Online] 2015;3(4): e39. Available from: 367 doi:10.2196/medinform.5215 368 22. Wheatley B. Transforming care delivery through health information technology. The 369 Permanente journal. [Online] Winter; 2013;17(1): 81–86. Available from: 4010 doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming 472 And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 373 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred 475 reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS 376 Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 377 25. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. 378 Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 379 26. McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3): 376 276–282. 	35	302		Interface Design. A Review of Recent Literature and Guideline Formulation. $Human$
 364 21. Hersh WK, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes 365 From Health Information Exchange: Systematic Review and Future Research Needs. 366 <i>JMIR Medical Informatics</i>. [Online] 2015;3(4): e39. Available from: 367 doi:10.2196/medinform.5215 368 22. Wheatley B. Transforming care delivery through health information technology. <i>The</i> 369 <i>Permanente journal</i>. [Online] Winter; 2013;17(1): 81–86. Available from: 370 doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming 372 And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 373 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred 376 reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> 376 <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.2307/2529310 378 <i>Biometrics</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 276–282. 	36	303	0.1	<i>Factors</i> . [Unline] 2015;57(5): 805–834. Available from: doi:10.1177/0018/20815576827
38365From Health Information Exchange: Systematic Review and Future Research Needs.39366JMIR Medical Informatics. [Online] 2015;3(4): e39. Available from:40367doi:10.2196/medinform.52154136822.Wheatley B. Transforming care delivery through health information technology. The42369Permanente journal. [Online] Winter; 2013;17(1): 81–86. Available from:43370doi:10.7812/TPP/12-030 [Accessed: 20th January 2021]4437123.Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming46372And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.32347373[Accessed: 22nd January 2021]4837424.Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred49375reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS50376Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.100009751378Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/252931053380276–282.5437638055380276–282.	37	364	21.	Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes
 <i>JMIR Medical Informatics.</i> [Online] 2015;3(4): e39. Available from: doi:10.2196/medinform.5215 368 22. Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal.</i> [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine.</i> [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 377 25. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. <i>Biometrics.</i> [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 380 276–282. 	38	365		From Health Information Exchange: Systematic Review and Future Research Needs.
40367doi:10.2196/medinform.52154136822.Wheatley B. Transforming care delivery through health information technology. The42369Permanente journal. [Online] Winter; 2013;17(1): 81–86. Available from:43370doi:10.7812/TPP/12-030 [Accessed: 20th January 2021]4437123.Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming46372And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.32347373[Accessed: 22nd January 2021]4837424.Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred49375reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS50376Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.10000975137725.Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.53378Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/25293105437926.McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3):55380276–282.	39	366		JMIR Medical Informatics. [Online] 2015;3(4): e39. Available from:
 Wheatley B. Transforming care delivery through health information technology. <i>The</i> Wheatley B. Transforming care delivery through health information technology. <i>The</i> <i>Permanente journal.</i> [Online] Winter; 2013;17(1): 81–86. Available from: doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 Iandis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. <i>Biometrics</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 276–282. 	40	367		doi:10.2196/medinform.5215
42369Permanente journal. [Online] Winter; 2013;17(1): 81–86. Available from:43370doi:10.7812/TPP/12-030 [Accessed: 20th January 2021]4537123.Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming46372And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.32347373[Accessed: 22nd January 2021]4837424.Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred49375reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS50376Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.10000975137725.Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.53378Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/25293105437926.McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3):56376276–282.	41	368	22.	Wheatley B. Transforming care delivery through health information technology. The
 doi:10.7812/TPP/12-030 [Accessed: 20th January 2021] 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 376 <i>Medicine</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 276-282. 	42	369		Permanente journal. [Online] Winter; 2013;17(1): 81–86. Available from:
 371 23. Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323 373 [Accessed: 22nd January 2021] 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 376 <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 377 25. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. <i>Biometrics</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 276–282. 	43	370		doi:10.7812/TPP/12-030 [Accessed: 20th January 2021]
46372And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.32347373[Accessed: 22nd January 2021]4837424.Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred49375reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> 50376 <i>Medicine</i> . [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.10000975137725.Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.53378 <i>Biometrics</i> . [Online] 1977;33(1): 159. Available from: doi:10.2307/25293105437926.McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i> . 2012;22(3):55380276–282.5611	44 15	371	23.	Chen C. Permanente K. The Kaiser Permanente Electronic Health Record: Transforming
 Ard Strategy and Strat	45 46	372		And Streamlining Modalities Of Care, 2009: Available from: doi:10.1377/hlthaff.28.2.323
 375 374 374 24. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred 375 376 376 376 376 377 25. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. 378 378 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 380 276–282. 	47	373		[Accessed: 22nd January 2021]
 374 24. Moner D, Elberatr A, retziarr J, Athnar DG, Athnar D, Antes G, et al. Treferred 375 reporting items for systematic reviews and meta-analyses: The PRISMA statement. <i>PLoS</i> 376 <i>Medicine</i>. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097 377 25. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. 378 <i>Biometrics</i>. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i>. 2012;22(3): 380 276–282. 	48	374	24	Moher D. Liberati A. Tetzlaff I. Altman DG. Altman D. Antes G. et al. Preferred
50375Teporting items for systematic reviews and meta-analyses. The PKISMA statement. PLos50376Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.10000975237725.Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.53378Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/25293105437926.McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3):55380276–282.565758	49	275	24.	reporting items for systematic reviews and mate analyses: The DDISMA statement, DLoS
51376Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.10000975237725.Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.53378Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/25293105437926.McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3):55380276–282.5657585811	50	275		Multiplice [Outline] 2000((7) Assolution device device analyses. The FKISWA statement. FLOS
5237725.Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.53378Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/25293105437926.McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3):55380276–282.565758	51	3/0	25	Medicine. [Online] 2009;6(7). Available from: doi:10.1371/journal.pmed.1000097
53 378 Biometrics. [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 54 379 26. McHugh ML. Interrater reliability: the kappa statistic. Biochemia medica. 2012;22(3): 55 380 276–282. 56 57 58 58 11	52	377	25.	Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.
54 379 26. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i> . 2012;22(3): 55 380 276–282. 56 57 11	53	378		<i>Biometrics</i> . [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310
55 380 276–282. 56 57 58 11	54	379	26.	McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i> . 2012;22(3):
56 57 58 11	55	380		276–282.
57 58 11	56			
20 II	57			**
5U	58 50			
60 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	60			For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

2			
3	381	27.	Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A
4	382	_ , ,	revised tool for assessing risk of hias in randomised trials. <i>The RMI</i> [Online]
5	383		2010.366(August) Available from: doi:10.1136/hmi.1/2008
6	202	20	Steme IA Hernén MA Desues DC Severió L Derlinen ND Viewensthen M et al
7	384	28.	Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, et al.
8	385		ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions.
9	386		<i>BMJ (Online)</i> . [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.i4919
10	387	29.	Drummond MF, Brien BJ, Torrance GW, Stoddart GL. Methods for the Economic
11	388		Evaluation of Health Care Programmes., 2nd ed. Oxford University Press: 1997.
12	389	30	Methods for the development of NICE public health guidance [Online] 3rd n National
13	200	50.	Institute for Clinical Excellence (NICE): 2018 Available from:
14	390		Institute for Chinical Excellence (NICE), 2018. Available from.
15	391		https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice-
16	392		public-health-guidance-third-edition-pdf-2007967445701
17	393	31.	Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S.
18	394		Guidance on the conduct of narrative synthesis in systematic reviews. A product from the
19	395		ESRC methods programme 2006 (April 2006) 1–92
20	396	32	Duval S. Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and
21	207	52.	- liveting for weblication his in mate analysis. Dispertuine [Online] Dispertuin Seriet
22	397		adjusting for publication bias in meta-analysis. <i>Biometrics</i> . [Online] Biometric Society;
23	398		2000;56(2): 455-463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed:
24	399		20th January 2021]
25	400	33.	Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al.
26	401		GRADE: an emerging consensus on rating quality of evidence and strength of
27	402		recommendations <i>BMI</i> [Online] 2008:336(7650): 924–926 Available from:
28	403		doi:10.1136/bmi 30480.470347 AD
29	403	24	Wernen I.D. Hernigen M. Anne C. Derri A. Werleine mith metionte and the multiple to design
30	404	34.	warren LR, Harrison M, Arora S, Darzi A. working with patients and the public to design
31	405		an electronic health record interface: A qualitative mixed-methods study. BMC Medical
32	406		Informatics and Decision Making. [Online] BMC Medical Informatics and Decision
33	407		Making; 2019;19(1): 1-8. Available from: doi:10.1186/s12911-019-0993-7
34	408		
35			
36			
37			
38			
39			
40			
41			
42			
43			
44			
45			
40			
47 70			
40			
49 50			
50			
57			
52			
55			
55			
56			
50			
57 58			10
50			12
57			

Section and topic	Item No.	Checklist item	Reported on Page No.
ADMINISTRATIV	E INFO	ORMATION	
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

 BMJ Open

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6-7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6-7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6-7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	7
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	-
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6-7
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	7

clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the

PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

BMJ Open

BMJ Open

Electronic Health Records, Interoperability, and Patient Safety in Health Systems of High-Income Countries: A Systematic Review Protocol

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-044941.R2
Article Type:	Protocol
Date Submitted by the Author:	27-May-2021
Complete List of Authors:	Li, Edmond; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; London School of Hygiene and Tropical Medicine Faculty of Infectious and Tropical Diseases, Clinical Research Department Clarke, Jonathan; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; Imperial College London, Centre for Mathematics of Precision Healthcare Neves, Ana Luisa; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; University of Porto, Center for Health Technology and Services Research / Department of Community Medicine, Health Information and Decision Ashrafian, Hutan; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer Darzi, Ara; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer
Primary Subject Heading :	Health informatics
Secondary Subject Heading:	Health policy, Public health, Health services research
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, Information technology < BIOTECHNOLOGY & BIOINFORMATICS, Information management < BIOTECHNOLOGY & BIOINFORMATICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT
	1

