

Clinical Trial Transparency at European Universities

Mapping unreported drug trials

30 April 2019

Bristol (UK), Bielefeld (Germany), Brussels (Belgium) & Amsterdam (NL)

“We advocate full transparency of which clinical trials are ongoing and ensuring all results are disclosed in a timely manner in accordance with the WHO Joint Statement on disclosure of results from clinical trials. This is consistent with the principal goal of medical research: to serve the betterment of humanity. In the case of clinical trials, full transparency on results advances both scientific understanding and timelines for product development and ultimately enables access to essential medicines.”

- Dr Tedros Adhanom Ghebreyesus, Director-General, [World Health Organisation](https://www.who.int/)

“Lack of transparency in clinical trials harms patients. The timely posting of summary results is an ethical and scientific obligation.”

- [Transparency International and Cochrane](https://www.transparencyinternational.org/)



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1 KEY FINDINGS AND RECOMMENDATIONS

Obligation to report the results of all trials

Failure to report clinical trial results is not a victimless crime. It has substantial negative consequences for patients and public health.

Since July 2014, [European Union rules](#) have required each and every clinical trial registered on the EU clinical trials registry to post summary results onto the registry within 12 months of trial completion (6 months for paediatric trials). These rules also apply to trials completed before 2014, and apply irrespective of whether a trial's outcomes have been published in the academic literature. Thus, all of the clinical trials identified in this report as missing summary results are in violation of European Union transparency rules that were designed to protect the interests of patients and taxpayers.

Key findings

Overall, 778 clinical trials run by 30 European universities (83% of due trials) are verifiably missing results on the European trial registry, in violation of EU transparency rules. Excluding UK universities, reporting rates are just 7%. The actual figure of due trials missing results is likely to be far higher.

- Only three universities perform well: University of Oxford, University College London, and King's College London. These universities have already posted over 80% of their trial results.
- Fourteen universities have failed to post a single clinical trial result. This includes all assessed universities in France, Italy, Norway and Sweden.
- The remaining 13 universities also perform weakly, with reporting rates ranging from 2-33%.

The fact that UK universities outperform their European peers by a wide margin is due to a [combination of pressure](#) from parliament, research funders, and the public. The strong performance by front-runner universities in the UK demonstrates that universities elsewhere in Europe can – and can be expected to – do far better.

Recommendations

- **UNIVERSITIES should post the summary results of all their clinical trials – past, present, and future – onto all registries where these trials are listed.** For ongoing and future trials, universities should post results within 12 months of their primary completion date. Furthermore, universities should sign up to the [WHO Joint Statement](#) and adopt the transparency policies set out therein.
- **NATIONAL MEDICINES REGULATORS** should review all trials that are listed as “ongoing” and update their status to “completed” if applicable. (See Annex III.)
- **NATIONAL RESEARCH FUNDERS** should sign up to the WHO Joint Statement to protect patients and prevent medical research financed by taxpayers from going to waste.
- **NATIONAL GOVERNMENTS** should put into place systems to monitor whether clinical trials conducted within their jurisdiction are posting their summary results onto public registries within 12 months, as per WHO best practices, and impose sanctions on trial sponsors who fail to make results public within that deadline. ([The UK is currently preparing to do this.](#))

2 REPORTING PERFORMANCE BY COUNTRY

This report assesses the reporting performance of the 30 European universities that have sponsored the largest number of clinical trials governed by the incoming EU Clinical Trials Regulation. Together, these universities have sponsored 4,575 clinical trials. Results are verifiably due for 940 of these trials. However, only 162 of verifiably due trials (17%) have made their results public on the EU Clinical Trials Register. The remaining 778 trials (83%) are in violation of EU transparency rules.

Most of the 778 clinical trials verifiably missing results were run by universities in Denmark (246 trials), Austria (225), and Germany (117).

