

Clinical Trial Transparency in Austria

Mapping unreported drug trials

February 25, 2020

Vienna, Austria and Bristol, UK

“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

“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.

European Union (EU) rules adopted in July 2014 require the sponsors (organisations that conduct a trial) of each clinical trial registered on the EU Clinical Trials Register to post those trials' summary results to 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.

Scope

The results presented in this report reflect EU Trials Tracker data on 14 Austrian trial sponsors with at least 5 registered trials as of January 2020. The data are based on the EU Clinical Trial Register, which includes all clinical trials of investigative medicinal products conducted within the European Union (EU). The report does not include trials of international pharmaceutical companies that are not headquartered in Austria but might have had study sites in Austria.

Key findings

Overall, the 14 largest clinical trial sponsors based in Austria have registered 693 clinical trials of investigative medicinal products on the EU Clinical Trial Register. Of these, 334 trials have verifiably been completed more than a year ago and should thus have results available. However, results are only available on the registry for 61 of those verifiably due trials (18.3%). Results are missing for the other 273 due trials (81.7%). This report focuses on the three largest medical universities, which are between them responsible for more than two-thirds of the trials run by Austrian trial sponsors.

- Austrian trial sponsors' results posting rate of 18.3% is far below the average European trial reporting rate of 64%.
- Only one sponsor, the **Central European Society for Anticancer Drug Research (CESAR)** has a perfect 100% reporting rate, albeit with only five trials. The performance of other sponsors ranges widely, from 0–90%. Six out of the 14 largest trial sponsors in Austria have not posted a single result.
- **Vienna Medical University** has by far the largest portfolio of trials, with at least 382 trials in total. Only 26 of its 202 verifiably due trials (13%) have posted results; 176 due trials are missing results. The medical universities of **Graz** and **Innsbruck** also perform weakly. Each has only uploaded 20% of its due trial results.
- For 63 apparently academic trials, it is difficult or impossible for outsiders to determine which university sponsored them. Up to 20 additional trials may have been registered directly by individual researchers, without direct university oversight.

Recommendations in brief

The Austrian Federal Office for Safety in Healthcare (BASG), the national regulator, and Austria's three largest academic trial sponsors are already taking significant steps to address the problem of underreporting. To be successful, we recommend the following measures:

- **Universities** should establish central oversight over their clinical trial registry entries, adopt policies that reflect WHO best practices, audit existing registry records, assume ownership of 'ghost trials' and upload missing clinical trial results.
- **The national regulator BASG** should review and update flawed registry data, directly contact trial sponsors whose results are overdue, and draw up plans to impose fines after the EU Clinical Trials Regulation comes into force.
- **The Austrian government** should use Research Ethics Committee records to monitor whether clinical trials are prospectively registered and upload their results to registries on time.

2 REPORTING PERFORMANCE BY SPONSORING ORGANISATION

On average, major Austrian trial sponsors have uploaded only 18.3% of their due clinical trial results. Performance varies strongly by sponsor. CESAR (100%) and Arbeitsgemeinschaft Medikamentöse Tumortherapie Gemeinnützige GmbH (90%) report results for (nearly) all their due trials. All other trial sponsors perform weakly. Six sponsors have not posted a single trial result (see Figure 1).

