

Clinical Trial Reporting by UK Universities: Progress Report January 2019

24 January 2019
Bristol and London, UK

"Many of these trials are funded with public money and the tax payer has a right to expect those who benefit from public funding to follow the rules and publish in full."

- [Norman Lamb MP](#), Chair of the Science and Technology Committee

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

- [Transparency International and Cochrane](#)



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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. For this reason, there is a universal ethical obligation to report the results of every clinical trial, regardless of where a trial was originally registered. Reporting trial results in line with global best practices requires posting their summary results onto trial registries within 12 months of trial completion for each and every trial, without exception, irrespective of legal requirements or whether a trial's outcomes have been published in the academic literature.

Key findings

- **Overall, 1,671 clinical trials run by UK universities are still missing results** on the American (1,575) and European (96) trial registries. To date, the 27 universities covered by this report have posted summary results for only 11% of their trials.
 - **The strongest performers on the European registry are Aberdeen (100% of trials reported) and King's College London (96%).** Across universities, 62% of due trials listed on the European registry now have results; 38% are still missing results.
 - **No UK university has yet achieved a strong reporting performance on the American registry.** 97% of due trials listed on the American registry still have no results.
 - **Around 800 university trials are in acute danger of becoming research waste.**
- **Some UK universities are already working hard to post missing trial results, but most have still not made any progress.** Eight universities have uploaded additional trial results over the past two months, with King's College London, Nottingham and Cardiff in particular making huge progress. However, 19 universities in our sample have not uploaded a single missing trial result in recent months, illustrating that calls for voluntary compliance alone will not fix the problem.

Recommendations

- **THE GOVERNMENT should fully adopt and implement all recommendations made in the Science and Technology Committee's 2018 report on clinical trials transparency.** This includes funding a national audit programme covering all clinical trials, and putting into place sanctions, including fines, for trial sponsors that do not post summary results onto registries within 12 months of the primary completion date of any interventional clinical trial.
- **THE GOVERNMENT should provide reporting support to non-commercial trial sponsors.** Many UK institutions still do not fully understand the relevant rules, and struggle in isolation to navigate the (unnecessarily complex) user interfaces of trial registries. A simple how-to manual and an online helpdesk would significantly support sponsors' efforts to upload trial results, and generate substantial efficiency gains for UK universities and NHS Trusts.
- **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 Declaration and adopt the transparency policies set out therein.