None of the assessed universities in France, Italy, Norway and Sweden have made a single clinical trial result public on the registry. Some universities in Belgium, Germany and the Netherlands have also not posted results for any of their clinical trials. Only some UK universities perform well, with some institutions now boasting reporting rates of over 80%.

Excluding UK universities, the average reporting rate across Europe is just 7%, even lower than the [11% reporting rate](#) researchers found for European universities in September 2018. Outside the UK, 730 out of 785 verifiably due trials (93%) are currently missing results.

Country	Universities assessed	VERIFIABLY DUE TRIALS			
		Total due	With results	Missing results	Reported
Austria	2	244	19	225	7.9%
Belgium	3	51	2	49	3.9%
Denmark	3	273	27	246	9.9%
Finland	1	13	2	11	15.4%
France	2	17	0	17	0%
Germany	3	120	3	117	2.5%
Italy	3	18	0	18	0%
Netherlands	6	23	2	21	8.7%
Norway	1	2	0	2	0%
Sweden	1	24	0	24	0%
United Kingdom	5	155	107	48	69.0%
Total	30	940	162	778	17.2%

The figures above are likely to significantly underestimate the true amount of clinical trials missing results in violation of EU rules. This is because many trials listed as “ongoing” on the European trial registry were in fact completed long ago. For example, universities in the Netherlands have run 967 trials in total, but only 23 of those (2.4%) are marked as “completed”. This number is completely implausible, as registry records show that many of those trials started over five years ago. (In the UK, where a registry update is ongoing, the proportion of “completed” trials in the cohort is 27.4%.)

Under the current reporting system, universities directly upload their summary results onto the EU registry – as trial sponsors, they are legally obliged to do this and the process is fully within their own control. However, universities cannot directly update the status (ongoing/completed) of their trials. Instead, they must notify their [national medicines regulator](#) when a trial is completed, and the regulator then updates the trial’s status on the registry to “completed”. In countries with implausibly low proportions of “completed” trials, such as the Netherlands, national regulators have very likely failed to update a large number of registry entries after trials were completed. These regulators should follow the positive example of the UK’s regulator, the MHRA, and systematically review and update the status of all clinical trials that have been conducted in their country. (See Annex III.)