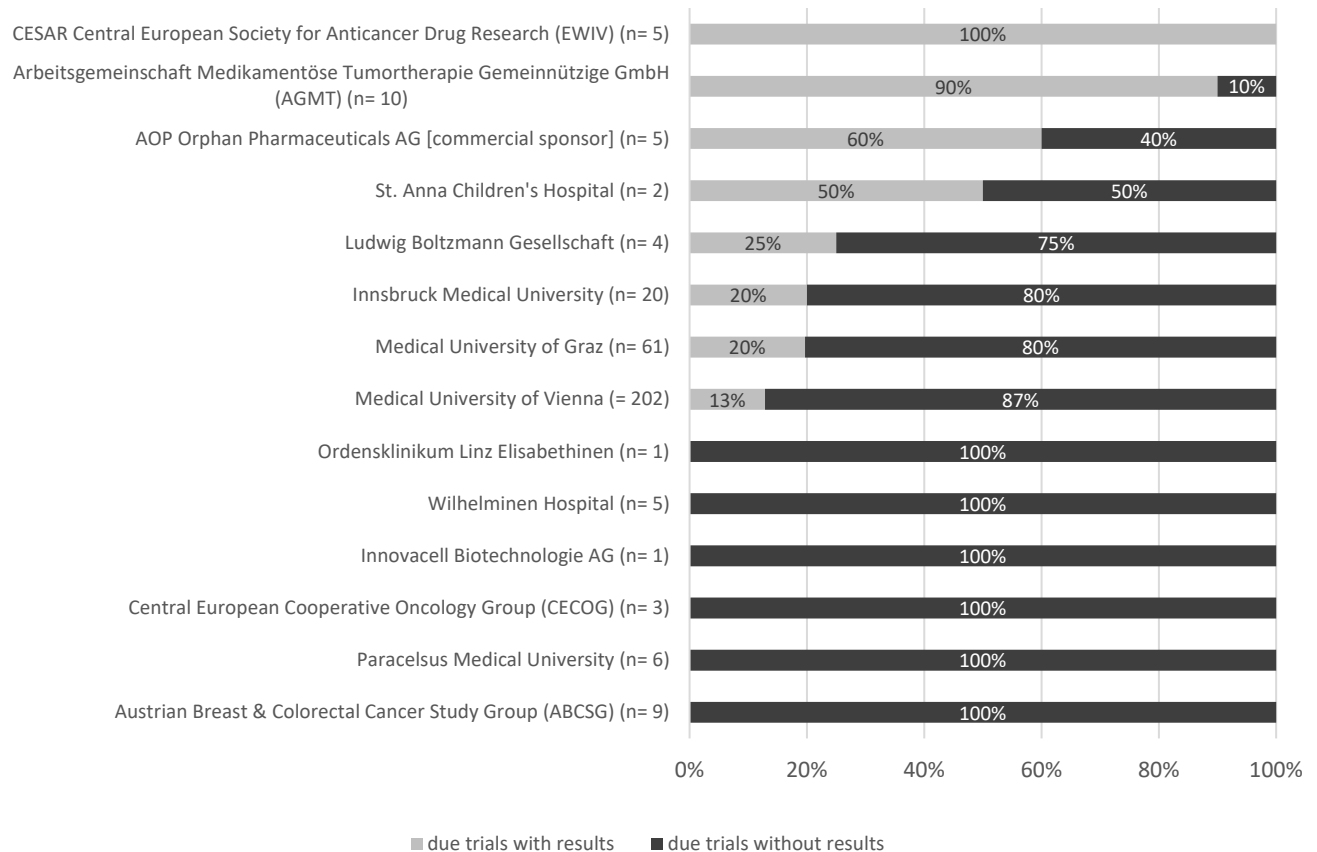


Figure 1: Percentage of due trials with and without reports of 14 major Austrian sponsoring organisations

3 CLINICAL TRIALS MISSING RESULTS BY SPONSORING ORGANISATION

In total, major Austrian trial sponsors have failed to make the results of 273 of their verifiably due trials public on the European trial registry, in violation of EU transparency rules.

With 176 due trials missing results, the Medical University of Vienna has by far the largest backlog of unreported trials, followed by the universities of Graz and Innsbruck. These three universities account for 241 of the 273 (attributable) clinical trials missing results (see Figure 2).

