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A transparency blueprint for the NHS

Reporting missing results of clinical trials sponsored by NHS Trusts

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MISSING TRIAL RESULTS OF NHS TRUSTS AND NHS FOUNDATION TRUSTS

The [report on clinical trials transparency](#) published by the House of Commons Science and Technology Committee on 30 October 2018 highlights the failure of several NHS Trusts and NHS Foundation Trusts to post the summary results of clinical trials they sponsored onto EudraCT, the European Union’s trial registry, within the required 12 month time frame.

These shortcomings are not limited to the few Trusts named in the Committee’s report. [EU Trials Tracker](#) data indicates that weak trial reporting on EudraCT is widespread among NHS Trusts and NHS Foundation Trusts across the country, with some [exceptions](#). There are strong indications that this shortcoming also extends to other WHO primary registries where Trusts have registered trials.

For example, six Trusts located in Greater Manchester have between them failed to post the summary results of at least 24 clinical trials onto EudraCT. The performance of these Trusts is just as disappointing on Clinicaltrials.gov, where all 38 of their due clinical trials are also missing results.

NHS Trust	EudraCT		CT.gov		Both registries	
	Results reported	Results missing	Results Reported	Results missing	Results reported	Results Missing
Christie NHS Foundation Trust	0	6	0	20	0	26
Manchester Mental Health and Social Care T.	0	2	0	0	0	2
Manchester University NHS Foundation Trust	0	13	0	15	0	28
Pennine Acute Hospital NHS Trust	0	1	0	1	0	2
Salford Royal NHS Foundation Trust	0	1	0	2	0	3
Wrightington, Wigan & Leigh NHS Fdn Trust	0	1	0	0	0	1
TOTAL	0	24	0	38	0	62

SCOPE AND SCALE OF THE PROBLEM

Sadly, the EU Trials Tracker data cited by the Science and Technology Committee only represents the tip of the iceberg, in two ways.

- Firstly, the tracker – an excellent tool that was designed to avoid giving any false positives – almost certainly understates the number of trials sponsored by NHS Trusts and NHS Foundation Trusts that are missing results on EudraCT. For example, it lists as overdue

neither trials with inconsistent completion data, nor the many trials that Trusts have erroneously left listed as still ongoing.

- Secondly, and more importantly, the tracker does not take into account the many trials sponsored by NHS Trusts that were exclusively, or additionally, registered on Clinicaltrials.gov and/or ISRCTN and that are missing results on those registries.

VIOLATION OF LAWS, REGULATIONS AND GLOBAL BEST PRACTICES

A failure to post clinical trial results onto EudraCT violates EU guidelines, and some of the trials missing results on Clinicaltrials.gov may be in breach of the U.S. FDA Amendments Act. Note that legally and administratively, responsibility for posting trial results rests with the Trusts that sponsored them, and not with individual investigators.

Merely updating EudraCT registry entries and adding missing summary results there, without also tackling entries made on other registries, is insufficient to achieve compliance with global best practices. WHO best practices explicitly require all clinical trials to post their results onto the registries where they are listed within 12 months of a trial's primary completion date, regardless of legal and regulatory requirements.

Thus, publication of trial results in an academic journal is not an acceptable substitute for posting summary results onto a public trial registry.

There are good reasons for the WHO's insistence 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 may 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.

WHY THIS IS IMPORTANT FOR THE NHS AND NHS PATIENTS

The data presented above raises serious concerns about research ethics, fiduciary stewardship (research waste), and data management practices within the NHS.

A failure to report clinical trials is [not a victimless crime](#). It [harms patients](#), leads to the misallocation of public health resources, and slows down the development of new drugs, vaccines, medical devices and treatments.

For example, trials missing results on EudraCT that were sponsored by Manchester University NHS Foundation Trust include trials that recruited, or set out to recruit, the following patients:

- Thirty [autistic children](#) aged 5-8 years
- Fifteen [infants and children with hyperinsulism](#)
- Sixty [pregnant women with diabetes](#)
- One hundred and fifty [patients who had suffered from heart attacks](#)
- One hundred and four [people with severe asthma](#)

This failure to fully report results is deeply unethical. Patients volunteer to participate in trials in the faith that trial results will be shared with them, and with the scientific community, in line with global best practices.

The [Declaration of Helsinki](#) explicitly states that:

“Researchers have a duty to make [publicly available](#) the results of their research on human subjects and are accountable for the completeness and accuracy of their reports... All medical research subjects should be given the option of being informed about the general outcome and results of the study” [emphasis added]

However, some NHS patients in the JustTreatment network have been unable to obtain the results of UK clinical trials they have participated in. Furthermore, patients typically do not have access to paywalled journals. In contrast, results on trial registries, including lay summaries, are a publicly accessible to everyone.

