Reporting Transparency and Completeness in Trials: Paper 4 - Reporting of randomised controlled trials conducted using routinely collected electronic records – room for improvement

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What's new?

- This review of publications of randomized controlled trials (RCTs) conducted using electronic health records (EHR) finds that EHR were used in different ways: approximately two-thirds of RCTs used the EHR to identify participants, and three-quarters used the EHR to ascertain the outcomes or as part of delivering the intervention.

- The reporting quality for RCTs conducted using EHRs was assessed using the 2021 CONSORT Extension for RCTs Conducted Using Cohorts and Routinely Collected Data (CONSORT-ROUTINE) checklist; reporting was inadequate for newly developed items specific to EHR trials. Most publications did not accurately describe the EHR used or report on the accuracy (e.g. completeness of record linkage) and validity of trial data (e.g. adjudication for outcomes) derived from the EHR.

- In a sample of EHR trials, reporting quality was also inadequate for key trial components covered by the CONSORT 2010 statement for RCTs, including the description of the trial design, the mechanism for concealing allocation and the source and role of the funder.

- The 2021 CONSORT Extension for RCTs Conducted Using Cohorts and Routinely Collected Data (CONSORT-ROUTINE) checklist will provide a benchmark to help improve and guide complete and transparent reporting.

Abstract

Objective: To describe characteristics of randomised controlled trials (RCTs) conducted using electronic health records (EHRs), including completeness and transparency of reporting assessed against the 2021 CONSORT Extension for RCTs Conducted Using Cohorts and Routinely Collected Data (CONSORT-ROUTINE) criteria.

Study design: MEDLINE and Cochrane Methodology Register were searched for a sample of RCTs published from 2011–2018. Completeness of reporting was assessed in a random sample using a pre-defined coding form.

Results: 183 RCT publications were identified; 122 (67%) used EHRs to identify eligible participants, 139 (76%) used the EHR as part of the intervention and 137 (75%) to ascertain outcomes.

When 60 publications were evaluated against the CONSORT 2010 item and the corresponding extension for the 8 modified items, four items were 'adequately reported' for the majority of trials. Five new reporting items were identified for the CONSORT-ROUTINE extension; when evaluated, one was 'adequately reported', three were reported 'inadequately or not at all', the other 'partially'. There were, however, some encouraging signs with adequate and partial reporting of many important items, including descriptions of trial design, the consent process, outcome ascertainment and interpretation.

Conclusion: Aspects of RCTs using EHRs are sub-optimally reported. Uptake of the CONSORT-ROUTINE Extension may improve reporting.

Running title: Reporting Completeness and Transparency of RCTs using EHRs; Word count: 3,096

1.0 Introduction

Electronic health records (EHR) are digital versions of medical records. Their primary use is clinical documentation of a patient's medical history (1). These data are collected prospectively and can provide a comprehensive longitudinal record of a patient's health. The availability of sequential electronic records provides an opportunity for the secondary use of these data for research purposes. EHR data have been widely used for observational studies and are increasingly being used in randomised controlled trials (RCTs) (2).

Common difficulties encountered when conducting RCTs include slow recruitment (3) and extensive monitoring and regulatory requirements (4) which increase the resources required to complete them. Large-scale RCTs are required to definitively answer research questions by robustly generating precise estimates of treatment effects and harms (5, 6). In response to these challenges, new approaches to conducting RCTs have been developed, including using existing sources of data, such as cohorts and routinely collected data (electronic health records, administrative databases, registries). EHRs offer the opportunity to conduct RCTs efficiently through automatic systems which can identify potential participants, assess their eligibility, record consent, randomise the participants, collect trial data and in some situations, deliver trial interventions (7). These potential gains in efficiency should, in theory, facilitate recruitment from more sites, and include hard to reach patient populations, thus allowing trialists to recruit a greater proportion of eligible patients. Therefore, RCTs using EHRs, particularly those that are closely integrated into care pathways, have the potential to increase efficiency, reduce cost, and generate results that are widely applicable.

The Consolidated Standards of Reporting Trials (CONSORT) 2010 Statement checklist is a 25-item instrument that was established to facilitate transparent and complete reporting of RCTs (8). RCTs published within journals that endorse the CONSORT statement are better reported than those published in journals that do not (9). The CONSORT 2010 statement was designed for parallel-group

trials, and extensions have been created to meet the reporting requirements of other RCT designs (10-12). This review forms part of a larger project developing a CONSORT extension for RCTs conducted using cohorts and routinely collected data (including EHRs, administrative databases and registries) (13). It is not known how well RCTs that use EHRs are reported. The purpose of this review was two-fold; firstly, to describe characteristics of RCTs conducted using EHRs published January 2011–March 2018, subsequent to the publication of the 2010 CONSORT statement (8), and, secondly, to describe the completeness and transparency of reporting of a random subset of trials conducted using EHRs in relation to reporting items developed for the 2021 CONSORT Extension for RCTs Conducted Using Cohorts and Routinely Collected Data (CONSORT-ROUTINE) (14).

2.0 Methods

This review examines reporting in trials using EHR data. The protocol is accessible on open science framework: https://osf.io/p6wa4/.

2.1 Inclusion and exclusion criteria

This review examined a subset of trials conducted using EHRs identified in a scoping review that supported the development of the 2021 CONSORT Extension for RCTs Conducted Using Cohorts and Routinely Collected Data (CONSORT-ROUTINE) (15). Eligible publications reporting RCTs had to either (i) describe using an EHR to identify potentially eligible participants (for further screening), or use the EHR to automatically identify (and facilitate recruitment of eligible) participants; or (ii) describe using an EHR to collect trial process(es) or clinical outcome data; or (iii) describe using the EHR for delivering the intervention (e.g., using clinical decision support systems embedded within the EHR), or any combination of the three uses. Methodological reviews, protocols and commentaries and studies that only assessed cost effectiveness were excluded.

2.2. Search strategy and publication selection

A search was performed to identify publications describing methodology, trial protocols or main publications specifically for RCTs that were conducted using EHRs. Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE and EBM Reviews–Cochrane Methodology Registry (Final issue, third Quarter 2012) were searched from January 2007 to March 2018 (Cochrane Methodology Register up to last update in July 2012). A MEDLINE search strategy was developed by a research librarian (MS) with input from the project team and were peer-reviewed using the Peer Review of the Electronic Search Strategy (PRESS) standard (16). The strategy was then adapted for the Cochrane Library Methodology Register (see Appendix 1 for search strategy). References were imported into Refworks, and duplicates were removed. The references were then imported into the systematic review software DistillerSR (Evidence Partners, Ottawa, Canada, (17)). A coding manual for inclusion and exclusion is available in Appendix 2.