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

2		
3 4	1	Electronic Health Records, Interoperability, and Patient Safety in
5	2	Health Systems of High-Income Countries: A Systematic Review
6	2	D 4 1
/ 0	3	Protocol
9	4	Edmond Li ^[1] , Jonathan Clarke ^[1,3] , Ana Luisa Neves ^[1,2] , Hutan Ashrafian ^[1] , Ara Darzi ^[1]
10	5	^[1] Imperial NIHR Patient Safety Translational Research Centre (PSTRC), Institute of Global
11	6	Health Innovation (IGHI). Imperial College London, London, United Kingdom
12	7	^[2] Department of Community Medicine Information and Health Decision Sciences (MEDCIDS)
13	8	/ Center for Health Technology and Services Research (CINTESIS) University of Porto Porto
14	9	Portugal
16	10	^[3] Centre for Mathematics of Precision Healthcare, Imperial College London, London, United
17	10	Kingdom
18	11	Kingdom
19	12	
20 21	13	
21	14	
23	15	
24	16	
25	17	
26	18	
27	19	
29	20	
30	20	
31	21	
32	22	
33 24	23	
35	24	
36	25	
37	26	
38	27	
39 40	28	
40	-° 29	
42	20	
43	21	Converse or ding outhor
44	20	Corresponding author
45 46	32	Name: Edmond Li
47	33	Email: <u>edmond.li19(a)imperial.ac.uk</u>
48	34	Address: Institute of Global Health Innovation, Room 1035/7, QEQM Wing, St Mary's Campus,
49	35	London W2 1NY
50	36	Keywords [MeSH terms]: electronic health records, electronic medical records, computerised
51	37	patient records, health information technology, health information exchanges, interoperability,
52 53	38	patient safety, patient harm, adverse events, health outcomes
54	30	Word count: 2752
55	<u>/</u> 0	Word Count. 2152
56	40	
57 58		1
59		1
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1		
2		
3	41	Abstract
4 5	12	Introduction
6	42	The availability and routing use of electronic health records (EUDs) have become commonpless
7	45 44	in healthcare systems of many high income countries. While there is an ever growing hedy of
8	44 15	literature pertaining to EHR use evidence surrounding the importance of EHR interoperability
9 10	45	and its impact on notions safety remains less clear. There is therefore a need and opportunity to
10	40	evaluate the evidence available regarding this relationship so as to better inform health
12	47	informatics development and policies in the years to come
13	40 49	information development and ponetes in the years to come.
14	50	Objective
15	50	
10 17	51	I his systematic review aims to evaluate the impact of EHR interoperability on patient safety in
18	52	nealth systems of high-income countries.
19	55	
20	54	Methods and analysis
21	55	A systematic literature review will be conducted via a computerised search through four
22	56	databases: PubMed, Embase, HMIC, and PsycInfo for relevant articles published between 2010
25 24	57	and 2020. Outcomes of interest will include: impact on patient safety, and the broader effects on
25	58	health systems. Quality of the randomised quantitative studies will be assessed using Cochrane
26	59	Risk of Bias Tool. Non-randomised papers will be evaluated with the Risk of Bias In Non-
27	60	Randomised Studies - of Interventions (ROBINS-I) tool. Drummond's Checklist will be utilised
28	61	for publications pertaining to economic evaluation. The National Institute for Health and Care
29	62	Excellence (NICE) quality appraisal checklist will be used to assess qualitative studies. A
30	63	narrative synthesis will be conducted for included studies, and the body of evidence will be
32	64	summarised in a summary of findings table.
33	65	
34	66	Ethics and dissemination
35	6/	This review will summarise published studies with non-identifiable data and therefore does not
30 37	68	require ethical approval. This protocol complies with the Preferred Reporting Items for
38	09 70	systematic Review and Meta-Analyses Protocols guidennes. Findings will be disseminated
39	70	ar members of the public were not involved in the design of this study
40	71	of members of the public were not involved in the design of this study.
41	12	
42 43	72	Article Summary
44	75	Strength and Limitation of the start
45	/4	Strengths and limitations of this study
46	15	Strengths
47	/0 77	• Inclusion of quantitative, qualitative, and mixed-methods studies can provide a
48 70	70	comprehensive overview of the multitude of ways in which interoperable EHRs may
50	/8 70	The proposed review attempts to answer a progratic question which is integral to
51	/9 00	• The proposed review altempts to answer a pragmatic question which is integral to influencing future health informatics development and policies.
52	0U Q 1	influencing future nearth informatics development and policies.
53	01 87	Limitations
54 55	82	• The beterogeneity of methods and outcomes assessed may obscure the true effect
56	84	interoperable EHRs have had on patient safety in the clinical setting
57	Т	incoroporable Errics have had on patient safety in the enhibit setting.
58		2
59		For peer review only - http://bmionen.hmi.com/site/about/quidelines.yhtml
60		For peer review only inter, / binjopen.onj.com/site/about/guidelines.xhtml

- Potential small sample size in subgroup analyses, may negatively impact the statistical
 power in quantitative data synthesis.
 - Limiting the search strategy to English-only publications may not capture studies
 exploring the EHR interoperability experiences of health systems in non-English
 speaking countries.

91 PROSPERO registration number [CRD42020209285]

- 92 This is an open access article distributed in accordance with the Creative Commons Attribution
- 93 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform
- 94 and build upon this work for any purpose, provided the original work is properly cited, a link to
- 95 the licence is given, and indication of whether changes were made. See:
- 96 https://creativecommons.org/licenses/by/4.0/.

2	
3	(
4	- (
5	
7	
, 8	1(
9	1(
10	1(
11	1(
12	1(
13	1(
14 15	1(
15	1(
17	1(
18	1(
19	1
20	
21	1
22	11
23 24	11
24 25	11
26	11
27	11
28	11
29	11
30	11
31	11
32 33	14
34	14
35	12
36	12
37	12
38	12
39	12
40 41	12
41	12
43	12
44	13
45	13
46	13
47	13
48	13
49 50	13
50	13
52	13
53	13
54	13
55	14
56	-
57	
58	

4

Introduction 97 98 Electronic health records (EHRs) have become an integral part of modern healthcare since their 99 initial mainstream implementation in the mid-late 2000s through the passing of the Health)() Information Technology for Economic and Clinical Health Act (HITECH) in the United States 01 and the NHS National Programme for IT initiative (NPfIT) in England (1-4). From the)2 documentation & retrieval of patient records and the prescription of medications, to coordinating complex care plans between different healthcare providers and electronic billing. EHRs fulfil a)3)4 multitude of roles for both clinicians and patients alike (5–9). 05)6 In order to achieve EHR's full potential, it is critical to improve interoperability - i.e., "the ability 07 of health information systems to work together within and across organisation boundaries in)8 order to advance effective delivery of healthcare for individuals and communities" (10). The lack)9 of universal interoperability is often cited as one of the many significant shortcomings of EHRs 0 currently in use, resulting in duplication in healthcare costs, increased clinician workload fatigue, and poses a potential risk to patient safety (2). This is especially problematic for patient 1 2 populations with chronic conditions, polypharmacy, and multiple comorbidities who are reliant 3 upon effective patient information sharing via EHRs to facilitate their care (11).

5 Poor EHR interoperability is detrimental to patient safety and costly for health systems. Its 6 consequences range from increased risks of medication errors, fragmentation of patient data, to 7 iatrogenic harm resulting from redundant testing, and additional healthcare expenditure (12–17). 8 In the fragmented EHR landscape of the United Kingdom, measuring the effect poor EHR 9 interoperability has in the National Health Service (NHS), remain challenging (18). Although 20 there is a growing body of literature investigating areas such as the facilitators and barriers to EHR greater adoption, technical capabilities, and usability (19,20), no systematic review has 21 been conducted exploring specifically the problem of interoperability amongst the assortment of 22 23 EHRs in use, how it affects patient safety, and ultimately the financial cost savings lost to health 24 systems.

25 26 In a recent systematic review by Dobrow et al. assessing the effects of EHR and HIT 27 interoperability on health systems, 130 publications were included, with the majority being 28 studies conducted in the United States, utilised quantitative methods, and focussed primarily on 29 acute healthcare settings. The authors noted the use of interoperable EHRs had a positive impact 30 on outcomes measures such as quality of care and productivity (19). However, in domains such 31 as stakeholder engagement, performance & reliability, security & privacy, information quality, 32 and ease of use, the benefits of interoperable EHRs was less clear (19). Amongst the 130 publications, 17 were reviews with the majority directed at exploring facilitators & barriers to 33 EHR implementation, and the general benefits and impact of EHR use. While this review did 34 35 focus on studies pertaining to the topic of interoperable EHRs, this was done so only from a broad perspective and included studies exploring a wide range of outcomes related to the effects 36 37 of EHR on healthcare rather than specifically on their implications to patient safety. 38 39 In another review by Hersh *et al.*, the authors explored how health information exchange (HIE)

 $\frac{139}{140}$ affected health systems on a variety of domains, including costs, healthcare utilisation, health

- $\frac{3}{4}$ 141 outcomes, healthcare worker attitudes, and sustainability. Despite the widespread routinely use
- $\frac{4}{5}$ 142 of HIE, the authors described a general lack of robust evidence on the quality, costs, efficiency,
- usage, and sustainability (21). However, there was some evidence demonstrating HIEs being
 associated with reduced utilisation and costs in emergency care settings despite methodological
- associated with reduced utilisation and costs in emergency care settings despite methodological
 issues being present in many of the included publications (21). Although this review was
- ambitious in the wide scope of interest regarding the effects of HIE use, patient safety was not a
- ¹⁰ 147 primary topic of focus. Another limitation of this study was that it only contained US-based
- ¹¹ 148 publications, and thus findings lack generalisability internationally to other health systems in
- $\frac{12}{13}$ 149 high-income countries (HIC) which are both organised, financed differently.

14 15 150 Research aim

1 2

16
 151 The overall aim of this literature review is to explore how EHR interoperability impacts patient
 152 safety, in the context of health systems in HICs. The results generated will aim to inform
 153 healthcare policymakers and help shape more effective EHR system implementation and

²⁰ 154 modernisation efforts in the coming years.

²¹ ²² 155 Methods and analysis

²³ 156 Search strategy

- A computerised search of the literature published in the last 10 years (2010 to 2020) search will
 be performed on PubMed/Medline, Embase, Cumulative Index to Nursing and Allied Health
 Literature (CINAHL), Health Management Information Consortium (HMIC), and PsycInfo. This
- ²⁸ 160 publication timeframe was chosen as it coincides with the mainstream implementation of EHRs
- ²⁹ 100 publication timenane was closen as it coincides with the mainstream implementation of Erros
 ³⁰ 161 in several HIC healthcare systems such as Kaiser Permanente in the US, and thus would select
- 162 for the most up to date, relevant evidence concerning EHR interoperability and patient safety
- 163 challenges faced by healthcare systems today to be included (22,23). The list of search strings
- ³³ 164 used will include both free text and controlled terms, whenever supported (Table 1) and will be
- ³⁴ 165 iteratively refined in consultation with the Imperial College St. Mary's campus medical librarian.
- ³⁶ 166 Grey literature sources will also be searched, including registrations in the International
- ³⁷ 167 Prospective Register of Systematic Reviews, reports of relevant stakeholder organisations (NHS
- 168 England, American Medical Informatics Association (AMIA), eHealth at WHO, and conference
- 169 proceedings (last 5 years) of several related conferences (AMIA, MedInfo, Medicine 2.0,
- 41 170 Medicine X)), in order to identify possible additional studies that meet the inclusion criteria.
 42
- 171 The search has also been restricted to HIC and articles published in English only.
- 44
45172Table 1: Concepts and database search terms

Electronic health records		Interoperability		Patient safety
 Electronic health records Electronic medical records Computerised medical records systems 	AND	 Interoperability Health information interoperability Systems integration 	AND	 Patient safety Patient adj1 incident* Adverse adj1 event* Patient adj1 outcome*

• Health	Patient adj1
information	harm
exchange / HIE	• Risk
• Health	managemen
information	
tashnalagy /	
HIT	
• Hospital	
information	
systems	
• Medical	
informatics	
Medical records	
linkage	

Study selection criteria

A summary of the population, intervention, comparison, outcomes, and type of studies being considered is provided in Table 2. This systematic review will focus on studies performed in high-income countries and published in English only. High-income countries will be defined in accordance with the World Bank's definition of "*countries where the gross national income*" (GNI) per capita is higher than \$12,536 USD" (24). Studies assessing the impact of EHR interoperability will be included. Interventions will include EHR systems interoperable with other health information technology systems both within and across healthcare facilities, as well as those used in tertiary and community settings. The primary outcomes to be considered in this review will be safety outcomes, including adverse events/incidents, safety-related patient experiences, and health outcomes. In addition, secondary outcomes would include studies exploring the broader impact of interoperable EHRs on health systems such as cost effectiveness and clinical culture amongst healthcare providers on the topic Quantitative, qualitative, and mixed methods studies will be included. Reference lists of the selected articles will also be screened for papers which may have been missed by the initial database search but still meet the eligibility criteria.

