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A technical review of three clinical trials register resources indicates where improvements to the search interfaces are needed

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Abstract

Clinical trials registers form an important part of the search for studies in systematic reviews of intervention effectiveness but the search interfaces and functionality of registers can be challenging to search systematically and resource intensive to search well.

We report a technical review of the search interfaces of three leading trials register resources: ClinicalTrials.gov, the EU Clinical Trials Register and the WHO International Clinical Trials Registers Platform. The technical review used a validated checklist to identify areas where the search interfaces of these trials register resources performed well, where performance was adequate, where performance was poor, and to identify differences between search interfaces.

The review found low overall scores for each of the interfaces (ClinicalTrials.gov

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55/165, the EU Clinical Trials Register 25/165, the WHO International Clinical Trials Registers Platform 32/165). This finding suggests a need for joined-up dialogue between the producers of the registers and researchers who search them via these interfaces. We also set out a series of four proposed changes which might improve the search interfaces.

Trials registers are an invaluable resource in systematic reviews of intervention effectiveness. With the continued growth in systematic reviews, and initiatives such as 'AllTrials', there is an anticipated need for these resources. We conclude that small changes to the search interfaces, and improved dialogue with providers, might improve the future search functionality of these valuable resources.

Background

Clinical trials registers form an important part of the search for studies in systematic reviews of intervention effectiveness.¹⁻⁸ Trials registers can be searched to identify newly registered, on-going, or recently completed but unreported studies (i.e. unpublished studies), and to review registered study protocols, for example, to identify adaptations to the design of a trial or changes to the outcomes measured over-time.^{1,3,4,7-26} They can also provide an alternative source of study data and study results for some studies.

The focus of research to date has been on which trials registers to search for systematic reviews and methods or strategies to search trials registers effectively.^{1,2,4,11,13,16,17,26-33} Whilst these studies indicate that there is value to be found in searching trials registers,^{1,3,4,7-26} the interfaces and functionality can be challenging to search systematically and resource intensive to search well.^{1,11,26,34}

We seek to explore these challenges in this study. Our hypothesis is that the search interfaces of trials registers have not kept pace with the developments seen in commercially available bibliographic databases.^{1,2,11} With initiatives such as 'AllTrials' – which calls 'for all past and present clinical trials to be registered and their full methods and summary results reported'³⁵ - and continued growth in systematic reviews of clinical effectiveness, we question if the search interfaces of trials registers are fit for purpose?

Study aim: The aim of this study is to undertake a technical review of leading trials registers to assess their suitability to identify trials. By technical review, we mean an evaluation of the technical aspects of the search interfaces and functionality of leading trials registers, which a user must navigate to complete a search. This aim is sub-divided into five objectives, namely:

1. to identify areas where the interfaces performed well;
2. to identify areas where the interfaces were adequate;
3. to identify areas where the interfaces performed poorly;
4. to identify differences in scoring across registers; and
5. to establish a list of any issues arising in review.

Methods

Below, we set out how we identified registers for review and the methods of the technical review to address the aim and objectives set out above.

Identifying trials registers for the technical review

Best practice guidance was reviewed to determine which registers were recommended (or simply mentioned) to search when undertaking a systematic review of intervention effectiveness. Eight sources of guidance were reviewed (See Table 1).

TABLE ONE HERE PLEASE

Two trials registers and one platform to search across registers were commonly recommended by almost all of the sources of guidance reviewed (See Table 1). These two registers and one platform were selected for this review on this basis.

The two registers were: ClinicalTrials.gov and the EU Clinical Trials Register. The platform was the WHO International Clinical Trials Registry Platform. The distinction between trials registers and the platform is important. The WHO International Clinical Trials Registry Platform offers access to multiple registers hence its designation as a platform. For ease of reporting, however, the phrase trials register resources is used throughout the rest of this article to refer to all three resources collectively. Table 2 summarises background information on these resources (See Table 2).

Undertaking the technical review

The technical review aimed to review the search interfaces of the trial register resources. To ensure a transparent evaluation across the three interfaces a validated checklist was used. The checklist developed by Bethel and Rogers, to assess the ability of bibliographic database platforms to process complex literature searches for systematic reviews, was chosen on the basis of its currency and relevance to the objectives of this study.³⁶

Bethel and Rogers identified ten basic features which they considered necessary in a bibliographic database interface to undertake and process a literature search for a systematic review. These ten features were: searching (functions), searching (syntax), field codes, controlled vocabulary, display (search), display (records), downloading, search history, performance and other. Within these ten categories, 55 individual criteria were identified as being either essential (n=37) or desirable (n=18).¹ Bethel and Rogers indicated a yes/no decision if a criterion exists or does not exist and then a score of 1-3 is assigned by a researcher to grade each criterion.³⁶

¹ An inaccuracy in the scoring criteria reported in the paper by Bethel and Rogers was identified. It is stated that there are 56 individual criteria (38 essential and 18 desirable) when, in fact, the checklist provided in the paper reports only 55 individual criteria, where 37 are essential and 18 desirable. We have taken the checklist at face-value and so use the 55 individual criteria.