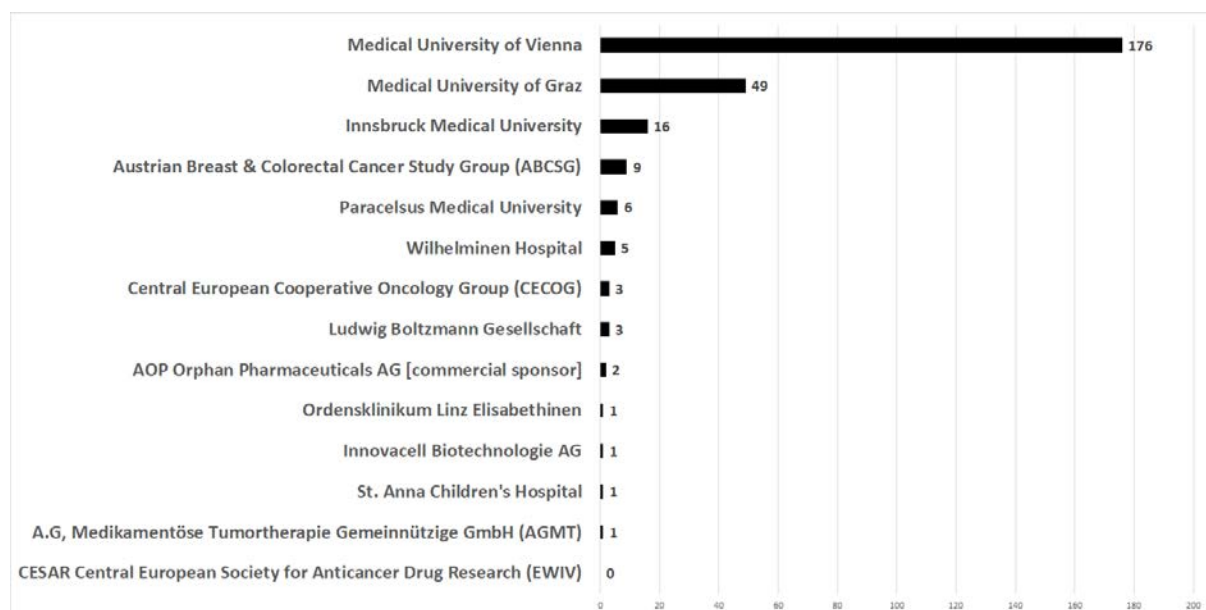


Figure 2: Number of due trials missing results for 14 major Austrian trial sponsoring organisations

Two of the three largest trial sponsors uploaded additional results during 2019. Between January 2019 and January 2020, the Medical University of Vienna and the Medical University of Graz uploaded more results than during all the previous years combined. In its statement, the Medical University of Innsbruck also assured that it will increase the upload of trial results (see Annex II).

Future TranspariMED reports will track Austrian sponsors' progress over time. Experience from the UK suggests that universities with large trial portfolios typically require at least one year to clear their legacy portfolios of unreported trials.

4 AUSTRIAN ACADEMIC GHOST TRIALS

As noted above, 273 trials attributable to individual major universities are missing results. However, the true number of unreported academic clinical trials in Austria is probably far higher.

- There are 63 ‘ghost trials’ that were conducted in Austria whose sponsor is identified with terms such as ‘University Clinic Internal Medicine I,’ which indicate that they were conducted by a university but make it difficult or impossible to determine which university ran them. Of these, 27 trials are due, but only 3 have posted results.
- A further 20 ‘ghost trials’ list individual researchers as their sponsor. Of these, 13 trials are due, but none have posted results.

Some examples of ambiguous sponsor names on the European database are listed below in Table 1.