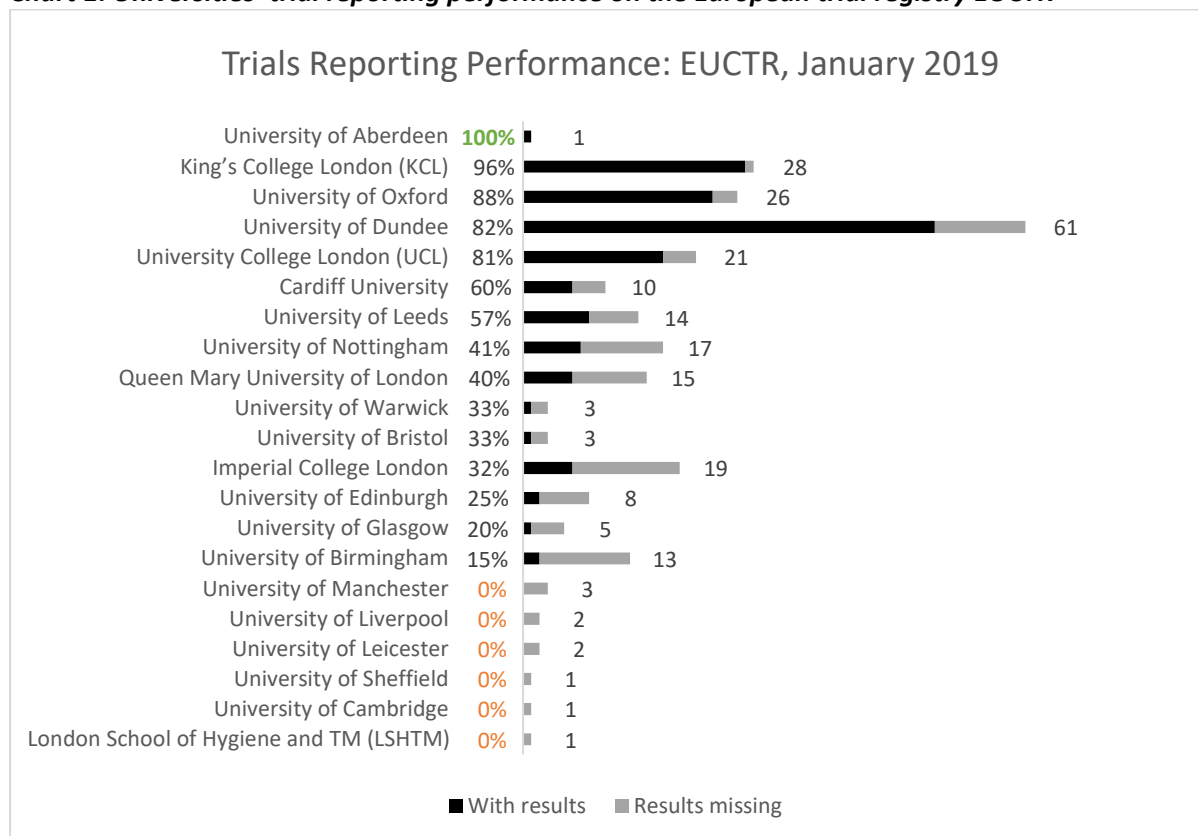
2 REPORTING PERFORMANCE ON THE EUROPEAN REGISTRY

In total, the 27 universities covered by this report have sponsored 254 clinical trials listed on the European registry whose results are verifiably due. 62% of these trials now have results on the registry. The remaining 38% of trials that were completed more than a year ago – 96 trials in total – are still missing results, in violation of European Union guidelines and global best practices.

The performance of UK universities varies widely. Among the universities with five or more due trials listed on the registry, the top performers are King's College London (96% reported), Oxford (88%), Dundee (82%) and University College London (81%). The major sponsors with the worst performance at present are Birmingham (15% reported), Glasgow (20%), and Edinburgh (25%).

The static snapshot below does not adequately capture the huge progress made by some universities. For example, only two months ago, Nottingham was the UK's weakest performer, with only 6% of its trials having posted results. By now, it has posted results for 41% of its due trials, and the university plans to achieve 100% compliance by the end of this month – a powerful example of the scope for rapid progress if a university takes decisive action.

Chart 1: Universities' trial reporting performance on the European trial registry EUCTR



Note: The absolute numbers in the chart above give the total number of trials listed on the registry per university. Liverpool School of Tropical Medicine (LSTM), Newcastle University, University of Exeter, University of Reading, University of Southampton, and University of Sussex have no due trials listed on the European registry and are thus not included in the chart above.