The authors reviewed the Bethel and Rogers checklist, initially with the intention of amending the scoring domains in view of potential differences between database hosts and trials register resources. It was, however, felt that the checklist was suitable for a technical review of the interfaces of both. One amendment was made to the scoring for each question. A score of 0 (zero) was used where a function did not exist in the interfaces. The original checklist gave a score of 1 where an 'interface did not perform the function or was so difficult to find that it was deemed 'ineffective'. We felt that there was a perceptible difference between an interface not performing a function well or being difficult to find **and** the function not existing. It could help interpretation of findings to specifically indicate which functionality does not exist. Our amended scoring, based on Bethel and Rogers, was:

- a score of 0 meant that the interface did not perform the function;
- a score of 1 meant that the function was so difficult to find that it was deemed ineffective;
- a score of 2 meant the interface performed the function, but was not intuitive or confusing terminology was provided; and
- a score of 3 meant the interface performed the function well.

The interfaces were independently reviewed by each author. The authors then met to reconcile scores awarded for each interface (as is common in resolving screening decisions in a systematic review) to produce a final and unified score for each criterion and each interface. We correlated a high total over-all score per interface to be a positive finding and maximal domain scores (3/3) as representing the best possible search experience for a user. Lower scores indicated areas where the user experience might be sup-optimal and might be improved. The unified scores were then used to address the research objectives set out above, namely to quantify areas where interfaces performed well, where performance was adequate, or performance was poor, and to generate areas of difference (disagreement) between scoring across interfaces. This allowed us to address objective five: to establish a list of any issues arising.

Findings

The checklist was applied independently by the authors in October 2019. The lead author used an Apple Macintosh (OS Mojave 10.14.4 using Firefox 68.0.1 (64-bit)) and the second and third authors used PCs (Windows 10 Enterprise using Chrome Version 78 (Official Build) (64-bit)). No issues with the three interfaces were reported at the time of this review and we believed them to be working correctly. The checklist was re-applied by the authors independently in September 2020 prior to submission. Whilst a note on the WHO ICTRP website indicates that a new version of the search interface was expected in late 2020, as late as Jan 2021, we have not been able to access this for testing.^{37,38}

The combined summary results across register resources are reported in Table 3 and the full combined scoring list is reported in Table 4 (See supporting information).

TABLE 3 HERE PLEASE

Below, we set out how the results relate to the objectives set out above. The amended scoring criteria from the Bethel and Rogers paper were used to guide this process (See methods). The scoring criteria rate 3 as the highest score indicating that the interface performed the function well and 0 to indicate that the function did not exist.

Objective 1: areas where the interfaces performed well (unified reviewer score of 3)

Three essential criteria of the checklist scored a unified score of 3 across the interfaces. These were: (2b) Phrase searching, (9d) compatible with major web-browsers and, (10b) results were consistent.

Objective 2: areas where the interfaces were adequate (unified reviewer score of 2)

One essential criterion of the checklist scored a unified score of 2 across the interfaces: (2a) the ability to search using Boolean terms.

There was near agreement between authors (where a criterion received a grade of 2 or 3, meaning it either performed adequately or well) for one criterion: (10a) 'Help facility is easy to locate and informative'.

Objective 3: areas where the interfaces performed poorly (unified reviewer score of 1 or 0)

No criteria received a 1 across all three interfaces, but 26 criteria of the checklist scored 0 because they were unavailable in all three. These 26 universally unavailable criteria largely fell within four domains ('Field codes', 'Controlled vocabulary', 'Display (search)', 'Search history'), with some also in 'Searching (syntax)', 'Display (records)' and 'Performance'.

Objective 4: areas of differences in scoring across interfaces

There were differences for 25 criteria, which largely appear within these domains: 'Searching (functions)', 'Searching (syntax)', 'Display (records)', 'Downloading', 'Performance' and 'Other'. Some of these features were available and scored highly in at least one interface but were unavailable in another (for example, (2i) 'Parenthesis', (6a) 'Option to choose fields to display' and (9b) 'Can handle large numbers of records >1000').

ClinicalTrials.gov scored better than the others for 14 criteria. These include six criteria for which it scored a 3 ((2i) 'Parenthesis', (2j) 'Combining parentheses within strings with Boolean', (6a) 'Option to choose fields to display', (6d) 'Ability to choose records and not lose this choice when you move onto the next page', (6e) 'Can move onto next record when in full record display' and (6f) 'Search term highlighted'), one criterion for which it scored a 2 and seven criteria for which it scored a 1.

The EU Clinical Trials Register scored better than others for three criteria, receiving a score of 2 for each ((2f) 'Left truncation', (2g) 'Single character truncation' and (2h) 'Masking within a word').

The WHO International Clinical Trials Registry Platform scored better than others for two criteria, one for which it was assigned a score of 3 ((2e) 'Right truncation') with the other receiving a score of 1 ((10c) 'Turn off any deduplication').

Objective 5: issues arising in review

The advanced search option in each interface is aimed at narrowing searches, not facilitating more sensitive or more complex searches. Only ClinicalTrials.gov provides an expert search option, but this is not visible unless the user has performed an initial search and then clicks 'Advanced Search' to modify the search. The use of 'expert search' allows for unlimited character entries which means longer, more sensitive searches can be entered, without having to run multiple searches in the basic or advanced search where there are limits to the number of characters which can be entered. ClinicalTrials.gov essentially has three search options; a basic search, an advanced search and an expert search.