Table 2: PICO inclusion criteria

Population	High-income countries utilising electronic health records
Intervention	EHRs with interoperability
Comparison	Usual care (i.e., existing baseline of interoperability)
Outcome	Impact on patient safety and quality of care

Screening

Articles to be included will be screened by two independent reviewers, following the process described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (25). The initial screening will be done by the first reviewer based on the publication titles, followed by a second screening based on the abstracts. Included abstracts will then be fully reviewed by two independent researchers to produce a unified selection of articles to be included in this review. Cohen's kappa will be calculated to ensure inter-rater

- agreement and consistency in the selection of studies to be included (26,27). Any disagreements

2		
3	200	will be resolved by consensus; if a Cohen's kappa value of less than 0.6 is reported, the
4	201	discrepancies will be addressed through discussions with a more experienced third investigator.
с С	202	Data extraction
7	202	Data extraction will be performed using a standardised extraction table for each of the two
8	203	investigators to summarize the obstractoristics and findings of each included study, including
9	204	norma of the first author, year of publication, study design, number of participants, retention rates
10	203	name of the first author, year of publication, study design, number of participants, retention rates,
11	200	setting characteristics, outcome measures, and main results. The content of the two summary
12	207	tables will then be aggregated and reviewed once more by both investigators, with any
13	208	disagreements being solved by the third senior investigator.
14 15	209	
16	210	Quality assessment
17	211	The quality of randomised controlled trials and cluster randomised trials will be assessed using
18	212	the Cochrane Risk of Bias Tool (28), and the quality of non-randomised intervention studies (i.e.,
19	213	case control, cohort, quasi-experimental) will be appraised using the 'Risk of Bias In Non-
20	214	Randomised Studies - of Interventions' (ROBINS-I) tool (29). For cost-effectiveness studies, the
21	215	Drummond's checklist for assessing economic evaluations will be used (30). The National
22	216	Institute for Health and Care Excellence (NICE) quality appraisal checklist will be utilised to
23	217	assess the selected qualitative studies (31). Two independent reviewers will score the selected
24 25	218	studies and any disagreements will be resolved by a third person. A risk of bias table along with
26	219	an overall, collective bias narrative will be produced to summarise the biases of outcomes
27	220	observed amongst the evaluated studies.
28	221	5
29	222	Narrative synthesis subgroup analysis and meta-analysis
30	222	A parrative synthesis, subgroup analysis, and mean analysis
31 22	223	summarise any solient findings observed (22)
32 33	224	summarise any sament midnigs observed (32).
34	225	In quantitative studies with homogeneous or comparable outcome mangures, whenever possible
35	220	antinuous and dichotomous outcomes will be pooled together in a meta analysis. If possible
36	227	effect sizes will be transformed in a common metric (Hedges' g the bios corrected standardized
37	220	difference in means) and classified as positive when in favour of the intervention. Hotorogeneity
38	229	will be assessed using I ² and the presence of publication bios will be evaluated using a funnel
39 40	230	will be assessed using 1 ² and the presence of publication bias will be evaluated using a fullier
40 41	231	plot and the Duval and Tweedle's tim and minimethod (55).
42	232	For both qualitative and quantitative studies that non-out commonship subserves a subserve
43	233	For boin quantative and quantitative studies that report comparable outcomes, a subgroup
44	234	analysis based on clinical settings (e.g., primary vs. secondary healthcare settings) will be
45	233	conducted to explore any patterns of relationships ascertained from the data. Infough a
46	230	standardised spreadsneet snared amongst the reviewers, the body of evidence will be organised
4/	237	in two separate Summary of Findings tables (for both qualitative and quantitative studies) in
40 10	238	accordance to the Grading of Recommendations Assessment, Development and Evaluation
50	239	(GRADE) criteria (34).
51	240	
52	241	Patient and public involvement
53	242	This systematic literature review saw no direct participation by patients or the public during the
54	243	design of this study. However, this study was designed following a series of structured
55	244	interviews with patients regarding their experience of attending multiple institutions for hospital
50 57		
57		

- care (35). As this literature review will be used to form the basis for subsequent studies exploring the topic including ones involving patients, findings from this review will be shared with patient research groups to gain feedback and encourage further discourse surrounding the topic of EHR interoperability and patient safety. Amendments Any amendments to this protocol will be documented with reference to saved searches and analysis methods, which will be recorded in bibliographic databases, Mendeley and Excel templates for data collection and synthesis. Discussion One of the primary strengths stemming from the almost exploratory nature of this systematic review is the ability to generate a succinct, comprehensive appraisal of the best evidence currently available regarding how EHR interoperability impacts patient care and safety. By publishing this review protocol beforehand, we demonstrate a clear, robust, and transparent approach to aggregating the anticipated assortment of literature on the subject in question. There are also some limitations to be acknowledged. By restricting the inclusion criteria to publications made in English only, this could potentially exclude relevant papers pertaining to interoperable EHR systems in non-English healthcare settings. However, this is expected to be minimal as the majority of the papers concerning this topic published from the United States and European countries and are primarily done so in English journals. It must also be noted that both the heterogeneity of measures and outcomes evaluated, as well as the potentially reduced number of studies in subgroup analyses, may negatively influence the statistical power in data synthesis, and may preclude pooling of data as a meta-analysis. With such diverse means of measuring and assessing the effects of EHR interoperability, this will likely make comparisons between studies difficult and may obscure the true measure of effect EHR interoperability has had in the clinical setting. To mitigate this risk, outcomes will be grouped whenever possible, and summarised as a narrative synthesis. However, this can also represent a strength, as it will provide a comprehensive overview on the subject, capitalising on various research methodologies and providing novel insights on the impact of interoperable EHR systems on patient safety. Acknowledgments We would like to thank Michael Gainsford (Library Manager and Liaison Librarian at Imperial College London) for his support and guidance provided to improve the composition of the search terms and procedural aspects of the overall search strategy. Authors' contributions
 - Conception and design of the work: EL, ALN, and JC wrote the manuscript. HA, and AD
 281 provided critical revision of drafts for important intellectual content. All authors provided input
 282 into drafts of the manuscript and agree on the contents of the final version.
 - ⁵³ 283 Funding statement

This research was supported through the Imperial College National Institute for Health Research
 (NIHR) Patient Safety Translational Research Centre (PSTRC) and the Imperial College

1		
2	• • • •	
4	286	Biomedica
5	287	[215938/Z/
6	288	this protoc
7		~
8	289	Compet
9	290	The author
10		
12		
13		
14		
15		
16 17		
17		
19		
20		
21		
22		
23 24		
25		
26		
27		
28		
29		
30 31		
32		
33		
34		
35		
30		
38		
39		
40		
41		
42 43		
44		
45		
46		
47		
48 40		
50		
51		
52		
53		
54		
55		
50 57		
58		
-		

60

al Research Centre (BRC). JC acknowledges support from the Wellcome Trust

/19/Z]. However, the funder/sponsor has had no role in development and drafting of ol.

ing Interests

rs declare that there are no competing interests.

tor peer terier only

1 2			
3	201	Dof	oronoos
4	291	Rei	
5	292	l.	Colicchio TK, Cimino JJ, Del Fiol G. Unintended consequences of nationwide electronic
0 7	293		health record adoption: Challenges and opportunities in the post-meaningful use era.
8	294		Journal of Medical Internet Research. [Online] 2019;21(6): 1–9. Available from:
9	295	2	$\frac{d01:10.2196}{13313}$
10	296	2.	Roman LC, Ancker JS, Jonnson SB, Senathirajan Y. Navigation in the electronic health
11	297		record: A review of the safety and usability literature. <i>Journal of Biomedical Informatics</i> .
12	298	2	[Unline] Elsevier Inc.; 2017;67:69–79. Available from: doi:10.1016/J.jbi.2017.01.005
13 14	299	3.	Justinia 1. The UK's National Programme for 11. Why was it dismantied? <i>Health Services</i>
15	300		Management Research. [Unline] 2017;30(1): 2–9. Available from:
16	301	4	doi:10.11///0951484816662492
17	302	4.	Wachter RM. Making II work : namessing the power of health II to improve care in
18	303		England. National Advisory Group on Health Information Technology in England.
19	304 205		[Online] 2010; /I. Available from: https://www.gov.uk/covernment/wilcode/avators/wilcode/attachment_dots/file/550866/We
20	305		https://www.gov.uk/government/upioads/system/upioads/attachment_data/me/550866/wa
21	207		chier_Review_Accessible.pul%0Antips.//assets.publishing.service.gov.uk/government/upr
23	202	5	Value CS. Kristof C. Jones D. Mitchell E. Martinez A. Derriers to Electronic Health
24	200	5.	Riuse CS, Klistol C, Jolles D, Mitchell E, Martinez A. Darnels to Electronic realtin Pagord Adoption: a Systematic Literature Pavioy. <i>Journal of Medical Systems</i> [Online]
25	210		Lournal of Modical Systems: 2016:40(12) Available from: doi:10.1007/s10016.016.0628
26	211		Journal of Wedical Systems, 2010,40(12). Available from doi:10.100//s10910-010-0028-
2/	317	6	7 Avaad O Allouhani A Alhajaa EA Farhan M Abusaif S Al Hrouh A et al. The role of
20 29	212	0.	Ayadu O, Alloudalli A, Alliajaa EA, Falliali M, Adusell S, Al Illoud A, et al. The fole of
30	313		study International Journal of Madical Informatics [Online] Elsevier: 2010:127(April):
31	315		63_67 Available from: doi:10.1016/j.jimedinf.2019.04.014
32	316	7	Evans RS Electronic Health Records: Then Now and in the Future <i>Yearbook of Medical</i>
33	317	1.	Informatics [Online] 2016:25(S 01): S48_S61 Available from: doi:10.15265/IVS-2016-
34 25	318		s006
36	319	8	Gagnon MP Payne-Gagnon I Breton E Fortin IP Khoury L Dolovich L et al Adoption
37	320	0.	of electronic personal health records in Canada: Percentions of stakeholders. International
38	321		Journal of Health Policy and Management [Online] 2016;5(7): 425–433 Available from:
39	322		doi:10.15171/jihpm 2016.36
40	323	9	Campanella P Lovato E Marone C Fallacara L Mancuso A Ricciardi W et al The
41 42	324	2.	impact of electronic health records on healthcare quality a systematic review and meta-
43	325		analysis. The European Journal of Public Health. [Online] 2016:26(1): 60–64. Available
44	326		from: doi:10.1093/eurpub/ckv122
45	327	10.	Reis ZSN, Maia TA, Marcolino MS, Becerra-Posada F, Novillo-Ortiz D, Ribeiro ALP, Is
46	328		There Evidence of Cost Benefits of Electronic Medical Records, Standards, or
47	329		Interoperability in Hospital Information Systems? Overview of Systematic Reviews. JMIR
48 ⊿0	330		Medical Informatics. [Online] 2017;5(3): e26. Available from:
50	331		doi:10.2196/medinform.7400
51	332	11.	World Health Organization (WHO). eHealth in the Region of the Americas: breaking
52	333		down the barriers to implementation. [Online] 2016. Available from:
53	334		http://iris.paho.org/xmlui/bitstream/handle/123456789/31286/9789275119259-
54	335		eng.pdf?sequence=6&isAllowed=y
55 56	336	12.	Zaheer S, Pimentel SD, Simmons KD, Kuo LE, Datta J, Williams N, et al. Comparing
57			
58			10
59			
60			For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