Titles and abstracts were screened independently by two reviewers. A 'liberal accelerated' method (where titles and abstracts are screened by one reviewer and only excluded publications are screened by a second reviewer) was used to identify publications for inclusion for full-text review (18). This was done in random order so that reviewers were blind to whether the other reviewer had already made a decision on any given title and abstract. Full texts were screened independently by two reviewers, and discordances were resolved in consultation with a third reviewer.

2.3 Data extraction

Data were extracted into a pre-defined form using the DistillerSR system. Items extracted from each trial publication included: research question, unit of randomisation (cluster or individual), setting, location, disease of interest, use of EHR in the trial, intervention, type of EHR related interventions, comparator, primary outcome, whether primary outcome was assessed using EHR, country where the

RCT was conducted and the sample size (number of clusters and/or participants randomised) (19). These items are presented for all trials and separately for cluster versus individually randomised RCTs. The initial data extraction was completed by one person and was independently validated by another using the DistillerSR Quality Control function.

Because of the large number of EHR trials identified (183) and for feasibility, a simple random sample of sixty publications of the included full-text publications were evaluated for reporting characteristics; randomisation was performed using the 'random study identifier' function within DistillerSR. A sample size of 60, assuming that 50% of publications exhibit a certain level of reporting, provides a precision (95% confidence interval) of ±13.2%.

2.4 Evaluation of completeness and transparency of reporting

We evaluated the completeness and transparency of all new and modified items included in the 2021 CONSORT Extension for RCTs Conducted Using Cohorts and Routinely Collected Data (CONSORT-ROUTINE) (14). For modified items, we first assessed reporting against the CONSORT 2010 checklist item. Then, we assessed only the modified portion of the item. We did this in order to determine whether any cases of inadequate reporting lacked information specific to the 2021 CONSORT Extension for RCTs Conducted Using Cohorts and Routinely Collected Data (CONSORT-ROUTINE), specifically, or if reporting was inadequate based on CONSORT guidance available at the time of publication.

The reporting of items was categorised into 'adequately reported', 'partially reported', 'inadequately or not reported' and 'not applicable'. A coding manual was devised to ensure objective assessment of reporting (Appendix 3) based upon similar previous reviews (20, 21). The data extraction rules and coding manual were piloted on five publications by four authors to clarify wording and calibrate agreement between reviewers. A second reviewer validated the final assessment of completeness and

transparency of reporting; disagreements were resolved by a third reviewer. Reviewers were not blinded to author or journal names due to lack of evidence that this reduces bias (9, 22).

Results were synthesized by totalling the number and percentage of publications adequately, partially, and inadequately or not at all for each item.

3.0 Results

The database searches identified 2,085 unique titles and abstracts for review, of which 1,537 were excluded after review of titles and abstracts and 365 after full-text review, leaving 183 publications that met inclusion criteria and were included in the description of RCTs using EHRs. Of these, 60 were randomly selected for review of reporting completeness and transparency (See Figure 1 for selection diagram and Appendix 4 for references).

3.1. Characteristics of eligible trial publications

Of the 183 RCT publications included, 122 (67%) reported identifying participants using the EHR, 139 (76%) used the EHR for delivering the intervention and 137 (75%) for outcome ascertainment; 80 (44%) used the EHR to perform all three functions (Figure 2).

Characteristics of the 183 RCTs using EHRs are presented in Table 1. The majority were conducted in North America (N=143, 78%), or set in primary care, accident & emergency or outpatient clinics (N=144, 79%). The most common speciality or thematic of interest was internal or general medicine (N=112, 61%). The most common interventions tested were implementation interventions using guideline or reminder-based interventions (N=87, 48%) to improve evidence based care; in trials where the EHR was used for delivering the intervention, the intervention was most commonly a clinical decision support tool (N=91/139, 65%).

There were 84 cluster RCTs and 99 individually randomised trials. The proportion of RCTs that tested a clinical decision support tool differed between cluster RCTs (59 of 84, 70%) and individually randomised trials (32 of 99, 32%). Overall, the most common outcome was the uptake of a treatment or service (cluster RCT, 36 of 84, 43% versus individually randomised RCT, 29 of 99, 29%). The majority of trials used the EHR to identify the primary outcome (64 of 84, 76%, cluster RCT versus 54 of 99, 55%, individually randomised RCT). For cluster trials that used EHR systems, the median number of participants was 4,447 (interquartile range [IQR] 613–20,904) with a median of 27 clusters (IQR 15–56); for individually randomised trials, the median number of participants was 415 (IQR 123–2,239).

3.2. Baseline assessment of completeness and transparency of reporting

Results for all included trials are available at https://osf.io/zjv7k/.

CONSORT 2010 items with Modifications in CONSORT-ROUTINE

When publications were evaluated against the original version of the eight CONSORT 2010 items that were modified in the extension, four items were 'adequately reported' for the majority of trials, including *Eligibility criteria,* 83%, *Outcome definition,* 73%, *Participant flow,* 75% and *Interpretation,* 80% (Table 2). Only 43%, 28% and 42% 'adequately reported' *structured summary (abstract), Trial design* and *Funding*, respectively. *Allocation concealment mechanism* was the most poorly reported item; 60% reported this 'inadequately or not at all'.

Of the eight items that were extension modifications, four were 'adequately reported' for the majority of trials, including *EHR use in the abstract,* 90%, *Description of trial design,* 85%, *Outcomes,* 68% and *Interpretation,* 52%.

Funding was poorly reported ('inadequately or not at all') in the extension modification *Funding (regarding cohort and routinely collected database),* 73%. Where applicable, the modified item

Eligibility criteria for trial participants (regarding information on codes/algorithms used to identify eligible participants, accuracy etc.) was 'inadequately or not at all' reported in 64% (27 of 42) of cases. Likewise, where applicable, the modified item *Participant flow (enhanced for cohort and routinely collected data)* was 'partially' reported in 48% (19 of 40) of cases. The item *Allocation concealment mechanism* was not coded separately, as the modification was a clarification of the original item.

New items in CONSORT-ROUTINE

Of the five new items that were evaluated, only one was 'adequately reported' for the majority of trials (>50%), *Informed consent* 58%. Three items were poorly ('inadequately or not at all') reported in the majority of trials; these items included *Eligibility (for cohort or routinely collected database),* 92%, *Description of record linkage,* 77% and where applicable, *List of codes, monitoring and adjudication for outcomes*, 79% *(*42 of 53).