Although help guides are provided for each interface (and scored well), they may not be up to date (at our latest check on 15th September 2020, the ClinicalTrials.gov 'How to search' pages were dated as last reviewed during 2017,³⁹ the EU Clinical Trials Register 'How to search' PDF guide was dated 28 April 2014,⁴⁰ and the WHO International Clinical Trials Registry Platform 'Search Tips' pages were undated).⁴¹ One guide included advice that was contradicted by our testing. If two words are entered into the EU Clinical Trials Register search box without using search operators, the AND operator is automatically included. This is contrary to the help guide, which states (in 1.1 Basic search) that the OR operator is the default. ClinicalTrials.gov have planned improvements to their interface and recently sought public involvement.⁴²

Technical issues occur with websites and databases. We noted an issue reported on the homepage of the EU Clinical Trials Register on 20-11-2019, which was still there on 15-01-2020: "We are currently experiencing technical issues with the EU Clinical Trials Register website. Trials which should be in public domain are currently not being shown. Our technical teams are working on it. We apologise for any inconvenience." More recently, in September 2020 we noted the following announcement on the WHO ICTRP homepage: "Due to heavy traffic generated by the COVID-19 outbreak, the ICTRP Search Portal can be slow or not responding. A new search platform will be setup to be able to cope with the high load." Checking the WHO ICTRP in December 2020 during peer review, we found no changes to the search interface. Moreover, we still found the search interface unstable, often being unable to complete test searches.

Discussion

We set out below the discussion section of this study. We discuss the findings of the technical review within the context of relevant evidence before setting out the implications for practice and research and the limitations of the work.

1. Contextualising the findings

The purpose of this study was to critically appraise the search interfaces of the trials register resources. Before we set our findings in context, it is important to acknowledge a number of things which the resources do well which would not be picked up by the checklist. First, they offer free access to trials and trials data. There is evidence that this access to study records is valuable in decision-making contexts and initiatives such as 'AllTrials' continue to highlight the importance of open access to study data. Secondly, they facilitate access to data often with limited resources. As we acknowledge below (see limitations) these resources are not commercial concerns and their ability to make changes which might improve the user experience depends on funding. We acknowledge that this funding is likely constrained. Thirdly, as we find, some of the search functionality available performed well. It should be noted that Bethel and Rogers, in their review of commercial database hosts, also identified shortcomings in the interfaces and search functionality of commercially available bibliographic databases.³⁶

The study finds comparatively low overall scores for each of the interfaces (ClinicalTrials.gov 55/165, the EU Clinical Trials Register 25/165, International Clinical Trials Registry Platform 32/165). This suggests that the interfaces are not entirely adequate to the task of identifying trials generally or for systematic reviews specifically. It would be valuable to explore these findings in greater depth, not only through the agenda set out below, but also in a wider call for joined-up dialogue between the people who provide trials register resources (and maintain/develop their interfaces) and their users.⁴³ A workshop which (re)examined the use of and access to trials within the context of the 'AllTrials initiative' (and for systematic reviews of trials more generally) would seem highly desirable based on the findings of this review. It might be possible to weight the findings from this work by their value for the user as a mechanism to prioritise any future changes.

Whilst the scores were generally poor overall, differences between the interfaces were identified. The functionality available and scoring for ClinicalTrials.gov was on the whole better than either the EU Clinical Trials Register or International Clinical Trials Registry Platform in similar domains. This may indicate that some of the functionality we call for below is technically possible to install since it is – in many cases – already present in ClinicalTrials.gov (and in a few cases in other interfaces).

The differences in scoring between interfaces notwithstanding, it is not, however, the case that ClinicalTrials.gov can be searched exclusively and to the exclusion of the EU Clinical Trials Register and International Clinical Trials Registry Platform.⁴⁴ Studies indicate that it remains necessary to search all three resources to ensure the comprehensive identification of trials.^{11,30,45} It may be necessary for users to spend time familiarising themselves with the search functions of each of the resources each time they search, such is the variability between interfaces and opportunity for error.

2. implications for practice: an agenda for change

The findings for objectives 2-5 suggest a proposed agenda for change. This agenda is nested in prevailing best practice guidance, and the findings of empirical studies, both of which suggest that searching trials register resources is necessary in systematic reviews of intervention effectiveness. It is acknowledged that some of the items called for are available in some of the interfaces but they are not present in all interfaces.

Proposed change 1: updating the help guides for the interfaces

It is suggested that the help guides are revised for currency and comprehensiveness, and that the content reported in these guides is checked for accuracy. As indicated in our findings (objective 5: issues arising), contradictory guidance between the help guide and the findings of this technical review were identified. We note that we took the help guides at face value and that we have not compared them to independent guides⁴⁶ or further tested the 'contact us' functions for any of the resources.