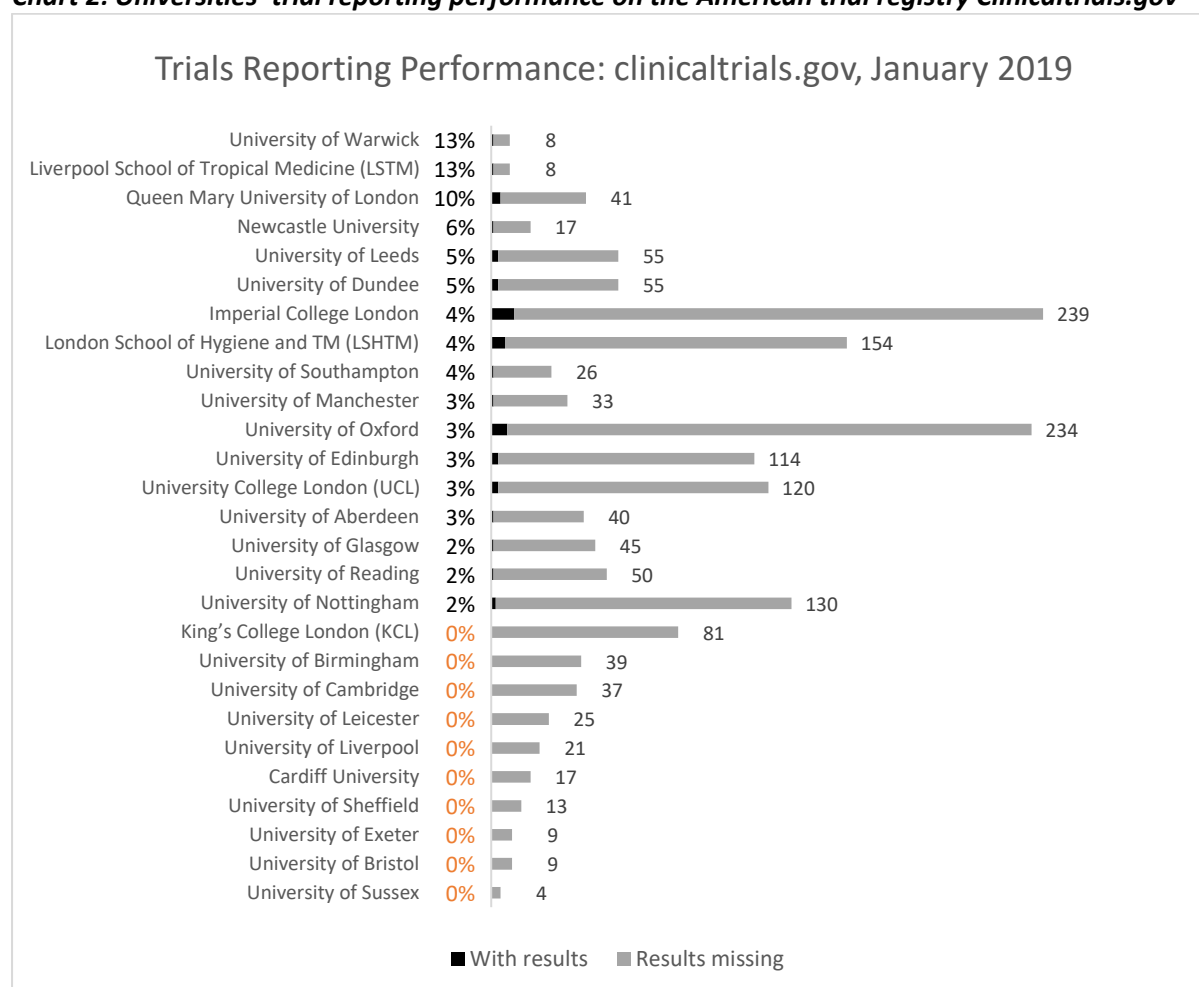
3 REPORTING PERFORMANCE ON THE AMERICAN REGISTRY

In total, the 27 universities covered by this report have sponsored 1,624 clinical trials listed on the American registry whose results are due. 97% of these trials are missing results on the registry. The medical discoveries made around 800 UK university trials are at risk of being lost forever unless their results are uploaded onto registries soon.

The American registry contains most trials run by UK universities. At present, the performance of all universities is still weak on this registry, and many universities still seem to be limiting their results posting efforts to the European trial registry. This is deeply worrying as around half of all trials with no results on registries have not reported their results anywhere else either. Around 800 UK university trials are currently at risk of becoming research waste, and their scientific insights lost forever, unless their results are uploaded soon (see below) – and most of these are located on the American registry.

Universities' inconsistent approach to clearing their backlogs of unreported trials on different registries makes no sense from an ethical, scientific, public health, or financial stewardship perspective. For public health bodies, doctors and patients, it makes no difference on which registry a trial was registered: they need access to the results of all clinical trial to be able to determine how safe and effective different drugs, medical devices and treatments are. On the positive side, at least one UK university, Bristol, has already [started the process](#) of uploading missing trial results onto the American registry.

Chart 2: Universities' trial reporting performance on the American trial registry Clinicaltrials.gov



Note: The absolute numbers in the chart above give the total number of trials listed on the registry per university.