3 REPORTING PERFORMANCE BY UNIVERSITY

Trial sponsor	Country	Total trials listed	VERIFIABLY DUE TRIALS				Link to results
			Total due	With results	Missing results	Reported %	
Copenhagen University and Hospital	Denmark	447	175	14	161	8%	http://eu.trialtracker.net/sponsor/copenhagen-university-and-hospitals
Medical University of Vienna	Austria	375	188	14	174	7%	http://eu.trialtracker.net/sponsor/medical-university-of-vienna
Hospitals of Paris (AP-HP)	France	229	8	0	8	0%	http://eu.trialtracker.net/sponsor/hospitals-of-paris-ap-hp
KU Leuven	Belgium	226	16	2	14	13%	http://eu.trialtracker.net/sponsor/ku-leuven
Karolinska Institutet	Sweden	205	24	0	24	0%	http://eu.trialtracker.net/sponsor/karolinska-institutet
Radboud University	Netherlands	198	3	1	2	33%	http://eu.trialtracker.net/sponsor/radboud-university
Charité-Universitätsmedizin Berlin	Germany	189	66	1	65	2%	http://eu.trialtracker.net/sponsor/charite-universitatsmedizin-berlin
Erasmus University	Netherlands	178	3	0	3	0%	http://eu.trialtracker.net/sponsor/erasmus-university
University of Amsterdam	Netherlands	175	5	0	5	0%	http://eu.trialtracker.net/sponsor/university-of-amsterdam
Aarhus University	Denmark	151	63	11	52	18%	http://eu.trialtracker.net/sponsor/aarhus-university
Agostino Gemelli University Poly	Italy	148	11	0	11	0%	http://eu.trialtracker.net/sponsor/agostino-gemelli-university-polyclinic
VU University Medical Centre	Netherlands	141	4	0	4	0%	http://eu.trialtracker.net/sponsor/vu-university-medical-centre
Leiden University	Netherlands	139	1	0	1	0%	http://eu.trialtracker.net/sponsor/leiden-university
Utrecht University	Netherlands	136	7	1	6	14%	http://eu.trialtracker.net/sponsor/utrecht-university
Ghent University	Belgium	133	29	0	29	0%	http://eu.trialtracker.net/sponsor/ghent-university
University of Oxford	UK	129	29	27	2	93%	http://eu.trialtracker.net/sponsor/university-of-oxford
University College London	UK	126	32	26	6	81%	http://eu.trialtracker.net/sponsor/university-college-london
AOU di Bologna, P.S. Orsola-Malp.	Italy	125	1	0	1	0%	http://eu.trialtracker.net/sponsor/aou-di-bologna-policlinico-sorsola-malpighi
Imperial College London	UK	124	32	8	24	25%	http://eu.trialtracker.net/sponsor/imperial-college-london
Medical University of Graz	Austria	112	56	5	51	9%	http://eu.trialtracker.net/sponsor/medical-university-of-graz
Helsinki University	Finland	106	13	2	11	15%	http://eu.trialtracker.net/sponsor/helsinki-university
Odense University Hospital	Denmark	96	35	2	33	6%	http://eu.trialtracker.net/sponsor/odense-university-hospital
King's College London	UK	95	43	40	3	93%	http://eu.trialtracker.net/sponsor/kings-college-london
University of Birmingham	UK	92	19	6	13	32%	http://eu.trialtracker.net/sponsor/university-of-birmingham
Université libre de Bruxelles	Belgium	90	6	0	6	0%	http://eu.trialtracker.net/sponsor/universite-libre-de-bruxelles
Hospices Civils de Lyon	France	88	9	0	9	0%	http://eu.trialtracker.net/sponsor/hospices-civils-de-lyon
Heidelberg University	Germany	86	23	0	23	0%	http://eu.trialtracker.net/sponsor/heidelberg-university
Vita-Salute San Raffaele University	Italy	84	6	0	6	0%	http://eu.trialtracker.net/sponsor/vita-salute-san-raffaele-university
University of Oslo	Norway	79	2	0	2	0%	http://eu.trialtracker.net/sponsor/university-of-oslo
University of Munich (Ludwig Max.)	Germany	73	31	2	29	7%	http://eu.trialtracker.net/sponsor/university-of-munich-ludwig-maximilians
TOTAL		4,575	940	162	778	Avg. 17%	http://eu.trialtracker.net/

Data extracted from the EU Clinical Trials Register via the EU Trials Tracker. Accurate as of 01 April 2019.

4 WHY DO UK UNIVERSITIES PERFORM BETTER THAN THEIR PEERS?

On average, UK universities perform far better than their peers in other countries. The weakest of the five assessed UK universities has a reporting rate of just 25%, and the two strongest performers - University of Oxford and King's College London – have already reported over 90% of trial results. In contrast, with one exception, not a single university assessed in mainland Europe has a reporting rate of more than 20%.

UK universities have become European leaders in transparency due to pressure from parliament, research funders, and the public.

- **Parliamentary pressure:** The Science and Technology Committee of UK parliament held an enquiry into research integrity during 2018-2019. Committee members were shocked to discover that many universities were routinely violating transparency rules. In early 2019, the Chairman of the Committee [wrote to all UK universities](#) warning them that if they did not upload the missing trial results by summer 2019, they would be called before the Committee to explain themselves.
- **Pressure from research funders:** Britain's two public medical research funding bodies, the NIHR and the MRC, as well as the non-profit Wellcome Trust, in 2017 all signed the [WHO Joint Statement on Public Disclosure of Results from Clinical Trials](#). By signing up, these funders committed themselves to adopting policies on trial registration and trial reporting that are in line with WHO best practices, and monitoring their grantees' compliance with these rules. (The MRC has already conducted an [excellent review](#) of the clinical trials it had funded.) In coming years, UK universities that fail to post the results of trials onto registries on time may not be able to receive further research funding.