Table 1: Entries with unclear sponsor names

Information entered to register
Abteilung für Herz-Thorax-Gefäß Anästhesie & Intensivmedizin
Akademische Eigenstudie, Sektion für Hygiene und Medizinische Mikrobiologie
Institut für Spezifische Prophylaxe und Tropenmedizin
Institute of Specific Prophylaxis and Tropical Medicine
Department für Kinder- und Jugendheilkunde, Pädiatrie I
Department of General Psychiatry
Klin. Abtlg. für Thorax- & Hyperbare Chirurgie
Klinik f. Innere Med., Fachabteilung Hämatologie
Pediatric Cardiology
Sektion Chirurgische Forschung
Sektion Chirurgische Forschung, Univ.Klinik f.Chirurgie
UK für Anästhesiologie und allgemeine Intensivmedizin
Univ. hospital, Dpt. of anaesthesia
Univ. Klinik für Anästhesiologie
Univ.-Klinik für Kinder- und Jugendheilkunde
Universitätsklinik für Kinder- und Jugendheilkunde
Universitätsklinik für Klinische Pharmakologie
Universitätsklinik für Psychiatrie und Psychotherapie I
University Childrens Hospital

Assuming that all 83 ghost trials were conducted by the major universities in the ranking, the overall results posting rate of these Austrian universities is 15.6%. This puts them ahead of German universities (6.7% of results reported) but far behind American (68.9%), UK (72.1%) and Irish (85.7%) universities.

Note that while an individual researcher may be able to legally act as the ‘sponsor’ of a trial, such a sponsorship arrangement is suboptimal from a patient and scientific perspective because that researcher’s retirement or death is likely to prevent the trial’s results from ever being reported. In contrast, sponsorship by an institution with strong clinical trial governance systems and processes should ensure continuity in the fulfilment of sponsor obligations regardless of any person’s individual circumstances.

Note: The above data on ‘ghost trials’ may not be precise; please see the methodology in Annex IV for details. See also the BASG statement in Annex III. BASG and trial sponsors can use this spreadsheet of the clinical trials conducted by Austrian sponsors to identify academic ghost

trials (highlighted in red) and trials sponsored by individual investigators (in blue) and allocate them to the correct institution.

5 EXAMPLES OF DATA QUALITY ISSUES IN AUSTRIAN TRIALS

Background

Once a university has completed a trial, it should notify the BASG of the date the trial was completed. The BASG should then update the trial's status on the European database. (The university cannot directly do this itself.) Thus, trials should be marked as 'ongoing' or as 'completed' in the database; in the latter case, a completion date should be entered.

Inconsistent data

A search of the [EU Trials Tracker](#) shows that among them, the three Austrian universities have sponsored 52 clinical trials flagged by the Tracker as having 'inconsistent [completion] data', leaving unclear whether they are due to post results. (For this reason, these 52 trials were omitted from the reporting data presented earlier in this report.)

Of the 52 trials with inconsistent data:

- 44 trials are marked as 'completed', but the completion date is missing.
- 6 trials have a completion date but are nonetheless marked as 'ongoing'.
- 2 trials are marked neither as 'ongoing' nor as 'completed'.

This data illustrates that all participants in the process have not lived up to their responsibilities: The European Medicines Agency has designed a database that allows incomplete and contradictory data to be uploaded.

- The BASG has been uploading incomplete and contradictory data (see Annex III for BASG's response).
- Universities have failed to notify the BASG of erroneous data in their trial portfolios and have not followed up to ensure that the BASG corrects this data.

Other quality issues

In addition, numerous trials that were completed long ago are still falsely listed as 'ongoing'. For example, the Medical University of Vienna's trial 2005-000105-65 is still listed as 'ongoing' even though its results were presented at a conference in 2012.

Meanwhile, the title of a cancer trial ([2011-002195-16](#)) was entered in German by the Medical University of Vienna, making it difficult for medical researchers in other countries to locate. Even though the original entry was made in 2012, no corrective action has been taken.