Proposed change 2: improving the ease of searching

The following technical changes are indicated by this review. Some of these changes may already be present in some registers but not all:

- Ability to use right truncation and ability to use parentheses to control the order in which Boolean operators are applied (or clear guidance that this is already possible);
- Introduction of a search history feature. Retention of searches previously run within the same session would allow searchers to build searches and compare searches;
- Short-cut to combining search lines with Boolean operators and the ability to build searches line-by-line. The ability to select and then combine search lines would allow combinations of searches to be run. In many interfaces to bibliographic databases, this functionality is facilitated through the ability to click on the search lines to be run. This could be linked to the introduction of a search history feature;
- Ability to search within specific fields and combine them with Boolean operators. We recognise that study data are not bibliographic in nature, and that there are a greater number of fields in a register compared to a bibliographic database, but there are some fields in these three trials register resources which it may be helpful to search specifically, which would help broaden study identification; and
- Ability to vary how results are displayed (such as having an option to choose fields to display and highlighting of search terms (NB: already available in ClinicalTrials.gov)).

Proposed change 3: downloading

The trials register resources do not present bibliographic data in the form of a structured abstract as is common in the reporting of original articles in bibliographic databases.¹ Instead, study data are reported according to the structural design of the register and each of the interfaces reviewed here exports in slightly different formats with differing amounts of study data.⁴⁷ This potentially makes study selection (i.e. screening) more complicated and less efficient because researchers may need to revert to the resource to obtain the fullest information to accurately screen a study record.²⁷ If there is a delay between study identification and study selection, it is possible that a different version of a study record could be viewed, or error introduced where data were updated.

Development of specific export options to facilitate direct export from trials register resources to bibliographic management tools for screening and study citation would be desirable.⁴⁸ Ideally, this development would happen across the interfaces and with input from the searching and wider research community, so that formats are standardised and data needed for review are highlighted. Data reported in registers would ideally be standardised which may offer efficiencies to registering studies too. The World Health Organization has a trial registration data set which is a 24-point list which is the minimum amount of trial information that must appear in the register in order for a given trial to be considered fully registered.⁴⁹ At the moment, some bibliographic tools (e.g. EndNote) offer an export filter, but it is a crude alternative when compared to comparable exports from bibliographic databases and it is less efficient than a simple export function.^{48,50}

Proposed change 4: researcher account

The ability to save and re-run search strategies, review search history and set alerts on studies of interest from within a password protected user account in the trials register resources themselves, would improve their functionality. The ability to set up auto-alerts on studies of interest, such that when a study record was altered (or updated), an automatic alert e-mail could be sent to alert an author highlighting the need to check a study record would be valuable for transparency and surveillance. Specific detail on what has been changed would be helpful too. RSS (Really Simple Syndication) feeds potentially offer a solution here in ClinicalTrials.gov and the EU Clinical Trials Register, but there is little empirical guidance on using this method in this way.

3. implications for research

Our technical review presented here, and the review by Bethel and Rogers,³⁶ may indicate a need for further technical reviews to source issues and identify an evaluation agenda for resources used in systematic reviews and other forms of evidence syntheses. These types of technical review may locate well with other types of review which examine resource use through the lens of effectiveness. Where effectiveness evaluations examine the effect of using one resource compared to another resource (see for instance, Wright *et al.* (2014) and Levay *et al.* (2016)^{51,52}), a technical review takes a step back to examine how the resources produce their results. Harmonising both types of review might lead to more nuanced understandings of the process of study identification.

Further research might examine the effect and efficiency of searching trials register resources through other interfaces or in other ways. For example, using a Google over-lay search or web-scraping the registers;^{1,50} evaluating the effectiveness and coverage of searching for trials via other resources (e.g. CENTRAL); or more simply by exporting ICTRP records to Excel to search as opposed to searching via the ICTRP interface. Evaluation studies which compared the effectiveness and efficiency of study identification using these methods would represent a valuable contribution to information retrieval research.^{50,53}

We repeat the call for increased and joined-up dialogue between the people who provide trials register resources (and maintain/develop their interfaces) and their users.⁴³ Thinking through how people use these resources and the data within them might benefit both groups.⁴³ For instance, it could help prioritise potential changes to the search interfaces, or be used to identify key data to prioritise for export filters.

4. Limitations

The agenda for change recognises that trials register resources are different to bibliographic databases. Bibliographic databases are – in most cases – commercial concerns which charge for access and so can afford to invest in their searching interfaces. The trials register resources reviewed in this study do not charge a fee to register studies and all rely on limited funding. Researchers may, accordingly, anticipate a more limited range of search functionality. We have attempted to situate the agenda above in this context and the agenda seeks to locate changes with this in mind.

The extent to which the checklist used for this technical review reflects the needs of day-to-day searching is to some extent unclear. The use of this checklist may overstate the importance of some domains reflecting the desire for perfection (or frustrations) of the checklist authors and authors of this study. The checklist could usefully be subject to further validation and use as part of its development. The language used to describe some of the items in the checklist could also usefully be supported by a brief description, since the naming of some domains was not always clear.

Conclusions

The principal finding of this technical review is that the interfaces performed poorly when evaluated using a validated checklist. Our conclusions are two-fold:

First, we set out a proposed, four-stage agenda of possible changes to the three interfaces, based on the findings of this review. This proposal is situated in the acknowledgement that the trials register resources we evaluated are not commercial concerns and they may have limited funding and resources to implement change. Updating the help guides, small technical changes to the searching interfaces, improvement in downloading of data, and the possibility of researcher accounts would improve the scoring seen in this evaluation if it were repeated. We associate higher scores with improved search interfaces to draw these conclusions.