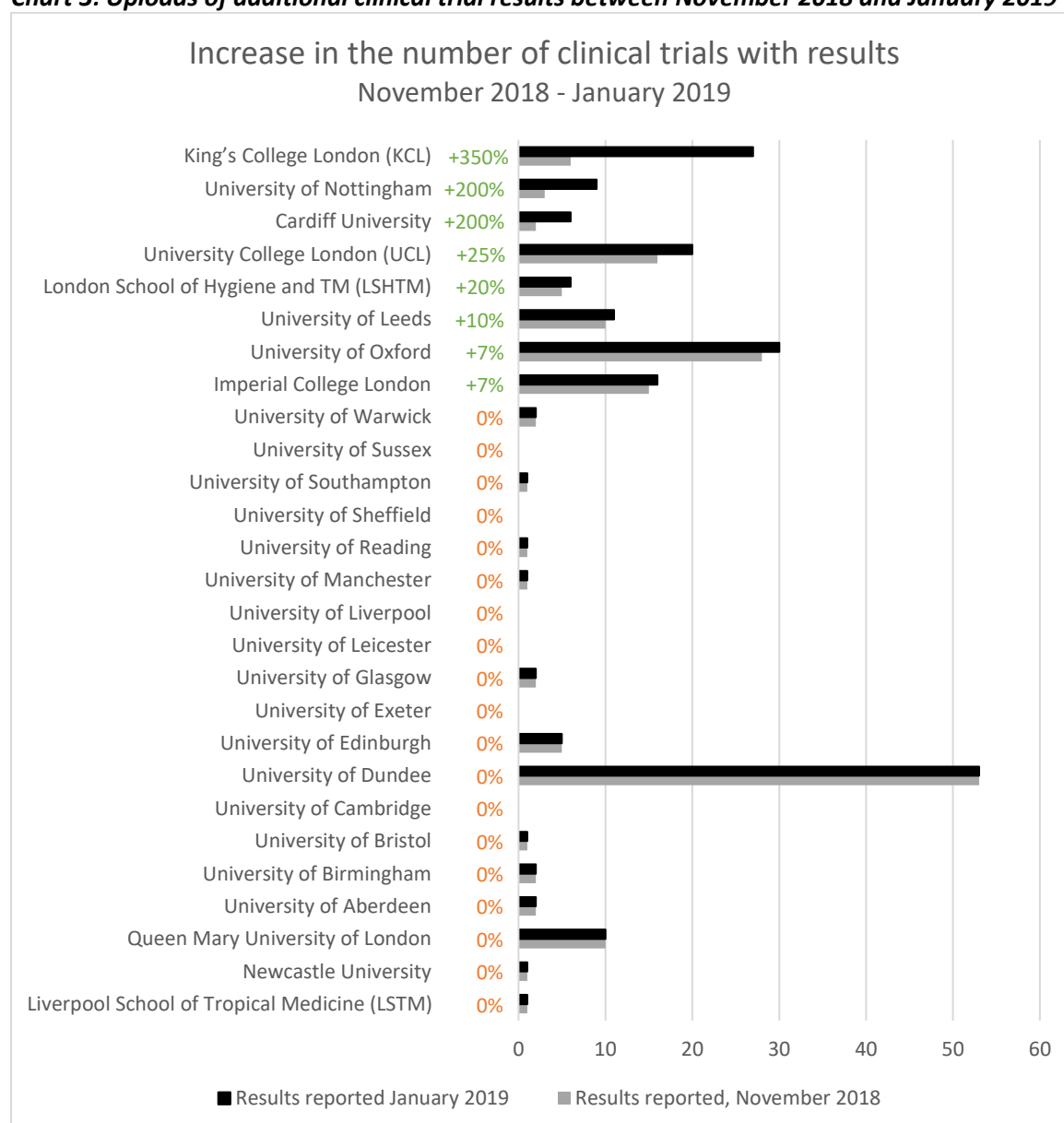
4 EFFORTS TO POST MISSING SUMMARY RESULTS

Some universities have made impressive progress in clearing their backlogs of unreported clinical trials over the past two months, but the majority of UK universities still seem to be failing to tackle the issue.

King's College London (KCL) has run the UK's most impressive registry cleanup operation, uploading 21 trial results in just two months. The number of publicly available KCL trial results has rocketed by 350% as a result. Only one of its due trials is still missing results on the European registry today, an impressive achievement. Nottingham and Cardiff have also taken huge strides forward. Hopefully, these universities will soon also tackle their trials missing results on the American registry.

Disappointingly, many other universities seem not to have taken any action. Out of 27 universities, 19 have not uploaded a single additional trial result. (Note that registry cleanup programmes can take time to yield publicly visible results, so some of these 19 universities may simply be moving slowly.)

Chart 3: Uploads of additional clinical trial results between November 2018 and January 2019



5 WHY THIS MATTERS

Focus on research excellence

Excellence in reporting the results of research is an integral part of overall research excellence.

Therefore, this report focuses on research excellence rather than on narrow legal and regulatory compliance. It does this by assessing universities' performance on both the European trial registry EUCTR and the world's largest trial registry, the American Clinicaltrials.gov.

The inclusion of American trial data in assessing universities' performance is fully aligned with best practices set out by the World Health Organisation (WHO), Cochrane, Transparency International, and the AllTrials campaign (see below). We may additionally include [ISRCTN](#) registry data in future reports.