The new item *Description of the cohort or routinely collected database* was 'partially reported' in 67% of cases.

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│ 2,085   Unique titles/abstracts          │
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│         potential eligibility            │
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                    │                    │    • Publication on methodological       │
                    │                    │      issues (n=26)                       │
                    │                    │    • Protocol of an RCT (n=106)          │
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│ 183     Publications meeting eligibility │
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│ 60      Publications randomly selected   │
│         to evaluate completeness of      │
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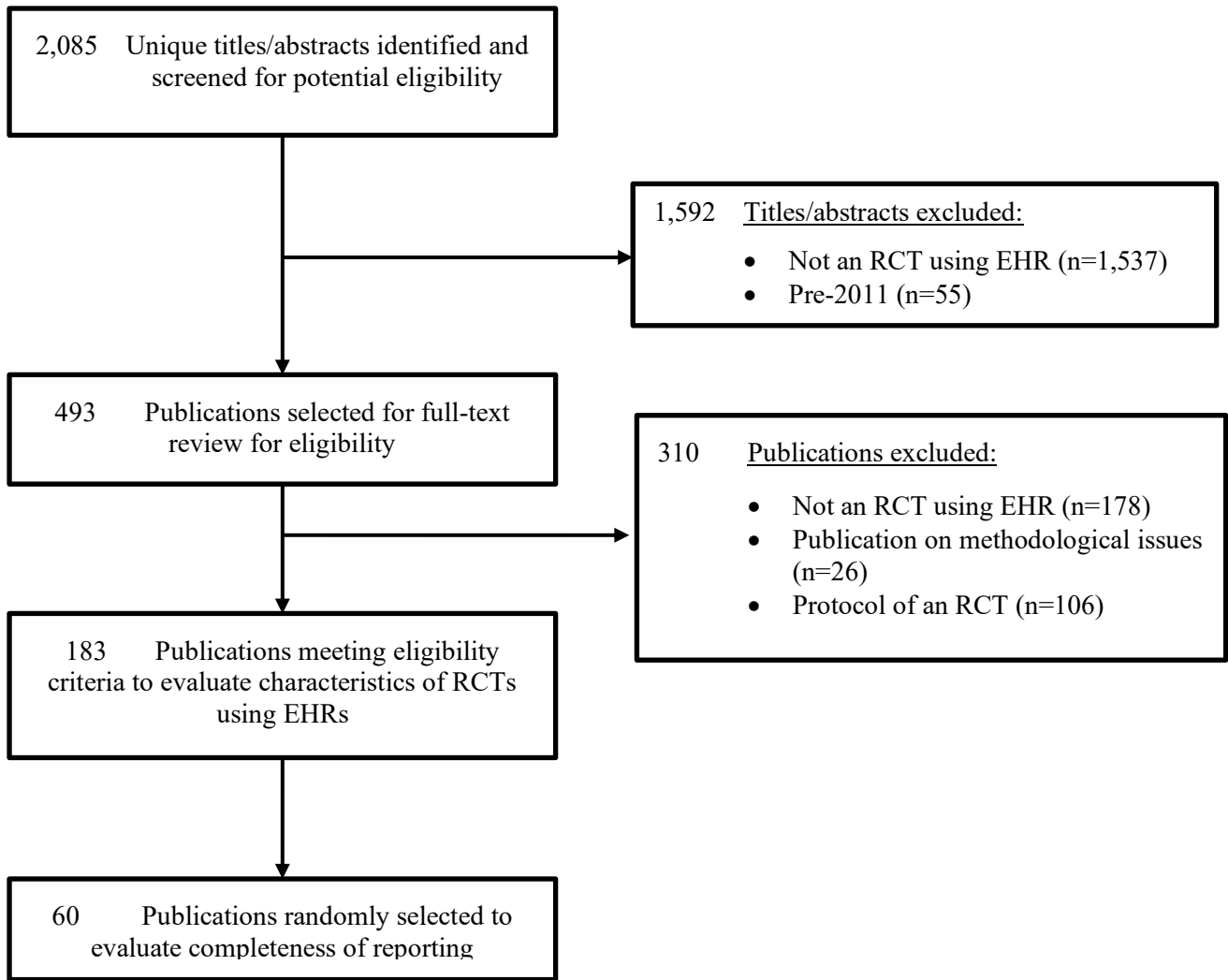
Figure 1. Flow diagram of publication selection process – trials conducted using electronic health records
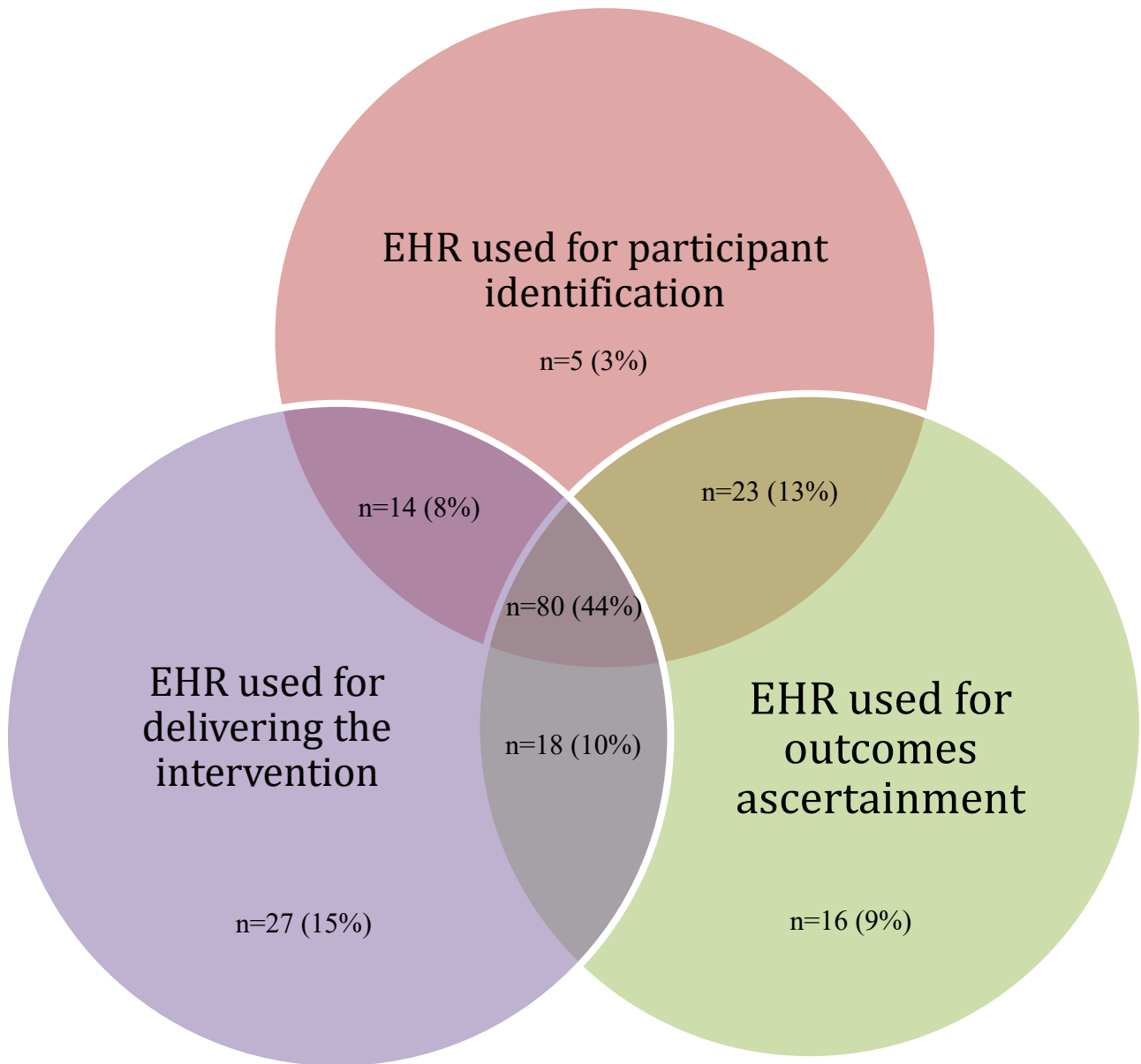
Figure 2. Description of how the electronic health records were used within the total sample of published RCTs meeting eligibility criteria (N=183)