Public pressure: A loose coalition of health integrity groups convened by TranspariMED that included Universities Allied for Essential Medicines (UAEM-UK), HealthWatch UK, Transparency International Health, and STOPAIDS engaged with parliament, the media and directly with universities to press for better trial reporting. TranspariMED and UAEM-UK also published [several reports documenting the performance of individual UK universities](#). In parallel, the [AllTrials campaign](#), which focuses mainly on the UK, strongly campaigned on the issue, including by regularly emailing its over 90,000 supporters. The [EBM Data Lab](#) at the University of Oxford, which is linked to the AllTrials campaign (and which built the EU Trials Tracker this report's data is drawn from), directly supplied the parliamentary Committee with data on individual universities' performance.

This pressure has had a huge impact on reporting rates by UK universities. For example, King's College London improved its reporting rate from 18% to 93% within only half a year. The University of Nottingham, singled out by the parliamentary Committee for its weak performance in 2018, has by now posted the summary results of over 95% of its trials. As far as TranspariMED is aware, every single medical university in the UK is currently working hard to upload missing clinical trial results onto the EU registry, and in [many cases](#) onto other registries such as ISRCTN and the US registry Clinicaltrials.gov as well. This demonstrates that where there is a will, there is a way – other universities in Europe too can solve this problem if they decide to do so. (See Annex II.)

The UK government is now working to put into place a [comprehensive national clinical trial monitoring system](#) that will track every single clinical trial conducted on UK soil – including commercial trials and multi-country trials – to ensure that it is registered and reports its results.

5 WHY THIS MATTERS

Relevance to public health and clinical practice

Failure to report clinical trial results is not a victimless crime. A 2017 [report](#) by Transparency International and Cochrane documents that a failure to fully report trial results has substantial negative consequences:

- Patients are harmed
- Public health agencies cannot make informed decisions
- Public health funds are wasted
- Medical progress is slowed down

Legal and regulatory framework

Since July 2014, [European Union rules](#) have required the summary results of each and every clinical trial registered on the EU trial registry EudraCT to post summary results onto the registry within 12 months of trial completion (6 months for paediatric trials). These rules also apply to trials concluded before 2014.

Thus, all of the clinical trials identified in this report as missing summary results are in violation of European Union transparency rules that were designed to protect the interests of patients and taxpayers.

Concerns about research waste

Unreported trials contribute nothing to progress in science and public health, and are therefore costly [research waste](#). In the past, unreported clinical trial results have [caused public health losses amounting to billions of Euros, and led to the death of countless patients](#). For this reason, the Declaration of Helsinki has made reporting the results of every clinical trial a [universal ethical obligation](#) for all medical researchers worldwide.

While not all trials lacking results on the European trial registry are completely unreported, the best available evidence suggests that [around half of all trials missing results on the registry](#) have also not reported their results in academic journals. Thus, hundreds of trials run by European universities are likely to be in acute danger of becoming research waste unless their results are made public soon.

We urge universities to review their clinical trial portfolios across the EU registry, the US registry Clinicaltrials.gov, and other [WHO primary trial registries](#), identify those trials that have remained completely unreported, and ensure that their results are made public as soon as possible.

Global best practices

[WHO standards](#) require every interventional trial to post its results on every public registry where it was registered within 12 months of its primary completion date. Importantly, the WHO has explicitly stated that publishing trial results in the academic literature is not an acceptable substitute for posting trial results onto public registries.

[Best practices jointly set out by Cochrane and Transparency International](#) also state that “Summary results for all clinical trials should be posted on the registries where they were originally registered within 12 months of study completion.” The two health integrity groups note that retrospectively posting the results of all past trials onto registries “would improve healthcare delivery and government

agencies' decision-making on resource allocations, as well as saving billions of dollars' worth of medical research from being lost forever."