2			
3	337		International and United States Undergraduate Medical Education and Surgical Outcomes
4	338		Using a Refined Balance Matching Methodology <i>Annals of Surgary</i> [Online] 2017:
5	330		Available from: doi:10.1097/SLA.00000000001878
6	340	13	Everson L Adler Milstein I Gans in health information evolution between hospitals that
7	240	13.	treat many shared potients. Journal of the American Medical Information According
8	341 242		treat many shared patients. <i>Journal of the American Medical Informatics Association</i> .
9 10	342		[Online] 2018;25(9): 1114-1121. Available from: doi:10.1093/jamia/ocy089
10	343	14.	Thompson MP, Graetz I. Hospital adoption of interoperability functions. <i>Healthcare</i> .
12	344		[Online] Elsevier Inc.; 2019;7(3): 100347. Available from:
13	345		doi:10.1016/j.hjdsi.2018.12.001
14	346	15.	Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges,
15	347		towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research</i> .
16	348		[Online] 2013;19(4): 286–292. Available from: doi:10.4258/hir.2013.19.4.286
17	349	16.	Warren LR, Clarke JM, Arora S, Darzi AW. Improving data sharing between acute
18	350		hospitals in England: an overview of health record system distribution and retrospective
19	351		observational analysis of inter-hospital transitions of care. <i>BMI Open</i> [Online]
20	352		2019.9(12): e031637 Available from: doi:10.1136/bmionen-2019-031637
21	352	17	Clarke IM Warren I.R. Arora S. Barahona M. Darzi A.W. Guiding interoperable
22	254	17.	clarke JW, watch LK, Alora S, Datahona W, Datzi AW. Outding incroperatic
23	254		Suring on LIS, 2019,1(1), 1 (Assilette from dei 10,1029/z4174(019,0072 st
24 25	333	10	Springer US; $2018;1(1): 1-6$. Available from: $d01:10.1038/s41/46-018-00/2-y$
25	356	18.	McAlearney AS, Sleck C, Hefner J, Robbins J, Huerta TR. Facilitating Ambulatory
20	357		Electronic Health Record System Implementation: Evidence from a Qualitative Study.
28	358		<i>BioMed Research International</i> . [Online] 2013;2013: 1–9. Available from:
29	359		doi:10.1155/2013/629574
30	360	19.	Dobrow MJ, Bytautas JP, Tharmalingam S, Hagens S. Interoperable Electronic Health
31	361		Records and Health Information Exchanges: Systematic Review. JMIR Medical
32	362		Informatics. [Online] 2019;7(2): e12607. Available from: doi:10.2196/12607
33	363	20.	Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records
34	364		Interface Design: A Review of Recent Literature and Guideline Formulation. Human
35	365		<i>Factors</i> [Online] 2015:57(5): 805–834 Available from doi:10.1177/0018720815576827
36	366	21	Hersh WR Totten AM Eden KB Devine B Gorman P Kassakian SZ et al. Outcomes
3/	367	21.	From Health Information Exchange: Systematic Review and Future Research Needs
38 20	268		IMIP Modical Informatics [Online] 2015:2(4): e20 Available from:
40	260		doi:10.2106/modinform 5215
41	270	22	Wheatley D. Transforming are delivery through health information technology. The
42	370	22.	wheatley B. Transforming care derivery through health information technology. The
43	3/1		Permanente journal. [Online] winter; 2013;17(1): 81–86. Available from:
44	372		doi:10./812/TPP/12-030 [Accessed: 20th January 2021]
45	373	23.	Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming
46	374		And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323
47	375		[Accessed: 22nd January 2021]
48	376	24.	World Bank. World Bank Country and Lending Groups – World Bank Data Help Desk.
49	377		[Online] The World Bank. p. 1–8. Available from:
50	378		https://datahelpdesk.worldbank.org/knowledgebase/articles/906519 [Accessed: 26th May
כו 51	379		2021]
52 53	380	25.	Moher D. Liberati A. Tetzlaff J. Altman DG. Altman D. Antes G. et al. Preferred
54	381		reporting items for systematic reviews and meta-analyses. The PRISMA statement <i>PLoS</i>
55	387		Medicine [Online] 2009:6(7) Available from: doi:10.1371/journal.nmed.1000007
56	502		memorie. [Simile] 2009,0(7). Tranuole from. doi:10.1571/journal.pined.1000097
57			
58			11
59			
60			For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

2			
3	383	26.	Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.
4	384		<i>Biometrics</i> . [Online] 1977:33(1): 159. Available from: doi:10.2307/2529310
5	385	27	McHugh ML Interrater reliability: the kappa statistic <i>Biochemia medica</i> 2012:22(3):
6 7	386	_/.	276–282
/ 0	387	28	Sterne IAC Savović I Page MI Elbers RG Blencowe NS Boutron L et al RoB 2: A
0	200	20.	revised tool for assessing risk of bigs in rendemised trials. The PML [Online]
10	200		2010.2(((Assessed) Assessing fisk of blas in failedonnised trials. <i>The Divid</i> . [Onnine]
11	200	20	2019,300(August). Available from: doi:10.1130/dmj.14898
12	390	29.	Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, et al.
13	391		ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions.
14	392		<i>BMJ (Online)</i> . [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.14919
15	393	30.	Drummond MF, Brien BJ, Torrance GW, Stoddart GL. Methods for the Economic
16	394		Evaluation of Health Care Programmes 2nd ed. Oxford University Press; 1997.
17	395	31.	Methods for the development of NICE public health guidance. [Online]. 3rd n. National
18	396		Institute for Clinical Excellence (NICE); 2018. Available from:
19	397		https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice-
20	398		public-health-guidance-third-edition-pdf-2007967445701
21	399	32.	Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S.
23	400		Guidance on the conduct of narrative synthesis in systematic reviews. A product from the
24	401		ESRC methods programme, 2006:(April 2006): 1–92.
25	402	33	Duval S Tweedie R Trim and fill. A simple funnel-plot-based method of testing and
26	403	55.	adjusting for publication bias in meta-analysis <i>Biometrics</i> [Online] Biometric Society
27	404		2000.56(2): $455-463$ Available from: doi:10.1111/i.0006-341X 2000.00455 x [Accessed:
28	405		2000,50(2): 455 405. Available from: doi:10.1111/j.0000 5417.2000.00455.x [//decisied.
29	405	34	Guyatt GH Oyman AD Vist GE Kunz R Falck-Vtter V Alonso-Coello P et al
30	400	54.	CPADE: an amorging consongue on rating quality of avidence and strength of
31 22	407		OKADE, an emerging consensus on rating quanty of evidence and strength of
32	408		Lecommendations. <i>DMJ</i> . [Omme] 2008,550(7050). 924–920. Available from.
34	409	25	dol:10.1136/bmJ.39489.4/034/.AD
35	410	35.	warren LR, Harrison M, Arora S, Darzi A. working with patients and the public to design
36	411		an electronic health record interface: A qualitative mixed-methods study. BMC Medical
37	412		Informatics and Decision Making. [Online] BMC Medical Informatics and Decision
38	413		Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7
39	414		
40			
41			
42 42			
45 44			
45			
46			
47			
48			
49			
50			
51			
52			
55 51			
55			
56			
57			
58			12
59			12

Section and topic	Item No.	Checklist item	Reported on Page No.
ADMINISTRATIV	E INFO	ORMATION	
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

 BMJ Open

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6-7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6-7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6-7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	7
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	-
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6-7
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	7

clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the

PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

BMJ Open

BMJ Open

Electronic Health Records, Interoperability, and Patient Safety in Health Systems of High-Income Countries: A Systematic Review Protocol

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-044941.R3
Article Type:	Protocol
Date Submitted by the Author:	05-Jun-2021
Complete List of Authors:	Li, Edmond; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; London School of Hygiene and Tropical Medicine Faculty of Infectious and Tropical Diseases, Clinical Research Department Clarke, Jonathan; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; Imperial College London, Centre for Mathematics of Precision Healthcare Neves, Ana Luisa; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer; University of Porto, Center for Health Technology and Services Research / Department of Community Medicine, Health Information and Decision Ashrafian, Hutan; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer Darzi, Ara; Imperial College London, Patient Safety Translational Research Centre, Institute of Global Health Innovation, Department of Surgery & Cancer
Primary Subject Heading :	Health informatics
Secondary Subject Heading:	Health policy, Public health, Health services research
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, Information technology < BIOTECHNOLOGY & BIOINFORMATICS, Information management < BIOTECHNOLOGY & BIOINFORMATICS, HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

1		
∠ 3		Flastronia Haalth Daaanda Interner anability and Dation (S. f. t. in
4	I	Electronic Health Records, Interoperability, and Patient Safety in
5 6	2	Health Systems of High-Income Countries: A Systematic Review
7	3	Protocol
8 0	4	Edmond Li ^[1] , Jonathan Clarke ^[1,3] , Ana Luisa Neves ^[1,2] , Hutan Ashrafian ^[1] , Ara Darzi ^[1]
10	5	^[1] Imperial NIHR Patient Safety Translational Research Centre (PSTRC), Institute of Global
11	6	Health Innovation (IGHI), Imperial College London, London, United Kingdom
12 13	7	^[2] Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS)
14	8	/ Center for Health Technology and Services Research (CINTESIS), University of Porto, Porto,
15	9	Portugal.
16 17	10	^[3] Centre for Mathematics of Precision Healthcare, Imperial College London, London, United
18	11	Kingdom
19	12	
20 21	13	
22	14 15	
23	15	
24 25	10	
26	17	
27 28	19	
28 29	20	
30	21	
31 32	22	
33	23	
34	24	
35 36	25	
37	26	
38	27	
39 40	28	
41	29	
42	30	
43 44	31	Corresponding author
45	32	Name: Edmond Li
46 47	33	Email: <u>edmond.li19@imperial.ac.uk</u>
48	34	Address: Institute of Global Health Innovation, Room 1035/7, QEQM Wing, St Mary's Campus,
49	35	London W2 1NY
50 51	36	
52	37	Keywords [MeSH terms]: electronic health records, electronic medical records, computerised
53	38	patient records, health information technology, health information exchanges, interoperability,
54 55	39	patient safety, patient harm, adverse events, health outcomes
56	40	
57		
58 59		1
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1		
2		
3 4	41	Abstract
5	42	Introduction
6	43	The availability and routine use of electronic health records (EHRs) have become commonplace
/	44	in healthcare systems of many high-income countries. While there is an ever-growing body of
0 9	45	literature pertaining to EHR use, evidence surrounding the importance of EHR interoperability
10	46	and its impact on patient safety remains less clear. There is therefore a need and opportunity to
11	47	evaluate the evidence available regarding this relationship so as to better inform health
12	48	informatics development and policies in the years to come. This systematic review aims to
13	49	evaluate the impact of EHR interoperability on patient safety in health systems of high-income
14 15	50	countries.
15	51	
17	52	Methods and analysis
18	53	A systematic literature review will be conducted via a computerised search through four
19 20	54	databases: PubMed, Embase, HMIC, and PsycInfo for relevant articles published between 2010
20 21	55	and 2020. Outcomes of interest will include: impact on patient safety, and the broader effects on
22	56	health systems. Quality of the randomised quantitative studies will be assessed using Cochrane
23	57	Risk of Bias Tool. Non-randomised papers will be evaluated with the Risk of Bias In Non-
24	58	Randomised Studies - of Interventions (ROBINS-I) tool. Drummond's Checklist will be utilised
25	59	for publications pertaining to economic evaluation. The National Institute for Health and Care
20 27	60	Excellence (NICE) quality appraisal checklist will be used to assess qualitative studies. A
28	61	narrative synthesis will be conducted for included studies, and the body of evidence will be
29	62	summarised in a summary of findings table.
30	63	
31	64	Ethics and dissemination
33	65	This review will summarise published studies with non-identifiable data and thus does not
34	66	require ethical approval. Findings will be disseminated through preprints, open access peer-
35	67	reviewed publication, and conference presentations.
36	68	
37	69	PROSPERO registration number [CRD42020209285]
39	70	This is an open access article distributed in accordance with the Creative Commons Attribution
40	71	4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform
41	72	and build upon this work for any purpose, provided the original work is properly cited, a link to
42	73	the licence is given, and indication of whether changes were made. See:
44	/4	nttps://creativecommons.org/licenses/by/4.0/.
45	75	Article Summary
46	15	Article Summary
47 48	76	Strengths and limitations of this study
49	//	Strengths
50	/8 70	• Inclusion of quantitative, qualitative, and mixed-methods studies can provide a
51	/9 00	offect patient safety and health systems
52	00 Q1	 Using robust methodology to examine the wealth of existing literature, the proposed
53 54	82	systematic review attempts to answer a pragmatic question which is integral to future
55	83	health informatics development and policies
56		
57		
58 59		
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