Secondly, we call for further technical reviews and greater collaboration between the people who manage the trials register resources and those who use them. Joined-up discussion and dialogue between all stakeholders seeks to identify proposals for innovation which are situated in the technical possibilities of trials data (as distinct from bibliographic data) and the resources available (principally, funding).

The trials register resources reviewed in this study offer free access to studies and trials data and they are a valuable source of data for researchers and decision makers. With the need for clear reporting of studies and study data they make an

important contribution to evidence synthesis. This technical review aims to contribute to their continuing development and use.

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Authors Contributions

CC identified the need for this study and developed the idea in discussion with RC and EK. CC, RC, and EK contributed equally to the design of the study, independently reviewed the registers, and contributed to the analysis. RC wrote the first draft of the findings section and table 4 and CC wrote the first draft of the rest of the paper. RC and US designed Table 4 and data were compiled by RC with input from CC. All authors then edited, revised, and approved this manuscript prior to submission.

Data availability statement

All data relied upon in the paper is reported in the paper.

Highlights

What is already known

The focus of research to date has been on which trials registers to search for systematic reviews and methods or strategies to search trials registers effectively.^{1,2,4,11,13,16,17,26-33} Whilst these studies indicate that there is value to be found in searching trials registers,^{1,3,4,7-26} the interfaces and functionality can be challenging to search systematically and resource intensive to search well.^{1,26,34} This technical review seeks to evaluate the search interfaces of three leading trials register resources to indicate a possible agenda for change.

What is new

We report the first technical review of three leading trials register resources: ClinicalTrials.gov, the EU Clinical Trials Register and the WHO International Clinical Trials Registry Platform. The technical review used a validated checklist and it reports an evaluation of the technical aspects of the search interfaces and functionality of leading trials register resources, which a user must navigate to complete a search.

Potential impact for RSM readers outside the authors' field

Clinical trials registers form an important part of the search for studies in systematic reviews of intervention effectiveness.¹⁻⁸ With initiatives such as 'AllTrials' – which calls 'for all past and present clinical trials to be registered and their full methods and summary results reported'³⁵ - and the continued growth in systematic reviews of clinical effectiveness, the search interfaces of trials register resources must evolve to meet the needs of researchers and decision-makers but within the scope of their funding. We highlight the need for improved dialogue between the people who provide these resources (and maintain/develop their interfaces) and their users, as well as indicating some changes to the search interfaces.

TABLE 1: GUIDANCE SEARCHED TO IDENTIFY WHICH TRIALS REGISTERS TO REVIEW

Guidance document (version, year of publication)	Trials Register Resource		
	ClinicalTrials.gov	WHO International Clinical Trials Registers Platform	EU Clinical Trials Register
1. Systematic Reviews: CRD's guidance for undertaking reviews in health care (2009) ¹⁰	√	√	X ⁺
2. The Cochrane Handbook (Version 6.0, 2019) ^{6,54}	√	√	√*
3. Institute for Quality and Efficiency in Health Care (IQWiG): General Methods (Version 5.0**, 2017) ⁵⁵	√	√	√
4. Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness. (EUnetHTA, Version 2, 2019) ⁵⁶	√	√	√
5. Searching for studies: a guide to information retrieval for Campbell systematic reviews (Version 1.1, 2017) ⁵⁷	√	√	√
	√*	√*	X**
6. Developing NICE guidelines: the Manual (last updated 17 July 2020) ⁵⁸			

	√	√	X
7. Institute of Medicine: Finding What Works in Health Care: Standards for Systematic Reviews (2011) ⁵			
	√	√	√
8. SuRe Info: Clinical effectiveness (last revised 20 May 2020) ²⁹			

Key: √ = trials register resource is recommended or mentioned in guidance as a resource to search. * Guidance pre-dates existence of the EU Clinical Trials Register (founded in 2011). √* = trials register resource recommended or mentioned in guidance supplement or appendix. X = there are no recommendations for this trials register resource evident in this guidance. ** Version 5 was used as it is available in English. There is a version 6 which is German language only at this time (2020). X** Mentions EudraCT, which is the main database searchable via the EU Clinical Trials Register, but the register as whole is not mentioned.

Abbreviations: CRD = Centre for Reviews and Dissemination; EUnetHTA = European Network for Health Technology Assessment; NICE = National Institute for Health and Care Excellence; SuRe Info = Summarized Research in Information Retrieval for HTA; WHO = World Health Organization.

Table 2: summary of trials register resources*ClinicalTrials.gov*

ClinicalTrials.gov is a web-based registry maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The registry was created in 1997 due to the Food and Drug Administration modernization act of 1997 (FDAMA) which required the US department of Health and Human Services (HHS), through NIH, to establish a registry of clinical trials. In 2007 the registration requirements to ClinicalTrials.gov were amended to ensure more types of trials and additional registration information were registered. ClinicalTrials.gov provides access to information on public and private clinical studies on a range of diseases and conditions for patients, health care professionals, researchers and the public. Studies included on the website are submitted/registered when they begin and the information is updated throughout the study. ClinicalTrials.gov contains studies from 209 countries.⁵⁹