Similarly, the trial reporting [benchmark set out by the AllTrials campaign](#) states that "A summary of results (...) should be posted where a trial was registered within one year of completion of a trial."

There are good reasons for this emphasis on posting all trial results onto registries:

- Posting results onto registries accelerates medical progress because the 12-month timeline permits far more rapid results sharing than the slow academic publication process allows.
- Posting results onto registries minimises the risk of a trial never reporting its results and becoming research waste, which can happen when a principal investigator dies or leaves their post during the prolonged process of submitting an academic paper to a succession of medical journals.
- Research shows that trial results posted on registries typically give a more comprehensive and accurate picture of patient-relevant trial outcomes than corresponding journal articles do.
- Results posted on registries are easier to locate and are open access.
- Registry reporting facilitates comparison of trial outcomes with a trial's originally stated aims, and thus discourages harmful research malpractices such as the 'silent' suppression, addition, or [switching of selected outcomes](#), [HARKing](#), and [p-hacking](#).

Please see the [report by Cochrane and Transparency International](#) for further details and links to the relevant literature.

No barriers to subsequent publication in academic journals

The International Committee of Medical Journal Editors has [explicitly stated](#) that the posting of summary results onto trial registries is not considered prior publication by academic journals. Thus, academic journals will accept articles reporting a trial's outcomes even if that trial's outcomes have already been made public in a trial registry. Because results reporting on registries is typically faster than academic publication, making trial results public on registries before they are published in an academic journal is now the norm in best practice scientific communications.

ANNEX I: USEFUL RESOURCES FOR UNIVERSITIES

[Achieving excellence in clinical trial reporting: University of Nottingham case study](#)

The University of Nottingham boosted its reporting rate on EUCTR from just 8% to over 95% within less than half a year. This Q&A explains how Nottingham did it, with useful tips for other universities.

[How to tackle clinical trial transparency: University of Bristol case study](#)

This case study, written by the former Head of Research Governance at the University of Bristol, contains useful hands-on advice on posting clinical trial results onto registries, and useful links.

[AllTrials blog: How to upload results and update entries on clinical trial registers](#)

Useful blog outlining the steps required to update and add results to the US clinical trials registry ClinicalTrials.gov and the EU Clinical Trials Register.

[Clinical trial registration and reporting rules - a quick primer](#)

Explains some of the basic rules governing clinical trial reporting on registries.

[WHO Joint Statement](#)

The statement sets out WHO best practices in clinical trial registration and reporting, with a focus on trial registries. Universities can assess their policies against WHO standards by using [this checklist](#).

[Clinical trial transparency: A guide for policy makers](#)

This report by Transparency International and Cochrane summarizes the academic literature on the causes and consequences of failures to register or report clinical trials, and flags relevant laws, regulations and best practices.

[CONSORT Statement](#)

The CONSORT Statement comprises a 25-item checklist and a flow diagram for reporting clinical trials in the academic literature.

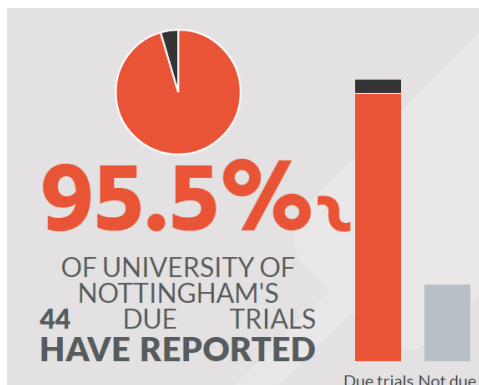
Need additional guidance or support?

Please check out TranspariMED's [collection of transparency tools](#) for universities.

TranspariMED is keen to learn from universities across Europe what additional resources and support would be helpful to support their trial reporting efforts. This will inform our ongoing work to [strengthen the European clinical trial transparency ecosystem](#).

Please email tillbruckner@gmail.com and share your experiences and suggestions.