2 3 4	84 85	Limitations
5 6 7 8	86 87 88	 The heterogeneity of methods and outcomes assessed may obscure the true effect interoperable EHRs have had on patient safety. Potential small sample size in subgroup analyses, may negatively impact the statistical
9 10 11 12	89 90 91	 power in quantitative data synthesis. Limiting the search strategy to English-only publications may not capture studies exploring EHR experiences in non-English speaking countries.
13 14 15	92 93	
16 17 18		
19 20 21 22		
23 24 25		
26 27 28 20		
29 30 31 32		
33 34 35		
36 37 38		
40 41 42		
43 44 45		
46 47 48		
49 50 51 52		
53 54 55		
56 57 58		
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Introduction

1

Electronic health records (EHRs) have become an integral part of modern healthcare since their initial mainstream implementation in the mid-late 2000s through the passing of the Health Information Technology for Economic and Clinical Health Act (HITECH) in the United States

documentation & retrieval of patient records and the prescription of medications, to coordinating complex care plans between different healthcare providers and electronic billing, EHRs fulfil a

In order to achieve EHR's full potential, it is critical to improve interoperability - i.e., "the ability of health information systems to work together within and across organisation boundaries in order to advance effective delivery of healthcare for individuals and communities" (10). The lack of universal interoperability is often cited as one of the many significant shortcomings of EHRs currently in use, resulting in duplication in healthcare costs, increased clinician workload fatigue,

populations with chronic conditions, polypharmacy, and multiple comorbidities who are reliant

and the NHS National Programme for IT initiative (NPfIT) in England (1-4). From the

and poses a potential risk to patient safety (2). This is especially problematic for patient

Poor EHR interoperability is detrimental to patient safety and costly for health systems. Its consequences range from increased risks of medication errors, fragmentation of patient data, to iatrogenic harm resulting from redundant testing, and additional healthcare expenditure (12–17).

In the fragmented EHR landscape of the United Kingdom, measuring the effect poor EHR interoperability has in the National Health Service (NHS), remain challenging (18). Although there is a growing body of literature investigating areas such as the facilitators and barriers to EHR greater adoption, technical capabilities, and usability (19,20), no systematic review has been conducted exploring specifically the problem of interoperability amongst the assortment of EHRs in use, how it affects patient safety, and ultimately the financial cost savings lost to health

In a recent systematic review by Dobrow *et al.* assessing the effects of EHR and HIT interoperability on health systems, 130 publications were included, with the majority being studies conducted in the United States, utilised quantitative methods, and focussed primarily on acute healthcare settings. The authors noted the use of interoperable EHRs had a positive impact on outcomes measures such as quality of care and productivity (19). However, in domains such as stakeholder engagement, performance & reliability, security & privacy, information quality, and ease of use, the benefits of interoperable EHRs was less clear (19). Amongst the 130 publications, 17 were reviews with the majority directed at exploring facilitators & barriers to EHR implementation, and the general benefits and impact of EHR use. While this review did focus on studies pertaining to the topic of interoperable EHRs, this was done so only from a broad perspective and included studies exploring a wide range of outcomes related to the effects

of EHR on healthcare rather than specifically on their implications to patient safety.

upon effective patient information sharing via EHRs to facilitate their care (11).

multitude of roles for both clinicians and patients alike (5–9).

2	
3	0.4
4	94
5	95
6	96
/ 0	97
9	98
10	99
11	100
12	101
13	102
14	102
15	103
10	104
18	105
19	106
20	107
21	108
22	109
23	110
24 25	111
25	112
27	113
28	114
29	115
30	115
31	110
32	11/
33 34	118
35	119
36	120
37	121
38	122
39	123
40	124
41	125
42	126
44	127
45	128
46	129
47	130
48	131
49 50	132
50 51	133
52	134
53	135
54	136
55	137
56	
57	
58	

60

systems.

In another review by Hersh *et al.*, the authors explored how health information exchange (HIE) affected health systems on a variety of domains, including costs, healthcare utilisation, health

- $\frac{3}{4}$ 138 outcomes, healthcare worker attitudes, and sustainability. Despite the widespread routinely use
- ⁴ ⁵ 139 of HIE, the authors described a general lack of robust evidence on the quality, costs, efficiency,
- usage, and sustainability (21). However, there was some evidence demonstrating HIEs being
 associated with reduced utilisation and costs in emergency care settings despite methodological
- associated with reduced utilisation and costs in emergency care settings despite methodological
 issues being present in many of the included publications (21). Although this review was
- ambitious in the wide scope of interest regarding the effects of HIE use, patient safety was not a
- ¹⁰ 144 primary topic of focus. Another limitation of this study was that it only contained US-based
- ¹¹ 145 publications, and thus findings lack generalisability internationally to other health systems in
- $\frac{12}{13}$ 146 high-income countries (HIC) which are both organised, financed differently.

¹⁴ 15 147 Research aim

1 2

The overall aim of this literature review is to explore how EHR interoperability impacts patient safety, in the context of health systems in HICs. The results generated will aim to inform healthcare policymakers and help shape more effective EHR system implementation and

151 modernisation efforts in the coming years.

21 22 23 24 25 25 26 27 28 29 29 20 21 21 22 23 24 25 26 27 27 28 29 29 20 21 21 22 23 24 25 26 27 27 27 27 27 27 27 27 27 28 29 29 20 20 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 22 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 21 2

²³ 153 Search strategy

- A computerised search of the literature published in the last 10 years (2010 to 2020) search will
 be performed on PubMed/Medline, Embase, Cumulative Index to Nursing and Allied Health
 Literature (CINAHL), Health Management Information Consortium (HMIC), and PsycInfo. This
 publication timeframe was chosen as it coincides with the mainstream implementation of EHRs
 in several HIC healthcare systems such as Kaiser Permanente in the US, and thus would select
- in several HIC nearthcare systems such as Kaiser Permanente in the US, and thus would select
 for the most up to date, relevant evidence concerning EHR interoperability and patient safety
- challenges faced by healthcare systems today to be included (22,23). The list of search strings
- ³³ 161 used will include both free text and controlled terms, whenever supported (Table 1) and will be
- ³⁴ 162 iteratively refined in consultation with the Imperial College St. Mary's campus medical librarian.
- For a sample of the search strategy, please see Supplement 1.
- ³⁷ 164 Grey literature sources will also be searched, including registrations in the International
- 165 Prospective Register of Systematic Reviews, reports of relevant stakeholder organisations (NHS
- 166 England, American Medical Informatics Association (AMIA), eHealth at WHO, and conference
- 41 167 proceedings (last 5 years) of several related conferences (AMIA, MedInfo, Medicine 2.0,
- Medicine X)), in order to identify possible additional studies that meet the inclusion criteria.
- 169 The search has also been restricted to HIC and articles published in English only.
- 45 46 170 Table 1: Concepts and database search terms

59

Electronic health records		Interoperability		Patient safety
 Electronic health records Electronic medical records 	AND	 Interoperability Health information interoperability Systems integration 	AND	 Patient safety Patient adj 1 incident* Adverse adj 1 event*

1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		
12		
13		
14		
15		
16		
17		
18		
19		
20		
21		
22		
23	171	
24		
25	172	
26	173	
27	173	
28	1/4	
29	175	
30	176	
31	177	
32	178	
33	179	
34	180	
35	100	
36	181	
37	182	
38	183	
39	184	
40	185	
41	186	
42	100	
43	10/	
44	188	

Computerised medical records			• Patient adj1 outcome*
systems			• Patient adj1
• Health			harm
information			• Risk
exchange / HIE			management
• Health			C
information			
technology /			
HIT			
• Hospital			
information	\frown		
systems			
• Medical	Ο.		
informatics			
Medical records			

5 172 Study selection criteria

linkage

A summary of the population, intervention, comparison, outcomes, and type of studies being considered is provided in **Table 2**. This systematic review will focus on studies performed in high-income countries and published in English only. High-income countries will be defined in accordance with the World Bank's definition of "*countries where the gross national income* (*GNI*) per capita is higher than \$12,536 USD" (24). Studies assessing the impact of EHR interoperability will be included. Interventions will include EHR systems interoperable with other health information technology systems both within and across healthcare facilities, as well as those used in tertiary and community settings. The primary outcomes to be considered in this review will be safety outcomes, including adverse events/incidents, safety-related patient experiences, and health outcomes. In addition, secondary outcomes would include studies exploring the broader impact of interoperable EHRs on health systems such as cost effectiveness and clinical culture amongst healthcare providers on the topic Quantitative, qualitative, and mixed methods studies will be included. Reference lists of the selected articles will also be screened for papers which may have been missed by the initial database search but still meet the eligibility criteria.