The EU Clinical Trials Register

The EU Clinical Trials Register is owned by the European Medicines Agency and contains studies from interventional clinical trials on medicines from the European Union (EU) or the European Economic Area (EEA). The register was created in 2004. Trials conducted outside of this area are included if they are part of a paediatric investigation plan or they are sponsored by a marketing authorisation holder. It is a primary register in the World Health Organization (WHO) registry network since 2011. The clinical trial information is provided by the company or organisation responsible for the clinical trial. The EU clinical trials Register contains studies from European Union or European Economic Area countries.⁶⁰

The WHO International Clinical Trials Registry Platform

The International Clinical Trials Registry Platform is part of the World Health Organization (WHO) registry network and was created in 2004 following a Ministerial Summit on Health Research. The aim of the WHO registry network is to provide "a network of international clinical trials registers to ensure a single point of access and the unambiguous identification of trials".⁶¹ The International Clinical Trials Registry Platform was created to ensure that a complete view of research is accessible to those involved in health care decision making. The International Clinical Trials Registry Platform publishes the International Clinical Trials Registry Platform search portal and supports the WHO registry network.⁶¹ It also provides access to both ClinicalTrials.gov and the EU Clinical Trials Register.

TABLE 3: RESULTS SUMMARY

	Overall score (of a possible 165)	Essential score (of a possible 111)	Desirable score (of a possible 54)
ClinicalTrials.gov	55	43	12
EU Clinical Trials register	25	19	6
WHO International Clinical Trials	32	29	3

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TABLE 4: COMBINED RESULTS IN FULL

	CRITERION	DEFINITION	ESSENTIAL OR DESIRABLE	CLINICAL TRIALS.GOV (NOTES)	EUCTR (NOTES)	WHO ICTRP(NOTES)
1. SEARCHING (FUNCTIONS)						
1a	Command line searches	Searches that incorporate syntax (e.g. field codes), with search terms in a single search box. Example: diabet*.ti,ab. AND Warwick.in.	E	1 (‘Expert Search’, where command line searches are possible, is not easy to find and is not mentioned in the help pages. It only appears as an option after performing an advanced search and then clicking ‘modify search’.)	0	0
2. SEARCHING (SYNTAX)						
2a	Boolean terms		E	2 (Boolean operators have to be in upper case. The help guide states this, but it is not clear from the search interface (See here .)	2 (Operators have to be in upper case. Automatic insertion of AND between words in the basic search is not clearly explained and is contradicted by the ‘How to search’ guide (2014 version), which states that OR is automatically inserted.)	2 ((Not case sensitive. Care needs to be taken if combining more than one Boolean term in a search because they are automatically combined in the following order of precedence: NOT, AND, OR (see here))

2b	Phrase searching		E	3 (Using quotation marks (See here).	3 (Using quotation marks (See here).	3 (Without quotation marks (see here).
2c	Adjacency terms	Operators which dictate that search terms are next to each other in any order.	E	0	0	0
2d	Proximity terms	Operators which dictate that search terms are near to each other in any order, sometimes within a number of words that can be specified.	E	0	0	0
2e	Right truncation	Symbol at the end of a root word, representing any number of characters. Example: diabet*.	E	0	2 (The asterisk symbol appears to work, but this is not mentioned in 'How to search'.)	3 (Notes in the 'Search tips' pages here : Truncation disables synonym searching Do not use truncation in the middle of a word or phrase (e.g. liv* cancer will not return any hits))

2f	Left truncation	Symbol at the beginning of a word, representing any number of characters. Example: *planned.	D	0	2 (The asterisk symbol appears to work, but this is not mentioned in 'How to search'. Tested: *marked (203) marked (200) unmarked (2) hallmarked (1) marked OR unmarked OR hallmarked (203))	0
2g	Single character truncation	Left-hand or right-hand truncation where the symbol represents a single character.	D	0	2 (The question mark symbol appears to work, but this is not mentioned in 'How to search'. Tested: mark? (37) marke OR marky OR marko OR markt OR marks (37))	0

2h	Masking within a word	Single character truncation within a word. Example: organi*ation to find both organisation and organization.	D	0	2 (The asterisk and question mark symbols appears to work within a word, but this is not mentioned in 'How to search'.)	0 (‘Search tips’ advises not to use truncation in the middle of a word or phrase.)
2i	Parenthesis	e.g. (diabetes diabetic) iodine	E	3	2 (Appears to work, but not mentioned in 'How to search'.)	0 (This feature was available and scored as a 2 in the initial review (October 2019), despite the ‘Search tips’ advising against using parenthesis. Re-checking the scoring prior to publication (September 2020) we found that this feature no longer worked so we revised the scores accordingly.)
2j	Combining parentheses within strings with Boolean	e.g. ((diabetes OR diabetic) AND iodine)	E	3	2 (Appears to work, but not mentioned in 'How to search'.)	0 (This feature was available and scored as a 2 in the initial review (October 2019) , despite the ‘Search tips’ advising against using parenthesis. Re-checking the scoring prior to publication (September 2020) we found that this feature no longer worked so we revised the scores accordingly.)