Table 1. Characteristics of trials conducted using electronic health records.

	Number (%) of cluster randomised trials (n=84)		Number (%) of individually randomised trials (n=99)		Total (n=183)	
Setting						
Primary Care, Accident & Emergency or Outpatient	71	(84.5)	73	(73.7)	144	(78.7)
Inpatient	9	(10.7)	16	(16.2)	25	(13.7)
Other	4	(4.8)	10	(10.1)	14	(7.7)
Country						
North America	65	(77.4)	78	(78.8)	143	(78.1)
Europe	18	(21.4)	12	(12.1)	30	(16.4)
Rest of the World	1	(1.2)	9	(9.1)	10	(5.5)
Speciality or Thematic of Interest						
Internal Medicine or General Medicine	53	(63.1)	59	(59.6)	112	(61.2)
Mental Health or Neurology	3	(3.6)	7	(7.1)	10	(5.5)
Vaccinations	8	(9.5)	7	(7.1)	15	(8.2)
Paediatrics	4	(4.8)	8	(8.1)	12	(6.6)
Behavioural Risk Factors*	8	(9.5)	9	(9.1)	17	(9.3)
Other	8	(9.5)	9	(9.1)	17	(9.3)
Intervention						
Guideline or Reminder-based	43	(51.2)	44	(44.4)	87	(47.5)
Other	29	(34.5)	46	(46.5)	75	(41.0)
Screening	12	(14.3)	9	(9.1)	21	(11.5)
Comparator						
Active Comparison Group	12	(14.3)	20	(20.2)	32	(17.5)
Usual care	71	(84.5)	74	(74.7)	145	(79.2)
Placebo	0	(0.0)	1	(1.5)	1	(0.5)
Unclear	1	(1.2)	4	(4)	5	(2.7)
Outcome						
Mortality, Disease Occurrence or Composite	4	(4.8)	5	(5.1)	9	(4.9)
No Primary Outcome	4	(4.8)	12	(12.1)	16	(8.7)
Other	19	(22.6)	14	(14.1)	33	(18.0)
Self-reported	7	(8.3)	22	(22.2)	29	(15.8)
Surrogate	14	(16.7)	17	(17.2)	31	(17.0)
Up Take of Treatment or Service	36	(42.9)	29	(29.3)	65	(35.6)
EHR used for Intervention**						
Clinical Decision Support	59	(70.2)	32	(32.3)	91	(49.7)
EHR not used for Intervention	19	(22.6)	25	(25.3)	44	(24.0)
Other	1	(1.2)	5	(5.1)	6	(3.3)
Personal Health Record	3	(3.6)	20	(20.2)	23	(12.6)
Telehealth	2	(2.4)	17	(17.2)	19	(10.4)
EHR for used for Primary Outcome(s)**						
No/Not Clear	20	(23.8)	45	(45.5)	65	(35.5)
Yes	64	(76.2)	54	(54.5)	118	(64.5)
Sample size						
Number of Clusters (median and IQR)	27	(15-56)				
Number of Participants (median and IQR)	4,447	(613-20,904)	415	(123-2,239)		
Total Number of Participants	2,311,604		302,055			

*Includes: Smoking, obesity, alcohol or opioid use.

**Definitions were adapted from Hemkens and Mc Cord, 2019, CMAJ (7)

Table 2. Completeness and transparency of reporting for 60 trial publications sampled that used the EHR to identify participants and outcomes (includes only new and modified CONSORT 2010 items)[1]