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 the failure to adequately 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
- Shareholders are exposed to substantial risks

There is a [universal ethical obligation](#) to report the results of every clinical trial, regardless of where a trial was originally registered.

Global best practices

[WHO best practices](#) 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." The AllTrials' over 700 supporter groups include key UK stakeholders such as the British Medical Association (BMA), the Health Research Authority (HRA), the National Institute for Health and Care Excellence (NICE), and the Association of Medical Research Charities (AMRC).

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](#).

Concerns about costly research waste at UK universities

A [recent study](#) by the team at Oxford University's reviewed a sample of 100 due trials missing results on the European registry and found that around half of those trials had not reported their results in the academic literature either. Assuming the ratio is similar for all trials run by UK universities, around 800 of the 1,671 UK university trials currently missing results across both registries are likely to not have reported their results anywhere. Universities urgently need to identify past trials at risk of becoming research waste, and rapidly upload their results to registries before they are lost forever.

Unreported trials contribute nothing to progress in science and public health, and are therefore costly [research waste](#), much it funded by public money. Between them, the 27 universities in our cohort received a [total of £344 million](#) in research grants from the Medical Research Council (MRC) in the year 2015-2016 alone. Thankfully, the MRC – widely recognised as a global clinical trial transparency frontrunner among public research funders – has begun routinely auditing its grantees' reporting performance and [publishing the audit results](#).

We encourage the MRC to [disclose the names of institutions and researchers](#) that have failed to publish trial results in its forthcoming 2019 audit. We also encourage the UK's other major public medical research funder, the National Institute for Health Research (NIHR), to follow the MRC's positive example and launch a similar trial audit programme as soon as possible, and to publish the names of non-reporting grantees. Encouragingly, NIHR too is [strongly committed to clinical trial transparency](#), and has already begun work on this issue.

Of the 1,671 UK university trials currently missing results, 1,575 (94%) are listed on the American trial registry, which most UK universities have yet to tackle. Our data shows that even universities committed to excellence in trial reporting on the European trial registry still have a long way to go until they meet global best practices across their full trial portfolios.

Many of the trials on the American registry are of crucial scientific and medical importance. For example, the ongoing [controversy around vaginal mesh implants](#) painfully illustrates that millions of patients' lives and wellbeing depends on medical devices being safe and effective. However, medical device trials currently [cannot be registered on the European registry](#), so UK universities usually register them on the American registry (or on the ISRCTN registry) instead. Note that some of the trials on the American registry may be [in violation of U.S. law](#), exposing UK universities to the [risk of steep fines](#).

We encourage UK universities to begin the process of uploading missing clinical trial results onto the American registry as soon as possible.

We encourage the UK government to phase in fines for universities that fail to upload trial results onto any trial registry, including the American registry.

Science and Technology Committee report on clinical trials transparency

In late October 2018, the House of Commons Science and Technology Committee issued a [report on clinical trials transparency](#), which recommended that “[e]very university should aim for 100% compliance,” that the UK’s Health Research Authority should monitor compliance, and that universities that fail to achieve compliance should be sanctioned, including through the imposition of fines. (See [here](#) for a summary.)

During Committee hearings, both Sam Gyimah MP, the Minister for Universities, and Dr Patrick Vallance, the Government Chief Scientific Adviser, stated that universities should, in their words, “[sort it out](#)”.

Importantly, the national audit programme proposed by the Committee [would cover all clinical trials](#) conducted in the UK. This includes trials registered on the European and American registries, the ISRCTN registry, and all other [WHO primary registries](#), as well as the [minority of trials that universities fail to register in the first place](#).

The report was [welcomed by transparency advocates and patients](#), and the Health Research Authority [responded positively to its recommendations](#). The UK government is expected to issue a formal response to the report before the end of January 2019.

We encourage the government to fully adopt and implement all recommendations made in the Science and Technology Committee’s 2018 report on clinical trials transparency. This includes funding a national audit programme covering all clinical trials, and putting into place sanctions, including fines, for trial sponsors that do not post summary results onto registries within 12 months of the primary completion date of any interventional clinical trial.

ANNEX I: USEFUL RESOURCES FOR UNIVERSITIES

[How to tackle clinical trial transparency](#)

This brief 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.

[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](#). Some of the basic rules governing trial reporting on registries are [explained here](#).

[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.