2k	Combining parentheses within strings with adjacency		E	0	0	0
2l	Combining parentheses within strings with proximity		E	0	0	0
2m	Combining parentheses with single field codes		E	1 (Advanced search facilitates searching in one or more specific fields, but will only combine fields with the AND operator to narrow the search. 'Expert Search' can then be selected to view the search with parentheses and field codes, whereupon the search terms and Boolean operator(s) can be changed.)	0	0

2n	Combining parentheses with multiple field codes		E	1 (As 2m above. More than one field code cannot be used with a single search term. For example, this search in 'Expert Search' works: AREA[ConditionSearch] diabetes AND AREA[InterventionSearch] (metformin AND (rosiglitazone OR pioglitazone)), but this does not: AREA[ConditionSearch] diabetes AND AREA[InterventionSearch][TitleSearch] (metformin AND (rosiglitazone OR pioglitazone)))	0	0
2o	Short cut to combining strings with AND/OR (e.g. OR/1-10)		D	0	0	0
3. FIELD CODES						

3a	Available to use		E	1 (‘Advanced search’ facilitates searching in one or more specific fields, but will only combine fields with the AND operator, which narrows the search. Field codes are only visible (within straight brackets) in ‘Expert Search’ after searching in the equivalent fields in ‘Advanced Search’. No list of field codes is available. See also 2m and 2n above.)	0 (Some fields are available for filtering to narrow the search (e.g. country, phase of trial), but the opportunity to specify other fields, such as title or sponsor, is not available. No list of field codes that can be added directly to the search is provided. See help guide.)	0 (Some fields are available for filtering to narrow the search (e.g. phase of trial) and ‘Advanced Search’ provides the opportunity to specify other fields, such as title, condition and intervention and choose to combine them with the Booleans AND, OR, NOT. However, no list of field codes that can be added directly to the search is provided. It was not possible to re-test this feature in September 2020 Due to heavy traffic generated by the COVID-19 outbreak. The ICTRP Search Portal was slow or it did not respond.)
3b	Easily accessible		D	0	0	0
3c	Ability to combine (e.g. ti,ab)		E	0 (See 2n above.)	0	0 (See notes for 3a in this column above.)

4. CONTROLLED VOCABULARY

4a	Subject headings e.g. MeSH		E	<p style="text-align: center;">2</p> <p>(It is unclear on the search pages where the synonyms in 'Search details' are from. Exploration of the website indicates that record managers are encouraged to select condition terms and keywords from MeSH or another vocabulary, such as SNOMED CT, that has been mapped to MeSH within the Unified Medical Language System (UMLS) Metathesaurus. See section 6 of https://prsinfo.clinicaltrials.gov/definitions.html)</p> <p>When you enter a search term, mapping to synonyms occurs. It is not possible to switch this off or select which synonyms to include.</p> <p>In order to search using a specific controlled vocabulary term, you would first need to identify the term from the 'See studies by topic' pages or an external source (e.g. MeSH browser https://meshb.nlm.nih.gov/search).</p>	<p style="text-align: center;">0</p> <p>(Automatically searches for synonyms using a thesaurus, but these terms are not visible in the search. It is stated under the 'What's New' page that this thesaurus searching uses health and biomedical terms and other data provided in the Unified Medical Language System (UMLS) Metathesaurus.)</p>	<p style="text-align: center;">2</p> <p>(Synonyms: The standard and advanced search interfaces automatically look for trial records containing synonyms (unless truncation is used) of search words or phrases using the UMLS metathesaurus http://www.nlm.nih.gov/research/umls (description: Metathesaurus: Terms and codes from many vocabularies, including CPT®, ICD-10-CM, LOINC®, MeSH®, RxNorm, and SNOMED CT®)</p> <p>It is possible to switch this off, but not to select which synonyms to include.</p> <p>In order to search using a specific controlled vocabulary term, you would first need to identify the term from an external source (e.g. MeSH browser https://meshb.nlm.nih.gov/search). After running a search in the basic search form, the results are displayed and a link to 'Display Synonyms' is visible. When re-testing prior to publication (September 2020) this function was not working in Google Chrome, Firefox or IE even after the website had been added to the list of allowed sites.)</p>
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4b	Thesaurus available (displayed in hierarchy)		E	1 (‘See studies by topic’ provides a way of finding results for particular conditions, drug interventions and dietary supplements. It is possible to view topic terms by category, with two levels in the hierarchy. Click on a term in the lower level and you are presented with results. It is not possible to select more than one term.)	0	0
4c	Ability to choose multiple terms from the thesaurus		D	0	0	0
4d	Ability to combine controlled vocabulary terms with free- text		E	1 (You would first need to identify controlled vocabulary terms.)	0	0
4e	Ability to explode headings		E	0	0	0

4f	Ability to choose a narrower term		E	0 (You can only choose terms from one level (the second level))	0	0
4g	Scope note available		E	0	0	0
5. DISPLAY (SEARCH)						
5a	Option to view search history while using search screen	Search history means all searches from a session including previous iterations of the current search.	E	0 (In 'Advanced Search' and 'Expert Search', the current search is presented above the search form. In basic search it is presented below the search form. Search concepts are divided with a downward line (i.e.) indicating the Boolean 'AND'. The full search history is not available.)	0 (The current search is presented at the top of the page and the top of the results. The full search history is not available.)	0 (The current search (but without filters) is only presented at the top of the results. On clicking 'Back to Search', the current terms are present in the search boxes. The full search history is not available.)
5b	Build up searches line- by- line with the number of hits visible for each string		E	0	0	0