189 Table 2: PICO inclusion criteria

Population	High-income countries utilising electronic health records
Intervention	EHRs with interoperability
Comparison	Usual care (i.e., existing baseline of interoperability)
Outcome	Impact on patient safety and quality of care

⁵¹ 190 Screening

191 Articles to be included will be screened by two independent reviewers, following the process

192 described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses

- ⁵⁵ 193 (PRISMA) flow diagram (25). The initial screening will be done by the first reviewer based on
- 56 57

53

54

the publication titles, followed by a second screening based on the abstracts. Included abstracts will then be fully reviewed by two independent researchers to produce a unified selection of articles to be included in this review. Cohen's kappa will be calculated to ensure inter-rater agreement and consistency in the selection of studies to be included (26,27). Any disagreements will be resolved by consensus; if a Cohen's kappa value of less than 0.6 is reported, the discrepancies will be addressed through discussions with a more experienced third investigator. Data extraction Data extraction will be performed using a standardised extraction table for each of the two investigators to summarise the characteristics and findings of each included study, including name of the first author, year of publication, study design, number of participants, retention rates, setting characteristics, outcome measures, and main results. The content of the two summary tables will then be aggregated and reviewed once more by both investigators, with any disagreements being solved by the third senior investigator. Quality assessment The quality of randomised controlled trials and cluster randomised trials will be assessed using the Cochrane Risk of Bias Tool (28), and the quality of non-randomised intervention studies (i.e., case control, cohort, quasi-experimental) will be appraised using the 'Risk of Bias In Non-Randomised Studies - of Interventions' (ROBINS-I) tool (29). For cost-effectiveness studies, the Drummond's checklist for assessing economic evaluations will be used (30). The National Institute for Health and Care Excellence (NICE) quality appraisal checklist will be utilised to assess the selected qualitative studies (31). Two independent reviewers will score the selected studies and any disagreements will be resolved by a third person. A risk of bias table along with an overall, collective bias narrative will be produced to summarise the biases of outcomes observed amongst the evaluated studies. Narrative synthesis, subgroup analysis, and meta-analysis A narrative synthesis will be performed for all studies included in this systematic review to summarise any salient findings observed (32). In quantitative studies with homogenous or comparable outcome measures, whenever possible, continuous and dichotomous outcomes will be pooled together in a meta-analysis. If possible, effect sizes will be transformed in a common metric (Hedges' g – the bias-corrected standardised difference in means) and classified as positive when in favour of the intervention. Heterogeneity will be assessed using I² and the presence of publication bias will be evaluated using a funnel plot and the Duval and Tweedie's trim and fill method (33). For both qualitative and quantitative studies that report comparable outcomes, a subgroup analysis based on clinical settings (e.g., primary vs. secondary healthcare settings) will be conducted to explore any patterns or relationships ascertained from the data. Through a standardised spreadsheet shared amongst the reviewers, the body of evidence will be organised in two separate Summary of Findings tables (for both qualitative and quantitative studies) in accordance to the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE) criteria (34). For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1	9
2	0
2	1
2	2
2	3
2	4
2	5
2	6
2	7
2	8
2	9
3	0
3	1
3	2
3	3
3	4
3	5
3	6
3	7
3	8
3	9
4	0
4	1
4	2
4	3
4	4
4	5
4	6
4	7
4	8
4	9
5	0
5	1

239 Patient and public involvement

This systematic literature review saw no direct participation by patients or the public during the design of this study. However, this study was designed following a series of structured interviews with patients regarding their experience of attending multiple institutions for hospital care (35). As this literature review will be used to form the basis for subsequent studies exploring the topic including ones involving patients, findings from this review will be shared with patient research groups to gain feedback and encourage further discourse surrounding the topic of EHR interoperability and patient safety.

¹³ 247 14 248 Amendments

Any amendments to this protocol will be documented with reference to saved searches and analysis methods, which will be recorded in bibliographic databases, Mendeley and Excel templates for data collection and synthesis.

0 252 Discussion

One of the primary strengths stemming from the almost exploratory nature of this systematic review is the ability to generate a succinct, comprehensive appraisal of the best evidence currently available regarding how EHR interoperability impacts patient care and safety. By publishing this review protocol beforehand, we demonstrate a clear, robust, and transparent approach to aggregating the anticipated assortment of literature on the subject in question.

27 258

There are also some limitations to be acknowledged. By restricting the inclusion criteria to publications made in English only, this could potentially exclude relevant papers pertaining to interoperable EHR systems in non-English healthcare settings. However, this is expected to be minimal as the majority of the papers concerning this topic published from the United States and European countries and are primarily done so in English journals. It must also be noted that both the heterogeneity of measures and outcomes evaluated, as well as the potentially reduced number of studies in subgroup analyses, may negatively influence the statistical power in data synthesis, and may preclude pooling of data as a meta-analysis. With such diverse means of measuring and assessing the effects of EHR interoperability, this will likely make comparisons between studies difficult and may obscure the true measure of effect EHR interoperability has had in the clinical setting. To mitigate this risk, outcomes will be grouped whenever possible, and summarised as a narrative synthesis. However, this can also represent a strength, as it will provide a comprehensive overview on the subject, capitalising on various research methodologies and .3 providing novel insights on the impact of interoperable EHR systems on patient safety.

⁴⁶ 47 274 Ethics and Dissemination

This review will summarise published studies with non-identifiable data and therefore does not
 require ethical approval. This protocol complies with the Preferred Reporting Items for
 Systematic Review and Meta-Analyses Protocols guidelines. Findings will be disseminated
 through preprints, open access peer-reviewed publication, and conference presentations.

³₄ 279 Acknowledgments

280 We would like to thank Michael Gainsford (Library Manager and Liaison Librarian at Imperial

College London) for his support and guidance provided to improve the composition of the search
 terms and procedural aspects of the overall search strategy.

tor occurrent only

1 2			
2 3	• • •	D - (
4	283	Ref	erences
5	284	1.	Colicchio TK, Cimino JJ, Del Fiol G. Unintended consequences of nationwide electronic
6	285		health record adoption: Challenges and opportunities in the post-meaningful use era.
/	286		Journal of Medical Internet Research. [Online] 2019;21(6): 1–9. Available from:
ð	287		doi:10.2196/13313
10	288	2.	Roman LC, Ancker JS, Johnson SB, Senathirajah Y. Navigation in the electronic health
11	289		record: A review of the safety and usability literature. Journal of Biomedical Informatics.
12	290		[Online] Elsevier Inc.; 2017;67: 69–79. Available from: doi:10.1016/j.jbi.2017.01.005
13	291	3.	Justinia T. The UK's National Programme for IT: Why was it dismantled? Health Services
14	292		Management Research. [Online] 2017;30(1): 2–9. Available from:
15	293		doi:10.1177/0951484816662492
16	294	4.	Wachter RM. Making IT work : harnessing the power of health IT to improve care in
1/ 10	295		England, National Advisory Group on Health Information Technology in England.
10	296		[Online] 2016: 71. Available from:
20	297		https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/550866/Wa
21	298		chter Review Accessible pdf%0Ahttps://assets publishing service gov uk/government/upl
22	299		oads/system/uploads/attachment_data/file/550866/Wachter_Review_Accessible.pdf
23	300	5	Kruse CS, Kristof C, Jones B, Mitchell E, Martinez A, Barriers to Electronic Health
24	301	0.	Record Adoption: a Systematic Literature Review <i>Journal of Medical Systems</i> [Online]
25	302		Iournal of Medical Systems: 2016:40(12) Available from: doi:10.1007/s10916-016-0628-
26	303		Q
27	304	6	Avaad O Allouhani A Alhaiaa FA Farhan M Abuseif S Al Hroup A et al. The role of
29	305	0.	electronic medical records in improving the quality of health care services: Comparative
30	306		study International Journal of Medical Informatics [Online] Elsevier: 2019:127(April):
31	307		63-67 Available from: doi:10.1016/j.jimedinf.2019.04.014
32	308	7	Evans RS Electronic Health Records: Then Now and in the Euture <i>Yearbook of Medical</i>
33	309	1.	Informatics [Online] 2016:25(S 01): S48-S61 Available from: doi:10.15265/IVS-2016-
34 25	310		s006
36	311	8	Gagnon MP Payne-Gagnon I Breton F Fortin IP Khoury I Dolovich L et al Adoption
37	312	0.	of electronic personal health records in Canada: Perceptions of stakeholders <i>International</i>
38	312		<i>Journal of Health Policy and Management</i> [Online] 2016;5(7): 425–433 Available from:
39	317		doi:10.15171/iihnm 2016.36
40	215	0	Componella P. Loveto F. Marona C. Fallacara L. Manauso A. Picciardi W. et al. The
41	216	9.	impart of algorrania health records on healthcare quality: a systematic review and meta
42	217		analysis. The European Journal of Public Health [Online] 2016;26(1): 60, 64, Available
43 44	210		frame dai:10.1002/aumauh/alu:122
44 45	210	10	nom. doi.10.1095/eurpu0/ckv122
46	319	10.	Keis ZSN, Maia TA, Marcolino MS, Becerra-Posada F, Novilio-Ortiz D, Ribeiro ALP. Is
47	320		I here Evidence of Cost Benefits of Electronic Medical Records, Standards, or
48	321		Interoperability in Hospital Information Systems? Overview of Systematic Reviews. JMIR
49	322		Medical Informatics. [Online] 2017;5(3): e26. Available from:
50	323		doi:10.2196/medinform./400
51	324	11.	World Health Organization (WHO). <i>eHealth in the Region of the Americas: breaking</i>
52 52	325		down the barriers to implementation. [Online] 2016. Available from:
55 54	326		http://iris.paho.org/xmlui/bitstream/handle/123456789/31286/9789275119259-
55	327		eng.pdt?sequence=6&isAllowed=y
56	328	12.	Zaheer S, Pimentel SD, Simmons KD, Kuo LE, Datta J, Williams N, et al. Comparing
57			
58			10
59 60			For peer review only - http://bmiopen.bmi.com/site/about/guidelines.xhtml
00			

2			
3	329		International and United States Undergraduate Medical Education and Surgical Outcomes
4	330		Using a Refined Balance Matching Methodology <i>Annals of Surgery</i> [Online] 2017
5	331		Available from: doi:10.1097/SLA.00000000001878
6	222	12	Everson L Adler Milstein I Cons in health information evolution between heapitals that
7	222	15.	treat many shared notionts. Journal of the American Medical Information According
8	333		treat many shared patients. <i>Journal of the American Medical Informatics Association</i> .
9	334		[Online] 2018;25(9): 1114–1121. Available from: doi:10.1093/jamia/ocy089
10 11	335	14.	Thompson MP, Graetz I. Hospital adoption of interoperability functions. <i>Healthcare</i> .
17	336		[Online] Elsevier Inc.; 2019;7(3): 100347. Available from:
12	337		doi:10.1016/j.hjdsi.2018.12.001
14	338	15.	Tapuria A, Kalra D, Kobayashi S. Contribution of clinical archetypes, and the challenges,
15	339		towards achieving semantic interoperability for EHRs. <i>Healthcare Informatics Research</i> .
16	340		[Online] 2013:19(4): 286–292 Available from: doi:10.4258/hir 2013.19.4.286
17	341	16	Warren LR Clarke IM Arora S Darzi AW Improving data sharing between acute
18	242	10.	hospitals in England: an everyieve of health record system distribution and retrospective
19	242		hospitals in England, an overview of nearly record system distribution and recospective
20	343		observational analysis of inter-nospital transitions of care. <i>BMJ Open</i> . [Online]
21	344		2019;9(12): e031637. Available from: doi:10.1136/bmjopen-2019-031637
22	345	17.	Clarke JM, Warren LR, Arora S, Barahona M, Darzi AW. Guiding interoperable
23	346		electronic health records through patient-sharing networks. <i>npj Digital Medicine</i> . [Online]
24	347		Springer US; 2018;1(1): 1–6. Available from: doi:10.1038/s41746-018-0072-y
25	348	18.	McAlearney AS, Sieck C, Hefner J, Robbins J, Huerta TR, Facilitating Ambulatory
26	349		Electronic Health Record System Implementation: Evidence from a Qualitative Study
27	350		RioMed Research International [Online] 2013:2013: 1–9 Available from:
28	351		doi:10.1155/2013/629574
29	252	10	Debrow MI Dytautas ID Thermalingon S Hagans S. Interoperable Electronia Health
30	252	19.	Doblow MJ, Bylaulas JF, Tharmannigani S, Hagens S. Interoperable Electronic Health
31	353		Records and Health Information Exchanges: Systematic Review. JMIR Medical
32	354		Informatics. [Online] 2019; /(2): e1260/. Available from: doi:10.2196/1260/
33 24	355	20.	Zahabi M, Kaber DB, Swangnetr M. Usability and Safety in Electronic Medical Records
34 25	356		Interface Design: A Review of Recent Literature and Guideline Formulation. Human
36	357		Factors. [Online] 2015;57(5): 805–834. Available from: doi:10.1177/0018720815576827
37	358	21.	Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, et al. Outcomes
38	359		From Health Information Exchange: Systematic Review and Future Research Needs.
39	360		IMIR Medical Informatics [Online] 2015:3(4): e39 Available from:
40	361		doi:10.2196/medinform 5215
41	362	22	Wheatley B. Transforming care delivery through health information technology. The
42	262	<i>LL</i> .	Down an outo journal [Online] Winter: 2012:17(1): 91, 96, Available from:
43	202		Permanente journat. [Online] winter, 2013, 17(1). 81-80. Available from.
44	364		dol:10.7812/1PP/12-030 [Accessed: 20th January 2021]
45	365	23.	Chen C, Permanente K. The Kaiser Permanente Electronic Health Record: Transforming
46	366		And Streamlining Modalities Of Care. 2009; Available from: doi:10.1377/hlthaff.28.2.323
47	367		[Accessed: 22nd January 2021]
48	368	24.	World Bank. World Bank Country and Lending Groups – World Bank Data Help Desk.
49	369		[Online] The World Bank. p. 1–8. Available from:
50	370		https://datahelpdesk.worldbank.org/knowledgebase/articles/906519 [Accessed: 26th May
51	371		2021]
52	372	25	Moher D. Liberati A. Tetzlaff I. Altman DG. Altman D. Antes G. et al. Preferred
53 E1	372	23.	reporting items for systematic reviews and mate analyses. The DDICMA statement DI of
54 55	515		Modicine [Online] 2000;6(7) Available from doi:10.1271/journal.com.d. 1000007
56	3/4		<i>Medicine</i> . [Online] 2009,0(7). Available from: doi:10.15/1/journal.pmed.100009/
57			
58			11
59			11
60			For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