	Item[2]	CONSORT 2010 Items, CONSORT-ROUTINE modifications, and new CONSORT-ROUTINE items	n=60			
			Adequately reported N (%)	Partially reported N (%)	Inadequately or Not reported N (%)	Not applicable N (%)
Title and abstract						
	1b	CONSORT 2010: Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts).	26 (43%)	34 (57%)	0 (0%)	-
		Modified CONSORT-ROUTINE: Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts). **Specify that a cohort or routinely collected data were used to conduct the trial and, if applicable, provide the name of the cohort or routinely collected database(s)**	54 (90%)	6 (10%)	0 (0%)	-
Methods						
Trial design	3a	CONSORT 2010: Description of trial design (such as parallel, factorial) including allocation ratio	17 (28%)	25 (42%)	18 (30%)	-
		Modified CONSORT-ROUTINE: Description of trial design (such as parallel, factorial) including allocation ratio, **that a cohort or routinely collected database(s) was used to conduct the trial (such as electronic health record, registry) and how the data were used within the trial (such as identification of eligible trial participants, trial outcomes)**	51 (85%)	4 (7%)	5 (8%)	-
Cohort or routinely collected database	ROUTINE-1	New CONSORT-ROUTINE: Name, if applicable, and description of the cohort or routinely collected database(s) used to conduct the trial, including information on the setting (such as primary care), locations, and dates, (such as periods of recruitment, follow-up, and data collection)	13 (22%)	40 (67%)	7 (12%)	-
	ROUTINE-2	New CONSORT-ROUTINE: Eligibility criteria for participants in the cohort or routinely collected database(s)	6 (10%)	8 (13%)	46 (77%)	-
	ROUTINE-3	New CONSORT-ROUTINE: State whether the study included person-level, institutional-level, or other data linkage across two or more databases and, if so, linkage techniques and methods used to evaluate completeness and accuracy of linkage	0 (0%)	5 (8%)	55 (92%)	-
Trial participants	4a	CONSORT 2010: Eligibility criteria for participants	50 (83%)	7 (12%)	3 (5%)	-
		Modified CONSORT-ROUTINE: Eligibility criteria for trial participants, **including information on how to access the list of codes and algorithms used to identify eligible participants, information on accuracy and completeness of data used to ascertain eligibility, and methods used to validate accuracy and completeness (e.g., monitoring, adjudication), if applicable**	1 (2%)	14 (23%)	27 (45%)	18 (30%)
	ROUTINE-4	New CONSORT-ROUTINE: Describe whether and how consent was obtained	35 (58%)	6 (10%)	19 (32%)	-
Outcomes	6a	CONSORT 2010: Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	44 (73%)	8 (13%)	8 (13%)	-
		Modified CONSORT-ROUTINE: Completely defined pre-specified primary and secondary outcome measures, including how and when they were ascertained **and the cohort or routinely collected database(s) used to ascertain each outcome**	41 (68%)	8 (13%)	5 (8%)	6 (10%)
	ROUTINE-5	New CONSORT-ROUTINE: Information on how to access the list of codes and algorithms used to define or derive the outcomes from the cohort or routinely collected database(s) used to conduct the trial, information on accuracy and completeness of outcome variables, and methods used to validate	3 (5%)	8 (13%)	42 (70%)	7 (12%)

		accuracy and completeness (e.g., monitoring, adjudication), if applicable				
Allocation concealment mechanism	9	CONSORT 2010: Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned[3] Modified CONSORT-ROUTINE: Mechanism used to implement the random allocation sequence **(such as embedding an automated randomiser within the cohort or routinely collected database(s)),** describing any steps taken to conceal the sequence until interventions were assigned[3]	16 (27%)	8 (13%)	36 (60%)	-
Results						
Participant flow (a diagram is strongly recommended)	13a	CONSORT 2010: For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	45 (75%)	7 (12%)	8 (13%)	-
		Modified CONSORT-ROUTINE: For each group, the number of participants **in the cohort or routinely collected database(s) used to conduct the trial and the numbers screened for eligibility,** randomly assigned, **offered and accepted interventions (e.g., cohort multiple RCTs),** received intended treatment, and analysed for the primary outcome	6 (10%)	19 (32%)	15 (25%)	20 (33%)
Discussion						
Interpretation	22	CONSORT 2010: Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	48 (80%)	11 (18%)	1 (2%)	-
		Modified CONSORT-ROUTINE: Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence, **including the implications of using data that were not collected to answer the trial research questions**	31 (52%)	18 (30%)	11 (18%)	-
Other information						
Funding	25	CONSORT 2010: Sources of funding and other support (such as supply of drugs), role of funders	25 (42%)	29 (48%)	6 (10%)	-
		Modified CONSORT-ROUTINE: Sources of funding and other support **for both the trial and the cohort or routinely collected database(s),** role of funders	3 (5%)	13 (22%)	44 (73%)	-

[1]For modified items, modifications are shown in bold. For those items, only portion modified was evaluated. [2]Item numbers reflect numbers in original 2010 CONSORT checklist that were modified or new items. New items are designated by "ROUTINE". [3]2010 and modified items not rated separately because modification was minor.

4.0 Discussion

Trials use EHRs in different ways, typically to deliver an intervention or to collect data, but also to identify participants; 44% of the trials in our review used the EHR to perform all three functions. In our sample, the majority of RCTs using EHRs were conducted in the United States and in primary care, community or outpatient settings.

When a random sample of 60 publications (out of 183 identified) were compared to the CONSORT 2010 checklist items that had been modified in the 2021 CONSORT Extension for Trials Conducted Using Cohorts or Routinely Collected Data (CONSORT-ROUTINE) (14), only 4 (out of 8) were 'adequately' reported in the majority of publications based on CONSORT 2010 content. This indicates that inadequate reporting precedes the development of the reporting extension. Perhaps most worrying, however, was the finding that the allocation concealment mechanism (item 9) was reported 'inadequately or not at all' in 60% of cases, given the link between allocation concealment (23, 24) with selection bias. Regarding the extension modifications of these 8 items, 4 were assessed as 'adequately' reported and 3 items were poorly reported in the majority of trials. The remaining item was 'partially' reported in nearly half of trials.

For some modified items, the difference between the 2021 extension and 2010 items is marked. For items Structured summary and Trial design, which may overlap, the 2021 extension is reported much better, possibly due to mentioning the source of data. However, the opposite relationship is observed for Participant flow, Interpretation and Funding, which are reported much better for 2010 items, possibly due to a general lack of nuanced reporting of the genre.

When the sample of trials was assessed against new items in the 2021 CONSORT Extension for Trials Conducted Using Cohorts or Routinely Collected Data (CONSORT-ROUTINE), only 1 out of 5 items was 'adequately' reported in the majority of trial publications. Three items were poorly reported, and the remaining item was 'partially' reported in the majority of trials.

Similar reviews were conducted evaluating reporting in trials conducted using registries (25) and administrative datasets (26). For most items, the reporting was much better for such trials than for trials conducted using EHRs. Nevertheless, there is considerable room for improvement in the reporting for these three types of trials conducted using routinely collected data, specifically regarding the broader issues of record linkage, eligibility for the routinely collected database(s), codes and algorithms related to outcome definitions, the allocation concealment mechanism, aspects of participant flow and funding source for the database(s).

The CONSORT checklist is a minimum standard for reporting. Clearly, there are issues specific to the use of routinely collected data that ideally would be reported in greater detail including: a general description of the EHR(s) used; throughput – eligibility and participant flow for the EHR(s) versus the trial population; and for both data quality and completeness - the use of complex codes, algorithms and record linkage.