5c	Ability to edit previous lines of search as it develops		D	0	0	0
5d	Ability to insert new lines of search into existing search		D	0	0	0
5e	Ability to move search lines around within search		D	0	0	0
5f	Combine searches (with Boolean?)		E	0	0	0
5g	Renumber searches after deletion		D	0	0	0

5h	Refine search by update code		D	0	0	0
6. DISPLAY (RECORDS)						
6a	Option to choose fields to display		D	3 (This option is called 'Show and hide columns'. See here: customize your search results display.)	0 (It is not possible to select fields individually. 'Summary view' is displayed with selected fields. It is possible to see a detailed view with more fields for each named country by clicking on 'the Country ISO code'.)	0 (It is not possible to select fields individually. The results list is displayed with 6 fields. It is possible to see a detailed view with more fields for each record by clicking on its title.)
6b	Option to change the number of hits viewed per page		E	3	0 (20 per page)	3

6c	Option to view search history on record display screen	Search history means all searches from a session including previous iterations of the current search.	E	0 (The search that retrieved the displayed results, and any filters applied, can be viewed above the results display. Search concepts are divided with a downward line (i.e.) indicating the boolean 'AND'. Filters applied are shown below the search terms and above the results display, and there is also an option to show them along with other filters to the left of the results to enable easy modification of the filters. The full search history is not available.)	0 (The search that retrieved the displayed results is visible above the results display at the top of the screen. If filters are applied, these are visible above the results. The full search history is not available.)	0 (The search that retrieved the displayed results (without the filters) is visible above the results display at the top of the screen. The option to also display the synonyms is available but this was not working when we re-tested prior to publication (September 2020). The full search history is not available.)
6d	Ability to choose records and not lose this choice when you move onto the next page		E	3	0 (Under 'Download Options', if 'Selected Trials only' is clicked, check boxes to select trials appear, but any selections are lost when you move to the next page.)	0 (Tick boxes only become available after clicking on Export results to XML.)
6e	Can move onto next record when in full record display		D	3	0	0 (Record opens in a new window.)

6f	Search term highlighted		D	3 (See here: search term highlighting.)	0	0
7. DOWNLOADING						
7a	Select all results from complete set of records rather than page- by- page		E	3	0 (Limited to 'Trials shown on current page' (20 records).)	3
7b	Able to download large numbers of records (500+) in one go		D	3 (Plain text, Tab-separated, Comma-separated and XML (maximum 10,000). PDF (maximum 100).)	0 (Only available for trials with a EudraCT protocol. See help guide.)	3 (Export to CSV or XML.)
7c	A wide choice of export/ download options		E	2 (5 options, but no automatic import option, RIS option or clear instructions specifically for importing bibliographic information into reference management software.)	0 (Only plain text.)	0 (Only CSV or XML.)

8. SEARCH HISTORY						
8a	Can save search history	Search history means all searches from a session including previous iterations of the current search.	E	0	0	0
8b	Can share saved searched		D	0	0	0
8c	Export search history		D	0	0	0
8d	Edit saved searches		D	0	0	0

8e	Re- run saved searches		E	0 (Whilst it is not possible to save and re-run either the current search or the whole search history within the resource, advice is given in the Help pages on how to create an RSS feed for a specific search or use your browser bookmarks/favourites to save and revisit a specific search.)	0 (Whilst it is not possible to save and re-run either the current search or the whole search history within the resource, it is possible to create an RSS feed for a specific search or use your browser bookmarks/favourites to save and revisit a specific search.)	0
9. PERFORMANCE						
9a	Can handle long and complex searches, >50 lines long		E	0	0	0
9b	Can handle large numbers of records >1000		E	3	0 (Each download can be for no more than 20 records.)	3

9c	Is compatible with major reference management systems		E	1 (No automatic import option, RIS option or clear instructions specifically for importing bibliographic information into reference management software. However, this is possible for EndNote by downloading results in plain text, saving the file and then using EndNote (with the ClinicalTrials import filter) to import it.)	0	0
9d	Compatible with major web browsers: IE, Firefox and Google Chrome		E	3 (Tested running searches on IE and Google Chrome.)	3 (Tested on IE and Google Chrome)	3 (Tested on IE and Google Chrome. The site is unstable and 'crashes' frequently.)
10. OTHER						
10a	Help facility is easy to locate and informative		E	3	2 (Lack of information about some features (for example, truncation and use of parentheses), which appear to work.)	3

10b	Results are consistent		E	3 (Not systematically tested, but not noticed inconsistencies in previous experience.)	3 (Tested the same search on three days and got the same number of results. Also, we have not noticed inconsistencies in previous searches.)	3 (Not systematically tested, but not noticed inconsistencies in previous experience.)
10c	Turn off any deduplication		E	0	0	1 (Duplicate entries for a trial in different registries are grouped by matching the main trial identifier to secondary trial identifiers found in other trial records. See here. When downloading, only the main record is exported.)
	Overall score (of a possible 165)			55	25	32
	Essential score (of a possible 111)			43	19	29
	Desirable score (of a possible 54)			12	6	3

Abbreviations: EUCTR, the EU Clinical Trials Register; WHO ICTRP, the WHO international Clinical Trials Registers Platform;

Notes: Checklist taken from Bethel and Rogers ³⁶