ANNEX II: TRANSPARENCY CASE STUDY - NOTTINGHAM UNIVERSITY



The University of Nottingham is a European leader in clinical trial transparency. Over 95% of its due trials now have summary results posted on the European trial registry EUCTR – a steep increase from its 2018 reporting rate of only 8%.

In this Q&A, the University explains how it tackled its unreported trials, with useful tips for other European universities.

Image source: EU Trials Tracker, 27 April 2019
<http://eu.trialstracker.net/>

When did you start systematically uploading missing clinical trial results onto EudraCT (EUCTR)?

- The University of Nottingham audited its trial registrations on EudraCT in December 2018 and commenced immediate action to post or update missing results. This process was completed in March 2019.
- Over the same time period, the University reviewed and updated its policies, systems and processes to ensure summary results in future would be posted on the relevant registries in a timely manner by academics engaged in clinical trials academics. A new guide to [Trial Registration](#) was published on 17 December 2018.
- The guide has been regularly communicated to academic staff engaged in clinical trials research, alongside support and advice from our Research Governance team, to help them meet their responsibilities in registering trials and posting results.

How many results were missing when you started, and how many results have you uploaded since then?

- Some 46 trial results were identified in the audit as potentially missing. One trial was subsequently confirmed as not a [CTIMP](#) and one trial was confirmed as having been registered but subsequently cancelled. These records were corrected and all other trial results have now been uploaded.

How is the process organised? Who does what?

- The Head of Research Governance conducted detailed audits of each registry, producing a detailed analysis of missing results and senior responsible owners (SRO) for each trial. Each SRO was contacted with a request by the Head of Research Governance and Faculty Pro Vice-Chancellor to post their results and offered support and guidance to do so where required.
- In a significant number of cases, and in the interests of urgently addressing the backlog, the Head of Research Governance obtained the trial results from the SRO, requested EMA transfer

the studies to her account, updated the registry and then contacted the MHRA [UK's national medicines regulator] to advise them to alter the status of each trial on EudraCT to 'complete.'

How did you deal with old trials that were falsely listed as "ongoing" on EudraCT?

- Where trials were incorrectly listed as "ongoing" or incorrectly registered (see above), the Head of Research Governance liaised with the EMA and MHRA to [correct the record](#).

What resources were required? Did you have to hire additional staff? How long did it take per trial?

- To date, the audit and action process has been overseen and largely delivered through the personal efforts of the Head of Research Governance.
- The University is currently augmenting staff resource in the Research Governance team by an additional two posts to further quality assure data management and audit trails across our research portfolio, including trial registries, and to support our clinical trials community in meeting their responsibility in registering trials and posting results.
- The time taken to update each EudraCT record varied widely according to the availability and format of data, the challenges in posting it to the registry, and subsequent liaison with the EMA and MHRA to update the records. On average, each record took several hours to complete.

What are the major barriers you encountered, and how did you overcome them?

- In posting missing results, academics' results data and tables frequently needed to be re-formatted to suit EudraCT functionality. This was overcome by academics or the Head of Research Governance manually re-formatting the data, which was a time-consuming process.
- In a registry environment where multiple academics and students engaged in clinical trials are individually responsible for registering trials and posting results, it can prove difficult to maintain central records and oversight by the Research Governance team. To overcome this, the Head of Research Governance has introduced a standard procedure whereby she will obtain the EudraCT number and registration for CTIMPs so that all future studies are registered under her account. This will prevent the unintended loss of account details by individuals, support central monitoring, and ensure academics engaged in clinical trials can be reminded to post and maintain results.
- The Research Governance team maintain a database of all studies requiring a declaration of research sponsorship as defined in law and UK Department of Health policies. However, the University along with many others, also conducts research that does not require this declaration and the Governance team have no oversight of those studies. We are examining processes whereby these studies can also be tracked in future.

What are the three most important things other players in the clinical trial ecosystem can do to make trial reporting easier for universities?