Furthermore, because many Trusts fail to regularly update their registry entries, it is impossible to determine with confidence whether any given trial is currently recruiting patients or not. This makes it difficult for NHS patients and their doctors to locate appropriate trials that they could enrol in, undermining NHS efforts to enable and encourage more patients to participate in clinical trials.

THE PATH TO IMPROVED CLINICAL TRIAL TRANSPARENCY

The experiences of transparency front-runners [in the UK](#) and [beyond](#) illustrate that NHS Trusts and NHS Foundation Trusts can and should be expected to do better.

Noting NHS Improvement’s [role](#) of “overseeing foundation trusts and NHS trusts,” and its priority of “offer[ing] support to providers and local health systems to help them improve”, we encourage you to consider taking the following two steps:

- **Step 1: NHS Improvement should publish a strategy for cleaning up registry entries for all clinical trials past and present**, ensuring that the data they contain is complete, accurate and – where the primary completion point of a trial lies more than 12 months in the past – includes summary results. In addition, it should outline mechanisms that ensure that in future, all clinical trials [as defined by the WHO](#) will be [appropriately registered and reported](#) from the outset. The strategy should include a clear timetable with intermediate milestones and regular public progress reports.
- **Step 2: NHS Improvement should conduct a central audit of the registry entries of all clinical trials sponsored by NHS Trusts and NHS Foundation Trusts** across EudraCT, Clinicaltrials.gov, ISRCTN and all other [WHO primary registries](#). This audit would identify all applicable registry entries and flag gaps, inconsistencies, outdated information and missing

summary results within and [between](#) these entries, and thereby create a 'to-do' list for subsequent registry clean-up efforts.

LEADERSHIP BY NHS IMPROVEMENT: FASTER, BETTER, CHEAPER

We suggest that NHS Improvement take on this role because of its unique mandate, and because a centrally conducted audit using a standardised methodology and data entry tool would be far more efficient, effective and cost-effective than isolated audit efforts by the dozens of individual NHS Trusts and NHS Foundation Trusts, each of which would have to independently create their own audit frameworks and tools, creating a risk of uneven design and implementation. A centralised audit would provide reassurance to UK parliament, patients and taxpayers that the issue is being adequately and comprehensively addressed.

We believe that such an audit could be completed centrally, based on public registry entries alone (i.e. without input from individual Trusts), by one person within just 1-2 months. Once the audit framework and Excel tool have been developed, the actual auditing process is essentially a data entry job that requires no specialist skills. Please note that Dr Ben Goldacre during his oral testimony to the Science and Technology Committee made an offer to support precisely such audit efforts together with his team. TranspariMED can help NHS Innovation to identify additional individuals or teams with trial audit experience should it wish to consult with them and/or outsource this work.

The subsequent cleaning up of registry entries would take considerably more effort. Fortunately, several UK institutions have already gained experience in cleaning up their existing trial registry entries. The [lessons learnt by these transparency front-runners](#) could inform the efforts of NHS Improvement and individual Trusts. NHS Improvement may wish to explore whether tasking a central point person with managing data entry into trial registries for all Trusts during (and possibly after) the clean-up process could improve data quality and reduce costs.

WHAT IS THE ALTERNATIVE?

NHS Improvement has a high work load and capacity constraints. At the same time, due to the ethical, public health, scientific and fiduciary considerations outlined above, not resolving this issue is simply not an option.

This transparency blueprint seeks to make a constructive contribution to NHS decision-making and patient care. If NHS Improvement was to identify and fully implement an alternative solution that ensures that all clinical trials – past, present and future – sponsored by all NHS Trusts and NHS Foundation Trusts are appropriately registered and fully report their results across all trial registries in line with WHO best practices, we would equally welcome such an alternative course of action.

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NOTE ON METHODOLOGY FOR COUNTING UNREPORTED TRIALS

The scope of this study is limited to Trusts in Greater Manchester that have sponsored clinical trials listed on EudraCT whose a primary completion date lies 13 or more months in the past. (Tameside Hospital NHS Foundation Trust has registered [one trial on EudraCT](#), but that the results of that trial appear not to be due yet.) The following Trusts have not sponsored any clinical trials listed on EudraCT: Central Manchester University Hospitals NHS Foundation Trust, Royal Bolton Hospital NHS Foundation Trust, Stockport NHS Foundation Trust, Trafford Healthcare NHS Trust.

EudraCT data were extracted from the [EU Trials Tracker](#). Clinicaltrials.gov data was generated using a tool developed by Sean Lee from Universities Allied for Essential Medicines ([tool and methodology here](#)).

All data were extracted in October 2018.