6 RECOMMENDATIONS FOR AUSTRIAN UNIVERSITIES

Recommendations for universities

- **Excellence in reporting results is an integral part of overall research excellence.** As trial sponsors, universities—not individuals—are responsible for ensuring that their data on trial registries are complete and kept up to date, and that the results are posted on time. Universities should **establish central oversight** over their clinical trial registry entries, across all trial registries, and track all past and future trials. [This presentation by TranspariMED provides some guidance.](#)
- Going forward, universities should adopt **policies** that ensure that the summary results of all their interventional clinical trials are routinely and consistently uploaded to all registries where these trials are listed within 12 months of trial completion, as per WHO best practices. [This policy checklist may be helpful.](#)
- Looking back, universities should **audit** their existing trials across [all WHO primary registries](#) and [Clinicaltrials.gov](#) to identify trials whose data are incomplete or out of date or that are missing results on the registry. Universities should then draw up a plan for addressing the problem.
- For trials listed on the **European registry**, all missing results should be uploaded. These can be easily identified using the [EU Trials Tracker](#). Guidance on how to upload results can be found in [TranspariMED's collection of transparency tools](#) and in [these presentations](#).
- Universities should compile a spreadsheet listing all trials on the **European registry** with their correct completion dates and ask the BASG to update their status. (Only regulators can update the status of trials listed on the European registry. On other trial registries, universities can update the status of trials themselves.)
- During the audit of **other WHO primary registries and Clinicaltrials.gov**, universities will detect trials that are missing summary results on these registries. For each of these trials, they should check whether it has reported outcomes in an academic journal. Trials that have not had their results made public anywhere are in acute danger of becoming research waste. Universities should upload the summary results of these trials to the registry where they are listed, before the data is lost forever.

Need additional guidance or support?

The TranspariMED website hosts a collection of useful [transparency tools and case studies](#) of universities that have successfully fixed the problem.

TranspariMED is keen to hear from universities regarding what additional resources and support would be helpful to support their trial reporting efforts. Please email tillbruckner@gmail.com and share your experiences and suggestions.

7 POLICY RECOMMENDATIONS

'WHO calls for ethics committees, regulatory authorities, professional bodies, sponsors, investigators, and funding agencies to act in their jurisdictions to ensure results from all interventional clinical trials are reported and publicly disclosed.'

World Health Organization statement, 2015

'Legislation or supporting regulations... [should] require all clinical trials to be registered... prior to commencing the trial, public disclosure of [the] results of any newly conducted clinical trial, public disclosure of unreported results for clinical trials conducted in the past, [and] sanctions if a clinical trial is not registered and/or results are not reported.'

WHO, Pharmaceutical System Transparency and Accountability Assessment Tool, 2018

Recommendations for the Austrian government

The Austrian government should establish monitoring system to check whether sponsors of clinical trials conducted within its jurisdiction are posting their summary results to public registries within 12 months, as per WHO best practices, and impose sanctions on those trial sponsors who fail to make the results public within that deadline. This involves centrally following up on ethics approvals made by Research Ethics Committees to check whether trials were prospectively registered and their results uploaded on time. (The UK is currently preparing to do this.)

Recommendations for the BASG

- **The BASG should review all the trials it is responsible for on the European registry.**
- **Ghost trials.** The BASG should amend the registry entries for ghost trials (and if possible individual investigator–sponsored trials), so that their institutional sponsors are clearly identifiable. Note that one trial for which the BASG is responsible has a completely blank sponsor name field.
- **Incorrect trial status.** In addition, the BASG should systematically review the status of all the trials it has approved that are currently listed as 'ongoing' and **update their status** to 'completed' if applicable. This will make it easier for patients to find trials to participate in, and for public health agencies and researchers to gain an overview of the complete scientific evidence base on a medicine. (The British regulator MHRA (Medicines and Healthcare products Regulatory Agency) is already doing this.)
- **Sanctions.** Failure to report clinical trial results is not a victimless crime. The BASG should formulate and clearly communicate plans to impose fines for violating reporting requirements after the EU Clinical Trials Regulation fully comes into force.

8 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

[European Union rules adopted in July 2014](#) require each and every clinical trial registered on the EU Clinical Trials Registry to post summary results to 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 EU transparency rules that were designed to protect the interests of patients and taxpayers. Once the EU Clinical Trial Regulation comes into force, probably in late 2020 or 2021, national regulators will have the power to fine institutions for not uploading trial results to the European trial registry.