- EudraCT, as indeed most other registries, do not have functionality by which the trial scene can be set, the results discussed and contextualised, and next steps discussed. Introducing a common reporting format within or across registries would overcome the formatting issues discussed above, and introducing further functionality to capture context and next steps could enhance use and compliance by the clinical trials community.

- There is no clear agreed definition of what constitutes clinical research - despite the [WHO attempts at a definition](#). Registries are also used to comply with the [ICMJE Lancet paper 2004](#) in order to obtain subsequent publication of non-clinical (but medical) and physiology studies, regardless of whether the study is actually fits a definition of 'clinical research' or not. This leads to confusion over which studies do actually need to be publically registered and which do not. Many of these studies are student projects, which are often not novel research and add little to the knowledge base for medicine. Registries therefore could do well to have a mechanism by which researchers and sponsors can flag what type of study it is and whether the results are intended to either be published or contribute to the knowledge base of clinical application
- Registries also presently have no mechanism to remove records or alter the study status to reflect that a study never started or was so prematurely stopped that there are no results to post.

Based on what you have learned along the way, what would you do differently if you were going to start the process again today?

- We would have introduced the measures we now have in place, in particular the enhanced central audit and analysis and oversight procedures.
- Better engaging the clinical trials community in the importance of maintaining registry entries. The Head of Research Governance will now regularly review and provide updates at faculty board and committee level on how clinical trials researchers are making positive progress, as well as highlighting where further work is required to ensure compliance.

What is your advice for other non-commercial trial sponsors that want to improve their clinical trial reporting?

- Be prepared and willing to undertake some intensive activity to bring your records up to date, perhaps devoting a dedicated 'task team' to address this swiftly and comprehensively. Subsequently, and critically, set the parameters, expectations and guidance for maintaining registries and communicate these clearly to the clinical trials community so that responsibilities are clear and progress can be maintained as a matter of routine in the future.

TranspariMED would like to thank the University of Nottingham for sharing its experiences with the wider medical research community. This case study is also available as a stand-alone PDF download from the [collection of transparency tools](#) that TranspariMED has compiled for universities.

ANNEX III: TRANSPARENCY CASE STUDY – BRITAIN'S REGULATOR MHRA

As this report has shown, a significant but unknown number of completed clinical trials is currently falsely listed as 'ongoing' on European trial registry across all EU Member States, with negative consequences for public agencies, medical researchers and patients.

This brief describes how the UK's national medicines regulator, the MHRA, is successfully tackling the problem. We encourage all other [National Competent Authorities](#) (national medicines regulators) across Europe to initiate a similar registry data clean-up programme.

Why this is important

- Health technology assessment agencies, horizon scanners, systematic reviewers and researchers cannot reliably determine whether a trial is still ongoing or has been prematurely ended, terminated, or completed. This [makes it difficult to gain an overview](#) of the complete scientific evidence base on a medicine.
- Clinicians, patient groups and patients cannot reliably determine which trials may currently be recruiting patients, [making enrolment more difficult for patients and recruitment more difficult for sponsors](#). This drives up the cost and slows down the pace of medical research.
- Registry users often have to contact sponsors directly to clarify a trial's status, which is inefficient and wasteful.
- Compliance with EU reporting rules is undermined. Trial sponsors are unable to upload the summary results for completed trials if at least one of the member states involved has not marked the status as 'completed'. More broadly, the EMA, national regulators, and trial sponsors themselves cannot reliably determine from EUCTR data (or from the [EU Trials Tracker](#)) which trials are due to post their summary results.

How the MHRA is tackling the problem

Scope of work

The UK National Competent Authority, the MHRA, is currently systematically reviewing and updating the status of all clinical trials listed on EUCTR to ensure the correct trial status is shown to the public. The MHRA's work covers all clinical trials with at least one trial site located in the UK that are listed on EUCTR.

Two people within the MHRA are working on the updating process, in parallel with performing other responsibilities. Between them, they are spending 2-3 person-days per week on the task.