 26. Landis JR, Koch GG, The Measurement of Observer Agreement for Categorical Data. <i>Biometrics.</i> [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 27. McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica.</i> 2012;22(3): 276–282. 28. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A revised tool for assessing risk of bias in non-randomised studies of interventions. <i>BMJ (Online)</i>. [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.14898 29. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-1: A tool for assessing risk of bias in non-randomised studies of interventions. <i>BMJ (Online)</i>. [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.1499 20. Drummond MF, Brien BJ, Torrance GW, Stoddart GL. Methods for the Economic Evaluation of Health Care Programmes 2nd ed. Oxford University Press; 1997. 31. Methods for the development of NICE public health guidance. [Online]. 3rd n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 32. Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. 33. Duval S, Tweedre R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BML</i>. [Online] 2008;36(7635): 924	1			
 Jandis JR, Kolen GG. The Measurement of Observer Agreement for Categorical Data. <i>Biometrics.</i> [Online] 1977;33(1): 159. Available from: doi:10.2307/2529310 McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica.</i> 2012;22(3): 276–282. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. <i>The BMJ</i> [Online] 2019;366(August). Available from: doi:10.1136/bmj.14598 Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-1: A tool for assessing risk of bias in non-randomised studies of interventions. <i>BMJ (Online).</i> [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.14919 Drummond MF, Brien BJ, Torrance GW, Stoddart GL. <i>Methods for the Economic Evaluation of Health Care Programmes.</i>. 2nd ed. Oxford University Press; 1997. <i>Methods for the development of NICE public health guidance.</i> [Online]. 3rd n. National Institute for Clinical Excellence (NICE): 2018. Available from: https://www.nice.org.uk/process/mpd/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweedie R., Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics.</i> [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] Warren LR, Harrison M, Atrox S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>, [Online] BVC Medical Informatics and Sceision Maki	2	275	26	Lendie ID, Kash CC, The Measurement of Observer Assessment for Coteconical Data
 Johnsentes, Johnsen, J. J. J. 197, 197, 197, 197, 197, 197, 197, 197,	4	3/5	26.	Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data.
 Arice Carlos A., Sortan C., Sortan C., Sartan Sarta	5	3/6	27	Biometrics. [Online] $19/7,33(1)$: 159. Available from: doi:10.230//2529310
 JO-282. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. <i>The BMJ</i>. [Online] Sterne JA, Herrain MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-1: A tool for assessing risk of bias in non-randomised studies of interventions. <i>BMJ (Online)</i>. [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.i4919 Drummond MF, Brien BJ, Torrance GW, Stoddart GL. <i>Methods for the Economic Evaluation of Health Care Programmes.</i>. 2nd ed. Oxford University Press; 1997. <i>Methods for the development of NICE public health guidance.</i> [Online]. 3rd n. National Institute for Clinical Excellence (NICE): 2018. Available from: https://www.nice.org.uk/process/mg4/resources/methods-for-the-development-of-nice- public-health.guidance-third-edition-pdf-200767445701 Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple finnel-plot-based method of testing and adjusting for public-tation bias in meta-analysis. <i>Biometrics.</i> [Online] Biometrics Society; 2000;56(2): 455–463. Available from; doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 207 Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADF: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i> [Online] 2008;336(7650); 924–926. Available from: doi:10.1136/bmj.39489.470347.AD Warren I.R, Harrison M, Arora S, Dazri A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical</i> <i>Making</i>; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	6	3//	27.	McHugh ML. Interrater reliability: the kappa statistic. <i>Biochemia medica</i> . 2012;22(3):
 Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. <i>The BMJ</i>. [Online] 2019;366(August). Available from: doi:10.1136/bmj.14898 Sterne JA, Hernán MA, Reves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-1: A tool for assessing risk of bias in non-randomised studies of interventions. <i>BMJ</i> (Online). [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.14919 Drummond MF, Brien BJ, Torrance GW, Stoddart GL. <i>Methods for the Economic Evaluation of Health Care Programmes.</i>. 2nd ed. Oxford University Press; 1997. <i>Methods for the development of NICE public health guidance</i>. [Online]. 3rd n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweccife R. Trim and fill: A simple finnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x. [Accessed: 20th January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(705): 924–926. Available from: doi:10.1136/bmj39489.470347.AD Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;	7	378	• •	2/6-282.
 380 revised tool for assessing risk of bias in randomised trials. <i>The BMJ</i>. [Online] 2019;366(August). Available from: doi:10.1136/bmj.14898 382 29. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-1: A tool for assessing risk of bias in non-randomised studies of interventions. <i>BMJ</i> (Online). [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.14919 385 30. Drummond MF, Brien BJ, Torrance GW, Stoddart GL. <i>Methods for the Economic Evaluation of Health Care Programmes.</i>. 2nd ed. Oxford University Press; 1997. 387 31. <i>Methods for the development of NICE public health guidance</i>. [Online]. 37d n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/mgd/resources/methods-for-the-development-of-nice-public-health-guidance-third-edition-pdf-2007967445701 391 32. Popay, J, Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. 394 33. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from; doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] 398 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falek-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i> [Online] 2008;336(7650); 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 305 Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods dudy. <i>BMC Medical Informatics and Decision Making</i>; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 306 	8	379	28.	Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A
 2019;366(August). Available from: doi:10.1136/bmj.14898 29. Sterne JA, Hernán MA, Reeves BC, Savovi J, Berkman ND, Viswanathan M, et al. ROBINS-1: A tool for assessing risk of bias in non-randomised studies of interventions. <i>BMJ (Online)</i>. [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.14919 30. Drummond MF, Brien BJ, Torrance GW, Stoddart GL. <i>Methods for the Economic Evaluation of Health Care Programmes</i>. 2nd ed. Oxford University Press; 1997. 31. <i>Methods for the development of NICE public health guidance</i>. [Online]. 3rd n. National Institute for Clinical Excellence (NICF); 2018. Available from: https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 32. Popay, J., Robert, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. 334. Guyati GR, Torman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	9	380		revised tool for assessing risk of bias in randomised trials. <i>The BMJ</i> . [Online]
 Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-1: A tool for assossing risk of bias in non-randomised studies of interventions. <i>BMJ (Online)</i>. [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.i4919 Drummond MF, Brien BJ, Torrance GW, Stoddart GL. <i>Methods for the Economic Evaluation of Health Care Programmes.</i> 2nd ed. Oxford University Press; 1997. <i>Methods for the development of NICE public health guidance</i>. [Online]. 3rd n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x. [Accessed: 20th January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650); 924–926. Available from: doi:10.1136/bmj.39489.470347.AD Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	10	381		2019;366(August). Available from: doi:10.1136/bmj.l4898
 ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. <i>BMJ (Online)</i>. [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.i4919 Drummond MF, Brien BJ, Torrance GW, Stoddart GL. <i>Methods for the Ceconomic Evaluation of Health Care Programmes.</i>. 2nd ed. Oxford University Press; 1997. <i>Methods for the development of NICE public health guidance.</i> [Online]. 3rd n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;36(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD Warren I.R, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical</i> <i>Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	11	382	29.	Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al.
 BMJ (Online). [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.i4919 BS 30. Drummond MF, Brien BJ, Torrance GW, Stoddart GL. Methods for the Economic Evaluation of Health Care Programmes 2nd ed. Oxford University Press; 1997. Methods for the development of NICE public health guidance. [Online]. 3rd n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 2014 January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. [Online] 2008;336(7650); 924–926. Available from: doi:10.1136/bmj.3489.470.374.AD Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. BMC Medical Informatics and Decision Making. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	12	383		ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions.
 385 30. Drummond MF, Brien BJ, Torrance GW, Stoddart GL. Methods for the Economic Evaluation of Health Care Programmes 2nd ed. Oxford University Press, 1997. 387 31. Methods for the development of NICE public health guidance. [Online]. 3rd n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/pmg4/resources/methods-for-the-evelopment-of-nice- public-health-guidance-third-edition-pdf-20079674445701 391 32. Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. 394 33. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455-463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] 398 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falek-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650); 924-926. Available from: doi:10.1136/bmj.39489.470347.AD 402 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 	14	384		BMJ (Online). [Online] 2016;355: 4–10. Available from: doi:10.1136/bmj.i4919
 <i>Evaluation of Health Care Programmes.</i>. 2nd ed. Oxford University Press; 1997. <i>Methods for the development of NICE public health guidance.</i> [Online]. 3rd n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple funel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	15	385	30.	Drummond MF, Brien BJ, Torrance GW, Stoddart GL. Methods for the Economic
 Methods for the development of NICE public health guidance. [Online]. 3rd n. National Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nice.org.uk/process/pmd/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 Popay, J., Roberts, H., Sowden, A., Pettierew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	16	386		Evaluation of Health Care Programmes 2nd ed. Oxford University Press; 1997.
 Institute for Clinical Excellence (NICE); 2018. Available from: https://www.nicc.org.uk/process/pmg4/resources/methods-for-the-development-of-nice- public-health-guidance-third-edition-pdf-2007967445701 Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	17	387	31.	Methods for the development of NICE public health guidance. [Online]. 3rd n. National
 389 https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice-public-health-guidance-third-edition-pdf-2007967445701 301 32. Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. 334 33. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] 343 Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 35. Warren LR, Harrison M, Arora S, Dazzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	18	388		Institute for Clinical Excellence (NICE); 2018. Available from:
 public-health-guidance-third-edition-pdf-2007967445701 popay, J., Roberts, H., Sowden, A., Pettierew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 	19	389		https://www.nice.org.uk/process/pmg4/resources/methods-for-the-development-of-nice-
 30. 32. Popay, J., Roberts, H., Sowden, A., Pettierew, M., Arai, L., Rodgers, M., & Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. 33. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650); 924–926. Available from: doi:10.11136/bmj.39489.470347.AD 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 	20	390		public-health-guidance-third-edition-pdf-2007967445701
 Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC methods programme. 2006;(April 2006): 1–92. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 	21	391	32	Ponav I Roberts H Sowden A Petticrew M Arai I. Rodgers M & Duffy S
 Bisker and Construction and the construction of the const	22	392	52.	Guidance on the conduct of narrative synthesis in systematic reviews. A product from the
 375 376 377 378 38. 398 39. 398 31. 399 398 31. 399 398 31. 399 398 31. 399 31. 31. 31. 31. 32. 32. 33. 34. 35. 35. 36. 37. 37. 38. 39. 398 31. 31. 31. 32. 339 34. 34. 35. 34. 35. 34. 35. 34. 35. 34. 35. 34. 35. 35. 36. 37. 37. 38. 39. 31. 31. 31. 32. 33. 34. 35. 35. 36. 37. 37. 37. 38. 39. 39. 39. 30. 30. 31. 32. 33. 34. 35. 35. 36. 37. 37. 37. 38. 38. 39. 30. 30. 31. 31. 32. 33. 33. 34. 35. 35. 36. 37. 37. 37. 38. 39. 39. 30. 30. 31. 32. 33. 34. 35. 35. 36. 37. 37. 38. 39. 39. 30. 30. 31. 32. 33. 34. 35. 35. 36. 37. 37. 38. 38. 39. 39. 30. 30. 31. 32. 33. 34. 35. 35. 36. 37. 37. 38. 39. 39. 39. 30. 30. 31. 32. 33. 34.	25 24	393		ESRC methods programme 2006: (April 2006): 1–92
 394 39. Duval S, tweede K. Hin and JH. A single full terms full end of testing and adjusting for publication bias in meta-analysis. <i>Biometrics</i>. [Online] Biometric Society; 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 20th January 2021] 398 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 402 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 	25	304	22	Duval S. Twoodia P. Trim and fill: A simple funnal plat based method of testing and
adjusting for publication bias in meta-analysis. <i>Biometrics</i> . [Online] Biometric Society, 28 396 2000;56(2): 455–463. Available from: doi:10.1111/j.0006-341X.2000.00455.x [Accessed: 29 397 20th January 2021] 398 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i> . [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 400 401 402 403 an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i> . [Online] BMC Medical Informatics and Decision 38 405 406 407 408 409 401 402 403 404 405 406 406 407 408 409 50 51 52 53 54 55	26	205	55.	adjusting for publication biog in moto analysis. <i>Biometrica</i> [Online] Diametric Society
 396 2000,50(2): 453-465. Available from: doi:10.1111/j.0006-341A.2000.00435.X [Accessed: 20th January 2021] 398 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. 399 GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 400 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 	27	295		2000.56(2): 455, 462, Asiailable from dai:10.1111/j.0006.241X 2000.00455 x [A accessed:
 397 20th Jahuary 2021] 398 34. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. 399 GRADE: an emerging consensus on rating quality of evidence and strength of 400 recommendations. <i>BMJ.</i> [Online] 2008;336(7650): 924–926. Available from: 401 doi:10.1136/bmj.39489.470347.AD 402 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical</i> <i>Informatics and Decision Making.</i> [Online] BMC Medical Informatics and Decision 406 406 407 408 409 409 409 409 406 	28	390		2000,50(2): 455–465. Available from: doi:10.1111/j.0000-541X.2000.00455.x [Accessed:
 398 34. Guyatt GH, Oxman AD, Vist GE, Kunz K, Halck-Y Her Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. <i>BMJ</i>. [Online] 2008;336(7650): 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 402 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 	29	397	2.4	
31 399 GRADE: an emerging consensus on rating quality of evidence and strength of 24 400 recommendations. BMJ. [Online] 2008;336(7650): 924–926. Available from: 34 401 doi:10.1136/bmj.39489.470347.AD 34 402 35. 403 an electronic health record interface: A qualitative mixed-methods study. BMC Medical 37 404 Informatics and Decision Making. [Online] BMC Medical Informatics and Decision 38 405 Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 41 42 44 43 44 44 5 45 6 46 47 47 48 48 49 50 51 51 53 52 53 54 54 55 57	30	398	34.	Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al.
 400 recommendations. <i>BMJ</i>. [Online] 2008;336(7650); 924–926. Available from: doi:10.1136/bmj.39489.470347.AD 402 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical</i> <i>Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 407 408 409 50 51 52 53 54 55 56 	31	399		GRADE: an emerging consensus on rating quality of evidence and strength of
 401 doi:10.1136/bmj.39489.470347.AD 402 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical</i> <i>Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 	32	400		recommendations. <i>BMJ</i> . [Online] 2008;336(7650): 924–926. Available from:
 402 35. Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design an electronic health record interface: A qualitative mixed-methods study. <i>BMC Medical</i> <i>Informatics and Decision Making</i>. [Online] BMC Medical Informatics and Decision Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 	33	401		doi:10.1136/bmj.39489.470347.AD
403 an electronic health record interface: A qualitative mixed-methods study. BMC Medical 37 404 Informatics and Decision Making. [Online] BMC Medical Informatics and Decision 38 405 Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 406 406 41 41 42 43 44 45 46 47 47 48 48 49 50 51 51 52 53 54 54 55	24 25	402	35.	Warren LR, Harrison M, Arora S, Darzi A. Working with patients and the public to design
37 404 Informatics and Decision Making. [Online] BMC Medical Informatics and Decision 38 405 Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 39 406 40 44 42 44 43 44 44 45 46 47 48 49 50 51 51 52 53 54 54 55 56 57	36	403		an electronic health record interface: A qualitative mixed-methods study. BMC Medical
38 405 Making; 2019;19(1): 1–8. Available from: doi:10.1186/s12911-019-0993-7 39 406 40 44 43 44 44 45 46 47 48 49 50 51 51 52 53 54 54 55 56 57	37	404		Informatics and Decision Making. [Online] BMC Medical Informatics and Decision
39 406 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	38	405		Making; 2019;19(1): 1-8. Available from: doi:10.1186/s12911-019-0993-7
40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	39	406		
41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	40			
42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	41			
43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	42			
44 45 46 47 48 49 50 51 52 53 54 55 56 57	43			
45 46 47 48 49 50 51 52 53 54 55 56 57	44			
40 47 48 49 50 51 52 53 54 55 56 57	45 46			
 48 49 50 51 52 53 54 55 56 57 	40 47			
49 50 51 52 53 54 55 56 57	48			
50 51 52 53 54 55 56 57	49			
51 52 53 54 55 56 57	50			
52 53 54 55 56 57	51			
53 54 55 56 57	52			
54 55 56 57	53			
55 56 57	54			
57 57	55			
5/	56 57			
50 10	57 58			10
59	59			12