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 have led to the deaths 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, dozens of trials run by the universities covered in this report are in acute danger of becoming [research waste](#) unless their results are made public soon.

Universities should 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 sponsor of an 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 to 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 to 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’.

Why is posting trial results to registries so important?

There are good reasons why global best practices require posting the results of all trials to registries:

- Posting results to registries accelerates medical progress because the 12-month timeline permits far more rapid results sharing than the slow academic publication process allows.
- Posting results to registries minimises the risk of a trial never having its results reported 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 the comparison of trial outcomes with a trial’s originally stated aims and, thus, discourages harmful research malpractices such as HARKing, p-hacking and the ‘silent’ suppression, addition or switching of the selected outcomes.

Please see the report by Cochrane and Transparency International for further details and links to the relevant literature.

Uploading results to trial registries typically precedes publication in academic journals

There is no recorded case, ever, in which a manuscript was rejected by a journal because the trial results had already been uploaded to a trial registry.

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. The International Committee of Medical Journal Editors has explicitly stated that the posting of summary results to trial registries is not considered prior publication by academic journals. Thus, 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 the new norm in scientific communications.

ANNEX I: IMPROVING TRIAL REPORTING – LESSONS FROM UK UNIVERSITIES

On average, UK universities perform far better than their peers in Austria. On average, they have already posted the results for over 72% of their clinical trials to the European registry, and some individual UK universities have attained reporting rates of 100%. Why do UK universities perform so strongly?

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 the UK parliament held an enquiry into research integrity from 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 the UK universities, warning them that if they did not rapidly upload the missing trial results, they would be called before the Committee to explain themselves. This set off a race to fix the problem.
- **Pressure from research funders:** In 2017, Britain’s two public medical research funding bodies, the National Institute for Health Research (NIHR) and the Medical Research Council (MRC), as well as the non-profit Wellcome Trust, 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 to monitoring their grantees’ compliance with these rules. Two funders, Wellcome Trust and the MRC, have already published audit results. In the coming years, UK universities that fail to post trial results to registries on time may no longer be able to access public medical research funds.
- **Public pressure:** A loose coalition of health integrity groups convened by TranspariMED that included the 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 the 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 UK universities’ trial reporting performance. For example, King’s College London improved its reporting rate from 18% to 100% within less than a year. The University of Nottingham, starting from an even lower baseline, has by now posted the results of over 94% of its trials. (See their respective case studies for details on how they fixed the problem.) Many medical universities in the UK are also reviewing their data on other registries, such as the US registry Clinicaltrials.gov and ISRCTN. This demonstrates that where there is a will, there is a way—universities in Germany can solve this problem too if they decide to do so.

The UK government is now working to put a comprehensive national clinical trial monitoring system in place that will use Research Ethics Committee records to track every single clinical trial conducted on UK soil—including commercial and multi-country trials—to ensure that all trials are registered and reports their results.

ANNEX II: UNIVERSITY RESPONSES

TranspariMED invited the three universities with the largest number of unreported trials to provide a statement on their current clinical trial registry management efforts and future plans. All three universities responded. Their responses – in some case slightly edited for clarity – are below.

TranspariMED, Cochrane Austria and Transparency International Austria would like to emphasise that the responses given by all three universities show that these institutions are already working to upload missing clinical trial results, and are thus on the right track.

Response by Medical University of Vienna

The Medical University of Vienna fully supports the efforts undertaken by WHO, EMA and the European Commission, funding agencies and others to increase validity and reproducibility of clinical trial data (and research data in general) as well as the transparency of trials and clinical trial results and access to data for secondary analyses. This is anchored in the Good Scientific Practice Guidelines of the Medical University of Vienna.

In close cooperation of Ethics Committees, clinical trial support centers and the BASG (the Austrian Medical Agency) we continuously increase our efforts to raise awareness as well as to provide support structures to fulfill these legal and ethical standards.