[Tackling trials incorrectly listed as ‘ongoing’ on the European registry](#)

Many UK university trials that were completed years ago are currently [incorrectly listed](#) as still ‘ongoing’ on the European trial registry. Universities should use the [EU Trials Tracker](#) to identify these trials, and request the [MHRA to update](#) their status. King’s College London has already done so, and MHRA has by now updated the status of most of its trials, illustrating the feasibility of this approach.

[Identifying due trials missing results on the American registry](#)

Universities can use our dataset to obtain a complete list of all their due trials missing results on the American trial registry. The dataset is linked below, in the methodology section.

[Need for additional resources and support](#)

[TranspariMED](#) is keen to learn from universities what additional resources and support would be helpful to support their trial reporting efforts. This will inform our ongoing work to strengthen the UK clinical trial transparency ecosystem. Please email tillbruckner@gmail.com and share your experiences and suggestions.

Over the coming months and years, TranspariMED and UAEM will continue to document the sector’s progress by regularly publishing follow-on progress reports. Future reports may additionally incorporate trial reporting data from ISRCTN, the third trial registry commonly used by UK universities.

ANNEX II: UNIVERSITY TRIAL REPORTING DATA AS OF JANUARY 2019

University trial reporting data for the American and European trial registries, covering interventional clinical trials that are due to report results.

- American data downloaded from Clinicaltrials.gov on 08 January 2019
- European data extracted from the EU Trials Tracker on 11 January 2019

See the methodology section below for more details.

University	Clinicaltrials.gov reporting performance January 2019			EUCTR reporting performance January 2019		
	Due trials	With results	Results missing	Due trials	With results	Results missing
Cardiff University	17	0	17	10	6	4
Imperial College London	239	10	229	19	6	13
King's College London (KCL)	81	0	81	28	27	1
Liverpool School of TM	8	1	7	0	0	0
London School of Hygiene & TM	154	6	148	1	0	1
Newcastle University	17	1	16	0	0	0
Queen Mary University of London	41	4	37	15	6	9
University College London (UCL)	120	3	117	21	17	4
University of Aberdeen	40	1	39	1	1	0
University of Birmingham	39	0	39	13	2	11
University of Bristol	9	0	9	3	1	2
University of Cambridge	37	0	37	1	0	1
University of Dundee	55	3	52	61	50	11
University of Edinburgh	114	3	111	8	2	6
University of Exeter	9	0	9	0	0	0
University of Glasgow	45	1	44	5	1	4
University of Leeds	55	3	52	14	8	6
University of Leicester	25	0	25	2	0	2
University of Liverpool	21	0	21	2	0	2
University of Manchester	33	1	32	3	0	3
University of Nottingham	130	2	128	17	7	10
University of Oxford	234	7	227	26	23	3
University of Reading	50	1	49	0	0	0
University of Sheffield	13	0	13	1	0	1
University of Southampton	26	1	25	0	0	0
University of Sussex	4	0	4	0	0	0
University of Warwick	8	1	7	3	1	2
TOTAL	1624	49	1575	254	158	96

ANNEX III: METHODOLOGY AND LIMITATIONS

Authorship

Lead report writer: Dr Till Bruckner (TranspariMED)
EU registry data: Extracted by Sarai Kestra (UAEM) from the EU Trials Tracker (EBM Data Lab)
US registry data: Generated by Sean Lee (UAEM) via a [Python tool](#) he developed
Historical data: [2018 universities report](#) by UAEM and TranspariMED
Cover and charts: Ian Goodrich (unaffiliated volunteer)

Lead author contact: tillbruckner@gmail.com

Methodology

- Cohort selection

The 27 universities included in the study cohort are the same universities that are currently under assessment for the Global Health Report 2017-2019, which are being developed jointly by Universities Allied for Essential Medicines (UAEM) UK in collaboration with Students for Global Health and TranspariMED.

A [previous report by UAEM and TranspariMED](#) on the trial reporting performance of UK universities was published in November 2018, and included the same cohort. The selection methodology for universities is described in detail in that report.

- Reporting performance on the European registry ([EUCTR](#))

Data on the reporting performance on the European registry was manually extracted by SK using the [EU Trials Tracker](#) built by EBM Data Lab, University of Oxford, which uses information publicly available on EUCTR. To the best of the authors' 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 tracker data was extracted on 11 January 2019 and manually entered into a table by SK.