Prioritisation

The first phase of the work, which began in January 2019 and is ongoing (as of April 2019), covers all applicable trials for which an End of Trial notification was received since 2014, around 4,500 trials total. Once all trials in that cohort have been updated, the MHRA will begin tackling the remainder of trials in its portfolio.

Process

When a trial sponsor completes a trial, [EU Guidance](#) stipulates that the sponsor must send a "Declaration of the End of Trial Form" to the MHRA within 90 days (or 15 days if the trial has to be terminated early).

For the period 2014-2018, the MHRA conducted a search of its internal records to locate trials for which the “Declaration of the End of Trial Form” document had been received. The MHRA then cross referenced their internal record of each individual trial with that in the EUCTR and where the status was wrongly listed as ‘ongoing’ this was corrected to ‘completed’.

In addition, the MHRA responded to requests for updates it received from UK trial sponsors on an ongoing basis. (Following a 2018-2019 parliamentary enquiry into the issue, many non-commercial trial sponsors in the UK are [currently in the process of uploading overdue summary results](#) onto EUCTR.)

Achievements

Between the start of the process in January 2019 and early April 2019, the MHRA successfully reviewed (and if appropriate, updated) the status of over 1,700 clinical trials.

Resources required

Based on the MHRA’s experience, National Competent Authorities seeking to update the status of all trials in their own legacy portfolio should budget around 30 person-days per 1,000 trials in their portfolio.

Fixing the status of legacy trials only requires a one-off allocation of resources. Going forward, the MHRA has already put into place a system that ensures that the status of all trials newly reported by sponsors as “completed” will be routinely updated, on a weekly basis.

Future steps

MHRA expects to complete updating the status of all trials in the initial five year cohort (of trials for which an End of Trial notification was received since 2014) by September 2019. Once MHRA has finished updating the initial cohort of trials, it will start updating the status of the remaining (older) trials in its portfolio.

Note: This case study is also available as a stand-alone PDF download from the publications page on [TranspariMED’s website](#).

ANNEX IV: METHODOLOGY AND LIMITATIONS

Authorship

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Methodology

- Cohort selection

The 30 universities included in the cohort are those that have sponsored the largest number of clinical trials listed on the European trial registry, the EU Clinical Trial Register.

- University performance data

Data on universities' trial reporting performance was manually extracted using the [EU Trials Tracker](#) built by EBM Data Lab, University of Oxford. The EU Trials Tracker periodically collates and curates data that is publicly available on the EU Clinical Trial Register. To the best of the author's knowledge, to date no instances of a trial incorrectly flagged as being due and missing results by the EU Trials Tracker have been detected.

The data was extracted from the EU Trials Tracker on 04 April 2019. At that point, the EU Trials Tracker has last been updated on 01 April 2019. Thus, the data in this report is accurate as of 01 April 2019.

The EU Trials Tracker individually lists every trial flagged as overdue, and includes a link back to the original registry entry for every trial. Thus, all data in this report is externally replicable.

Limitations

- Undercounting of unreported trials

The EU Trials Tracker draws on registry data and thus significantly undercounts the number and proportion of unreported trials because many trials are falsely marked as "ongoing" in the registry. Please see the main text of the report and Annex III for details.

- Trials not listed on the EU Clinical Trial Register

The data in this report exclusively covers clinical trials that were registered on the EU Clinical Trial Register. Under EU rules, all clinical trials of investigative medicinal products ([CTIMPs](#)) conducted in the European Union must be registered on the EU Clinical Trial Register.

However, trials not covered by these rules, including trials of medical devices (e.g. pacemakers) and non-drug treatments (e.g. physiotherapy), cannot be registered on the EU Clinical Trial Register. Universities usually register such trials on other registries, notably the U.S. registry [Clinicaltrials.gov](https://clinicaltrials.gov). While reporting the results of such trials is also important, and WHO best practices clearly state that all trials should post results onto all registries where they are listed, such non-CTIMP trials are beyond the scope of this report.

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