The poor reporting of these items matters because fundamentally it is difficult to assess the quality of trial conduct if reporting is substandard *per se,* and it is not surprising that new or modified items were not necessarily well reported. But there were also some encouraging signs with adequate and partial reporting of many important items, such as descriptions of trial design, the consent process, outcome ascertainment and interpretation.

The description of the use of the EHR within published RCTs was broadly consistent with a previous descriptive review of such trials (7) where the majority of RCTs used the EHR as part of the intervention and to ascertain outcomes while a smaller proportion of RCTs used the EHR to identify eligible participants. The previous review was a descriptive study of RCTs that used an EHR, whilst our review used more comprehensive review methods, collected additional information on the characteristics of these RCTs and compared them by the level of randomisation (cluster vs. individual), while also evaluating the adequacy of reporting against existing and newly developed reporting standards.

We found that the transparency and completeness of reporting of RCTs conducted using EHRs to be sub-optimal, despite numerous reporting guidelines and publications. In particular, we found ongoing deficiencies in the adequacy of reporting key indicators of trial quality such as the mechanism for allocation concealment, clearly defined outcomes and the role of the funder (9, 11, 22, 27, 28). The randomisation process is fundamental to the integrity of the trial, and if poorly conducted, will increase the chances of a biased result. It is disappointing that such a fundamental component of any RCT is not well reported in these recent EHR based RCTs, despite the existence of evidence and recommendations (8, 27, 29, 30).

This review provides a contemporary benchmark to assess the reporting of new or modified items included in the 2021 CONSORT Extension for Trials Conducted Using Routinely Collected Data (CONSORT-ROUTINE). As this reporting extension was not available at the time these trials were published, we did not expect these items to be particularly well reported. It is completely reasonable that the codes and algorithms used to identify participants or ascertain outcomes (and their completeness and accuracy) including details on record linkage were not well reported in the published EHR trials examined, since these items are not suggested in existing CONSORT reporting guidance or extensions, although they are in the RECORD reporting guidance for observational studies using routinely recorded data, published in 2015 (31). These items are essential to understand the quality of the data (32), particularly the completeness and accuracy which are critical to internal validity and generalisability. Given that RCTs that use EHR data are increasingly common, this review highlights both the importance of transparency and completeness of reporting of specific aspects, and the deficiencies in reporting that exist.

Limitations include that the search may not have identified all published RCTs that used routinely collected data because the search strategy required the indication that electronic health records were involved either in the title, abstract or indexing. As a result, publications using a different term (e.g. RCHD) would not have been included. It is likely that this also resulted in several items being overestimated, since we may have selected examples of better reporting. Secondly, this review also only evaluated the reporting of new or modified items specific to trials conducted using EHRs and the corresponding CONSORT 2010 items.

Therefore, it does not provide any information on more general aspects of trial reporting covered by other (non-modified) items from the CONSORT 2010. Thirdly, we performed an assessment of reporting quality, which is inherently subjective. To minimise this, we performed all extractions systematically, in duplicate, and disagreements were resolved by a third party; but we did not monitor inter-rater agreement.

Conclusion

EHRs are used in a variety of ways to help conduct RCTs. In order to improve the poor quality of reporting of these RCTs, the research community, journal editors, reviewers and funders should endorse and implement adherence to CONSORT 2010, and this 2021 extension for trials conducted using cohorts or routinely collected data. Improved awareness will improve reporting. The CONSORT explanation and elaboration document and checklist for RCTs using cohorts and routinely collected data will be made available on the EQUATOR website and published elsewhere (14).

5.0 Acknowledgements

5.2. Declaration of Competing Interests

All authors have completed the ICJME uniform disclosure form and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years.

5.3 Availability of data and materials

Additional data beyond that reported in the main and supplementary materials can be requested from the corresponding author.

5.4 Author Contributions

Stephen J. McCall: Conceptualization, Protocol development & review, Project administration, Data curation, Formal analysis, Software, Investigation, Methodology, Validation, Writing – original draft.

Mahrukh Imran: Conceptualization, Protocol review, Data curation, Investigation, Methodology, Project administration, Software, Validation, Writing – review & editing.

Lars G. Hemkens: Conceptualization, Protocol review, Methodology, Supervision, Writing – review & editing.

Kimberly McCord: Conceptualization, Data curation, Investigation, Methodology, Validation, Writing – review & editing.

Linda Kwakkenbos: Conceptualization, Protocol review, Data curation, Funding acquisition, Investigation, Methodology, Supervision, Writing – review & editing.

Margaret Sampson: Conceptualization, Methodology, Search, Writing – review & editing.

Sena Jawad: Conceptualization, Data curation, Investigation, Methodology, Validation, Writing – review & editing.

Merrick Zwarenstein: Conceptualization, Methodology, Writing – review & editing.

Clare Relton: Conceptualization, Funding acquisition, Methodology, Writing – review & editing.

Sinéad M. Langan: Conceptualization, Methodology, Writing – review & editing.

David Moher: Conceptualization, Methodology, Writing – review & editing.

Ole Fröbert: Conceptualization, Protocol review, Funding acquisition, Methodology, Writing – review & editing.

Brett D. Thombs: Conceptualization, Protocol development & review, Data curation, Formal analysis, Funding acquisition, Methodology, Supervision, Writing – review & editing.

Chris Gale: Conceptualization, Protocol development & review, Funding acquisition, Methodology, Supervision, Writing – review & editing.

Edmund Juszczak: Conceptualization, Protocol development & review, Funding acquisition, Methodology, Supervision, Writing – review & editing and approval of the manuscript as submitted.

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26.   Imran M, Mc Cord K, McCall S, Kwakkenbos L, Sampson M, Fröbert O, et al. Trials conducted using administrative databases do not adequately report elements related to the use of databases. 2020 Unpublished (Under review).

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7.0 Appendices

Appendix 1. Electronic search strategy

Adapted from published protocol (15). Searches were run in both MEDLINE and Cochrane Methodology Register simultaneously. As an example, in the registries search, lines 1-11 are the MEDLINE search and lines 12-15 are tailored for the Cochrane Methodology Register. The final lines of each search isolate the records from each database, combine them so duplicate records can be removed, then isolate the remaining records so they can be downloaded and imported into Reference Manager using customized import filters.

Searching for RCTs conducted using Electronic Health Records

1. randomized controlled trial.pt.

2. controlled clinical trial.pt.

3. randomi?ed.ab.

4. placebo.ab.