- Reporting performance on the American registry ([Clinicaltrials.gov](#))

Data on the reporting performance on the American registry (Clinicaltrials.gov) was generated using an Excel pivot tool built by SL according to specifications developed by TB. A manual verification of 26 trials was performed by TB before publication of the 2018 report to assure the accuracy of results.

The tool uses the following criteria:

- Only interventional studies (clinical trials) are included
- University is listed as lead sponsor of a trial
- Trials with a 'withdrawn' status are excluded
- Primary completion date is at least 13 months in the past

Trials that did not present a primary completion date, be it tentative or actual, were simply treated as overdue. Trials that only gave a month and a year for a primary completion date were assumed to have completed the trial on the first of the month. To account for this, an additional 30 days (1 month) grace period was added to the 12 month post completion time period.

The dataset used for this analysis was downloaded from Clinicaltrials.gov on 08 January 2019 and analysed by SL using a Python tool. The full dataset [has been posted online](#) together with an [explanatory note](#) to enable external verification of the data presented in this report.

The Python tool itself [has been posted on Github](#) together with instructions for use and can be downloaded from there and used to by third parties to conduct similar assessments. The authors welcome critical feedback on the tool, which they plan to re-use for future follow-on assessments.

Limitations

- Trials not listed on EUCTR or Clinicaltrials.gov

Trials sponsored by universities that had not been registered on EUCTR or Clinicaltrials.gov were beyond the scope of this report. This includes trials registered on other [WHO Primary Registries](#), notably ISRCTN, and trials that have never been registered in the first place.

- Trials listed on both EUCTR and Clinicaltrials.gov

Some trials covered by this report were registered on both EUCTR and Clinicaltrials.gov. These trials were double counted in the performance data.

- Reporting performance on EUCTR

Some trials sponsored by the universities in the cohort were flagged as having “incomplete data” by the EU Trials Tracker. In keeping with the tracker’s established methodology, such trials were not included in the data set of due trials. In addition, the tracker is unable to identify completed trials erroneously listed as still “ongoing” on EUCTR; therefore, such trials were also not included in the data set of due trials.¹

- Reporting performance on Clinicaltrials.gov

Past studies of Clinicaltrials.gov reporting performance have commonly only included trials marked as ‘completed’ by the registry. This widespread but flawed approach results in a substantial undercounting of due trials. [Previous research by TranspáriMED](#) has shown that numerous completed trials sponsored by UK universities are falsely listed as not completed on various registries, presumably because university staff failed to update trials’ status after trial completion.

The Excel pivot tool used for generating Clinicaltrials.gov reporting data uses a trial’s primary completion point as the key criterion to determine whether or not a trial is due to post results. This approach is likely to slightly over-count due trials. For example, if a trial’s expected primary completion date is extended during the trial due to slower than expected patient recruitment, and university staff fails to update the registry entry accordingly, the expected primary completion date listed in the registry will be further in the past than the actual or currently expected primary completion date.

On balance, the approach used here has two significant advantages:

- In terms of accuracy, the number of trials falsely identified as overdue using this approach is assumed to be substantially lower than the number of trials falsely identified as not yet due when using the conventional approach.

¹ The number of trials falsely listed as “ongoing” on EUCTR is likely to be substantial. A [2018 study](#) of 10,492 trials registered on both Clinicaltrials.gov and EUCTR by Jessica Fleminger and Ben Goldacre showed that 33.9% of dual-registered trials listed as 'ongoing' on EUCTR were listed as 'completed' on ClinicalTrials.gov.

- In terms of faithfully depicting a university's registry management performance, this approach is preferable because it will never² falsely identify trials as overdue if a university keeps its registry entries up to date. Thus, the approach used here incentivises universities to keep their registry entries up to date. In contrast, the conventional approach creates perverse incentives for trial sponsors to postpone or neglect updating a trial's status to 'completed'.

Thanks

The authors thank the team at the EBM Data Lab in Oxford, whose EU Trials Tracker enabled them to rapidly generate reliable performance data for the European registry. The authors are also grateful to the members and staff of the House of Commons Science and Technology Committee for encouraging UK universities to aspire to excellence in reporting clinical trial results.

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² Trial sponsors can request an extension of the legal results posting deadline on Clinicaltrials.gov under certain circumstances. However, while such extensions have legal significance in terms of FDAAA compliance, they have no bearing on a trial's adherence to global best practices. Furthermore, it seems unlikely that UK universities have ever requested such extensions with U.S. authorities.