1 2		
3	407	Authors' contributions
4 5	408	Conception and design of the work: EL ALN and IC wrote the manuscript HA and AD
6	409	provided critical revision of drafts for important intellectual content. All authors provided input
7	410	into drafts of the manuscript and agree on the contents of the final version.
8 9		
10	411	Funding statement
11	412	This research was supported through the Imperial College National Institute for Health Research
12 13	413	(NIHR) Patient Safety Translational Research Centre (PSTRC) and the Imperial College
14	414	Biomedical Research Centre (BRC). JC acknowledges support from the Wellcome Trust
15	415	this protocol
16 17	410	
18	417	Competing Interests
19 20	418	The authors declare that there are no competing interests.
20 21	419	
22	420	Word count: 3886
23	421	
24 25		
26		
27		
28 29		
30		
31		
32 33		
34		
35		
30 37		
38		
39		
40 41		
42		
43		
44 45		
46		
47		
48 49		
50		
51		
52 53		
54		
55		
56 57		
58		13
59		Ear poor roviou oply http://bmiopon.hmi.com/citc/shout/swidelines.uhtml
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xntml

2
2
3
4
5
6
7
/
8
9
10
11
11
12
13
14
15
16
10
17
18
19
20
20
21
22
23
24
27
25
26
27
28
20
29
30
31
32
33
24
54
35
36
37
20
50
39
40
41
42
12
43
44
45
46
47
10
40 40
49
50
51
52
52
53
54
55
56
57
57
58
50

60

Supplement 1: Search strategy exploring main themes, utilizing search terms and related terminology derivations for each theme (electronic health records, interoperability, and patient safety).

#	Searches
1	exp Medical Records Systems, Computerized/ or exp Electronic Health Records/ or exp Hospital Information Systems/
2	limit 1 to (english language and yr="2010 - 2020")
3	exp Electronic Health Records/
4	limit 3 to (english language and yr="2010 - 2020")
5	exp Health Information Exchange/ or exp Medical Informatics/ or exp Decision Support Systems, Clinical/ or exp Medical Records Systems, Computerized/ or exp Medical Record Linkage/
6	limit 5 to (english language and yr="2010 - 2020")
7	exp Medical Informatics/
8	limit 7 to (english language and yr="2010 - 2020")
9	exp Hospital Information Systems/
10	limit 9 to (english language and yr="2010 - 2020")
11	exp Medical Informatics/
12	limit 11 to (english language and yr="2010 - 2020")
13	exp Health Information Interoperability/
14	limit 13 to (english language and yr="2010 - 2020")
15	exp Systems Integration/
16	limit 15 to (english language and yr="2010 - 2020")
17	exp Patient Safety/
18	limit 17 to (english language and yr="2010 - 2020")
19	(Patient adj1 incident*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
20	limit 19 to (english language and yr="2010 - 2020")
21	(Adverse adj1 event*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary

2
3
1
4
5
6
7
8
9
10
10
11
12
13
14
15
16
17
10
18
19
20
21
22
22
22
24
25
26
27
28
29
20
20
31
32
33
34
35
36
27
3/
38
39
40
41
42
12
4-J
44
45
46
47
48
49
50
50 F1
51
52
53
54
55
56
50
5/
58
59

	concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
22	limit 21 to (english language and yr="2010 - 2020")
23	(Patient adj1 outcome*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
24	limit 23 to (english language and yr="2010 - 2020")
25	(Patient adj1 harm).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
26	limit 25 to (english language and yr="2010 - 2020")
27	exp Risk Management/
28	limit 27 to (english language and yr="2010 - 2020")
29	2 or 4 or 6 or 8 or 10 or 12
30	14 or 16
31	18 or 20 or 22 or 24 or 26 or 28
32	29 and 30 and 31
	4

Section and topic	Item No.	Checklist item	Reported of Page No.
ADMINISTRATIV	E INFO	ORMATION	
Title:			
Identification	la	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
INTRODUCTION		06	
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5

alvaia Duotoaola) 2015 abaalvliste vooommandad ita DDIGMA D (Ducf natio • d Mata An ID ... - 14 .

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6-7
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6-7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6-7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6-7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	7
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	-
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6-7
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	7

* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important

clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the

PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.

 From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.