5. randomly.ab.

6. clinical trials as topic.sh.

7. trial.ti.

8. or/1-7

9. exp animals/ not humans.sh.

10. 8 not 9

11. exp Electronic Health Records/

12. (EHR or electronic health record*).ab,kf,ti.

13. (EMR or electronic medical record*).ab,kf,ti.

14. (PHR or personal health record*).ab,kf,ti.

15. (EPR or electronic patient record*).ab,kf,ti.

16. exp Health Records, Personal/

17. or/11-16

18. 10 and 17

19. limit 18 to yr="2007 - 2018"

20. (Electronic health record or electronic health records or EHR).ti,ab,kw.

21. (Electronic medical record or electronic medical records or EMR).ti,ab,kw.

22. (Electronic patient record or electronic patient records or EPR).ti,ab,kw.

23. or/20-22

24. limit 23 to yr="2007 - 2018"

25. 19 use medall

26. 24 use clcmr

27. 25 or 26

28. remove duplicates from 27

29. 28 use medall

30. 28 use clcmr

Appendix 2. Inclusion criteria algorithm

Eligible RCTs have to use EHRs. Publications that report (1) issues related to methods or reporting of EHR-based RCTs, or (2) a protocol from an RCT conducted using EHRs are excluded. If the RCT involved non-human subjects, it is excluded. Only RCTs that use EHRs as a source of data for conducting the trial, including activities such as identifying eligible participants for the trial or as an intervention or collecting trial outcomes, are eligible. To be included in the review, a publication had to meet one of the following criteria:

1. The EHR is used for identifying eligible participants. If the publication describes a trial in which the EHR was used to identify eligible trial participants, it will be included.

2. The EHR can be used as an intervention or component of an intervention, such as alerting physicians to deliver a screening procedure for some patients, and different trial arms may involve different access to EHR functions. If the publication describes an RCT that used the EHR as part of the intervention, it will be included.

3. The EHR is used to ascertain health outcomes. If the publication describes a trial that links to an EHR to ascertain health outcomes, as trial endpoints, it will be included.

Appendix 3. Coding manual for the completeness and transparency of reporting

Section/Topic	Item No.	CONSORT 2010 Item	CONSORT-ROUTINE	Adequately reported	Partially reported	Inadequately or not reported	Not applicable
Title and abstract							
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts). Specify that a cohort or routinely collected data were used to conduct the trial and, if applicable, provide the name of the cohort or routinely collected database(s) (Modified)	Did the authors clearly describe a (1) structured summary of (2) trial design, (3) methods, (4) results, and (5) conclusions Did the authors specify that a cohort or routinely collected data were used to conduct the trial?	Did the authors only report one, two, three or four element(s) of this item and not all five elements of the item? Did the authors describe methods that would typically require routinely collected data for components of the trials but not specify they used routinely collected data?	Did the authors not describe a structured summary of trial design, methods, results and conclusions? Did the authors not specify that routinely collected data were used to conduct the trial?	
Introduction							
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Description of trial design (such as parallel, factorial) including allocation ratio, that a cohort or routinely collected database(s) was used to conduct the trial (such as electronic health record, registry) and how the data were used within the trial (such as identification of eligible trial participants, trial outcomes) (Modified)	Did the authors clearly describe the trial design including allocation ratio? Did the authors clearly mention the (1) routinely collected database(s) that were used within the trial and (2) how the data were used within the trial (i.e. identification of participants, outcome measurement, other)?	All other cases, where applicable. Did the authors only report one element of this item and not both elements of the item?	Did the authors not describe the trial design including allocation ratio? Did the authors not describe the routinely collected database(s) that were used within the trial and not describe how the data were used within the trial (i.e. identification of participants, outcome measurement, other)?	
Cohort or routinely collected data							

	ROUTINE-1		Name, if applicable, and description of the cohort or routinely collected database(s) used to conduct the trial, including information on the setting (such as primary care), locations, and dates, (such as periods of recruitment, follow-up, and data collection) (New)	Did the authors clearly (1) name and (2) describe the routinely collected database(s) and (3) provide information on the setting, locations, and relevant dates (e.g. periods of recruitment, follow-up, and data collection)?	Did the authors only report one or two element(s) of this item and not all three elements of the item?	Did the authors not name and describe the routinely collected database(s) and not provide information on the setting, locations, and relevant dates (e.g. periods of recruitment, follow-up, and data collection)?	
	ROUTINE-2		Eligibility criteria for participants in the cohort or routinely collected database(s) (New)	Did the authors clearly describe the eligibility criteria for the routinely collected database(s)?	All other cases, where applicable.	Did the authors not describe all eligibility criteria for the routinely collected database(s)?	
	ROUTINE-3		State whether the study included person-level, institutional-level, or other data linkage across two or more databases and, if so, linkage techniques and methods used to evaluate completeness and accuracy of linkage (New)	Did the authors clearly state whether the study included (1) person-level, institutional-level, or other data linkage across two or more databases and (2) the methods of linkage and (3) methods used to evaluate completeness and accuracy of linkage?	Did the authors only report one element of this item and not all three elements of the item?	Did the authors not state whether the study included person-level, institutional-level, or other data linkage across two or more databases and not state the methods of linkage and methods used to evaluate completeness and accuracy of linkage?	
Trial participants	4a	Eligibility criteria for participants		Did the authors clearly describe the eligibility for the trial participants?	All other cases, where applicable.	Did the authors not describe all eligibility criteria for the trial participants?	
			Eligibility criteria for trial participants, including information on how to access the list of codes and algorithms used to identify eligible participants, information on accuracy and completeness of data used to ascertain eligibility, and methods used to validate accuracy and completeness (e.g., monitoring, adjudication), if applicable (Modified)	Did the authors provide information on (1) how to access the lists of codes and algorithms used to identify participants, including (2) methods used to assess accuracy and completeness, if applicable?	Did the authors only report one element of this item and not both elements of the item?	Did the authors not provide information on how to access the lists of codes and algorithms used to identify participants, and not provide the methods used to assess accuracy and completeness?	The trial did not use routinely collected data to identify participants
	ROUTINE-4		Describe whether and how consent was obtained (New)	Did the authors describe clearly whether and how consent was obtained?	All other cases, where applicable.	Did the authors not describe whether and how consent was obtained?	
Outcomes	6a	Completely defined pre-specified primary and secondary outcome		Did the authors clearly define the pre-specified primary and secondary	Did the authors only define the pre-specified primary and	Did the authors not define the pre-specified primary and secondary outcome measures	

		measures, including how and when they were assessed		outcome measures, including how and when they were assessed?	secondary outcome measures but <u>not</u> how and when they were assessed, or did they describe how and when outcomes were assessed but not the measures?	<u>and</u> <u>not</u> define how and when they were assessed?	
	ROUTINE-5		Completely defined pre-specified primary and secondary outcome measures, including how and when they were ascertained and the cohort or routinely collected database(s) used to ascertain each outcome (Modified)	Did the authors clearly describe the routinely collected database(s) used to ascertain each outcome?	All other cases, where applicable.	Did the authors <u>not</u> describe the routinely collected database(s) to ascertain each outcome?	The trial did not use routinely collected data to ascertain the outcome
			Information on how to access the list of codes and algorithms used to define or derive the outcomes from the cohort or routinely collected database(s) used to conduct the trial, information on accuracy and completeness of outcome variables, and methods used to validate accuracy and completeness (e.g., monitoring, adjudication), if applicable (New)	Did the authors clearly (1) describe information on how to access the list of codes and algorithms used to define or derive the outcomes from the routinely collected database(s), (2) including methods used to assess accuracy and completeness?	Did the authors only report one element of this item and not both elements of the item?	Did the authors <u>not</u> describe information on how to access the list of codes and algorithms used to define or derive the outcomes from the routinely collected database(s), <u>and</u> <u>not</u> describe the methods used to assess accuracy and completeness?	The trial did not use routinely collected data to ascertain the outcome
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Mechanism used to implement the random allocation sequence (such as embedding an automated randomiser within the cohort or routinely collected database(s)), describing any steps taken to conceal the sequence until interventions were assigned (Modified)	Did the authors clearly describe the mechanism used to implement the random allocation sequence (such as embedding an automated randomiser within the cohort or routinely collected database(s)), describing any steps taken to conceal the sequence until interventions were assigned?	All other cases, where applicable	Did the authors <u>not</u> describe the mechanism used to implement the random allocation sequence (such as embedding an automated randomiser within the cohort or routinely collected database(s)), describing any steps taken to conceal the sequence until interventions were assigned?	
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were		Did the authors define clearly for each group, (1) the number of participants who were randomly assigned, (2) received	Did the authors only report one or two elements of this item and not all three elements of the item or	Did the authors <u>not</u> describe clearly for each group, the number of participants who were randomly assigned, <u>and</u> <u>not</u> received intended	

Section	Item	Original description	Extension description	Yes	Partial	No
		analysed for the primary outcome		intended treatment and (3) were analysed for the primary outcome?	only presented this information for one group?	treatment and not were analysed for the primary outcome?
			For each group, the number of participants in the cohort or routinely collected database(s) used to conduct the trial and the numbers screened for eligibility, randomly assigned, offered and accepted interventions (e.g., cohort multiple RCTs), received intended treatment, and analysed for the primary outcome (Modified)	Did the authors clearly define, for each group, the number of participants in the routinely collected database(s) used to conduct the trial and the numbers screened for eligibility, randomly assigned, received intended treatment, and analysed for the primary outcome?	Did the authors only report some, but not all, elements of this item?	Did the authors not define, for each group, the number of participants in the routinely collected database(s) used to conduct the trial and not define the numbers screened for eligibility, randomly assigned, received intended treatment, and analysed for the primary outcome
Discussion						
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence, including the implications of using data that were not collected to answer the trial research questions (Modified)	Did the authors clearly provide an interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence? Did the authors describe the implications of using data that were not collected to answer the trial research questions? Note: the authors have to report information about the issues of using routine data.	All other cases, where applicable All other cases, where applicable	Did the authors not provide an interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence? Did the authors not describe the implications of using data that were not collected to answer the trial research questions?
Other information						
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Sources of funding and other support for both the trial and the cohort or	Did the authors clearly describe the sources of funding and the role of funders? Did the authors clearly describe the sources of funding for the database(s)	All other cases, where applicable Did the authors only report some, but not	Did the authors not describe the sources of funding and other support for the trial and the role of the funders? Did the authors not describe the sources of funding for routinely collected database(s)

routinely collected database(s), role of funders (Modified)	and trial and the role of the funder of the trial?	all, elements of this item?	and trial and not describe the role of the funder of the trial?	

Appendix 4. References of the 60 RCT publications assessed for completeness and transparency of

reporting

1. Abdel-Kader K, Fischer GS, Li J, Moore CG, Hess R, Unruh ML. Automated clinical reminders for primary care providers in the care of CKD: a small cluster-randomized controlled trial. American Journal of Kidney Diseases. 2011;58:894

2. Adams WG, Phillips BD, Bacic JD, Walsh KE, Shanahan CW, Paasche-Orlow MK. Automated conversation system before pediatric primary care visits: a randomized trial. Pediatrics. 2014;134:e691

3. Amemori M, Virtanen J, Korhonen T, Kinnunen TH, Murtomaa H. Impact of educational intervention on implementation of tobacco counselling among oral health professionals: a cluster-randomized community trial. Community Dentistry & Oral Epidemiology. 2013;41:120

4. Arts DL, bu-Hanna A, Medlock SK, van Weert HC. Effectiveness and usage of a decision support system to improve stroke prevention in general practice: A cluster randomized controlled trial. PLoS ONE. 2017;12:e0170974

5. Awdishu L, Coates CR, Lyddane A, Tran K, Daniels CE, Lee J, et al. The impact of real-time alerting on appropriate prescribing in kidney disease: a cluster randomized controlled trial. Journal of the American Medical Informatics Association. 2016;23:609

6. Beurden van, Anderson P, Akkermans RP, Grol RP, Wensing M, Laurant MG. Involvement of general practitioners in managing alcohol problems: a randomized controlled trial of a tailored improvement programme. Addiction. 2012;107:1601

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8. Carroll AE, Biondich PG, Anand V, Dugan TM, Sheley ME, Xu SZ, et al. Targeted screening for pediatric conditions with the CHICA system. Journal of the American Medical Informatics Association. 2011;18:485

9. Chiche L, Brescianini A, Mancini J, Servy H, Durand JM. Evaluation of a prototype electronic personal health record for patients with idiopathic thrombocytopenic purpura. Patient preference & adherence. 2012;6:725

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14. Enns E, Rhemtulla R, Ewa V, Fruetel K, Holroyd-Leduc JM. A controlled quality improvement trial to reduce the use of physical restraints in older hospitalized adults. Journal of the American Geriatrics Society. 2014;62:541

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