Not as an excuse but as an explanation: The web-based platform EudraCT is absolutely not user friendly, especially in an academic setting where investigators are dealing with the system from time to time only. The handling is not intuitive, the data requested are not in accordance with a scientific/research question and do not follow the general structure of data reports in scientific journals. All concerns that were raised by investigators regarding improvements to use the EudraCT results database have been systematically ignored. The doubt on the usefulness of data uploaded in the database hampers the motivation of researchers to add data onto EudraCT, despite that the Medical University of Vienna fully acknowledges this legal requirement. Furthermore, it is a pity that EudraCT data cannot be evaluated and not be compiled with our Ethics Committee data set. Therefore, follow-ups are cumbersome. Astonishingly, the EU Clinical Trials Tracker is able to do so. In this respect, we would also look forward to joining forces with TranspariMED to increase awareness on the EMA and European Commission's side for academic needs, frameworks and resource limitations.

[Note by TranspariMED: It is true that EudraCT is "absolutely not user friendly". See this report for more details. The European Medicine Agency has recently taken steps to facilitate results reporting on EudraCT, notably by improving the EMA helpdesk for trial sponsors.]

The report mentions also problems in regards to sponsor names that are difficult or impossible to link to any institution. Unfortunately, we are not aware of this problem and do not see any cases concerning Medical University Vienna.

[Regarding trials incorrectly listed as still "ongoing" on the registry:] This is in the responsibility of the Investigators of the Medical University Vienna, we do not assume that BASG did not update the status.

We would also like to emphasize the fact that we see first positive results of our initiatives to increase compliance and accuracy in status reporting. As a first step, this has already resulted in a relatively higher number of "completed" trials, but we are still lacking behind in reporting.

As member of the European Hospital Alliance (EUHA), we have jointly initiated a project to address this issue explicitly. Together with the experience of our partner organization Kings College London and the experts of BiH QUEST Center at the Charite we are confident to manage this aspect in a timely manner.

We will give centralized support to our Investigators for reporting results. This is a joint effort of all nine EUHA members and we will profit of the experience and positive results of Kings College London. Furthermore, investigators are automatically informed about their legal obligation to upload trial results onto EudraCT by the Ethics Committee immediately after submitting the end of trial notification.

We expect to reach a substantial increase [in the number of trials with results available on EudraCT] within this year.

Response by Medical University of Graz

The Medical University of Graz is fully aware of the importance of transparency regarding the results of clinical research and of the reporting responsibilities resulting from this. We take compliance to these obligations very seriously and include relevant information in our regular trainings on Good Clinical Practice. At the same time, we must acknowledge that additional measures have to be taken to improve the situation.

[Regarding trials incorrectly listed as still “ongoing” on the registry:] It has not been possible to research the reason for each individual trial within the given timeframe. The submission of “End of Trial notifications” lies with the Sponsor, not the BASG.

The university provides a specific guideline document for reporting study results in EudraCT, which is available to Principal Investigators on the University’s intranet platform. Also, regular trainings and refreshers about Good Clinical Practice are offered, which include information and guidance about reporting requirements and their importance.

The university’s Institutional Review Board and Coordination Center for Clinical Trials react to all notifications sent by trials registers, i.e. they complete data, regularly remind investigators to report, and provide centralized support for the completion of data. As EudraCT does not provide instruments like reminders, this activity has been focused on [the American trial registry] www.clinicaltrials.gov in the first phase but will be extended to EudraCT in the future.

[Note by TranspariMED: The European Medicines Agency has started sending out reminder emails, but this process started only recently and is progressing on a rolling basis. The Medical University of Graz may not yet have received any such reminders. The fact that Graz is also tackling its trials listed on ClinicalTrials.gov is highly laudable; note that this report does not contain any data on ClinicalTrials.gov results reporting.]

In response to the present situation, the Rectorate will issue a formal letter to all Principal Investigators to remind them to update study information in EudraCT and other relevant registers. Also, the university management plans to implement a centralized monitoring process to promote complete and accurate reporting.

The university expects to complete most entries by the end of the year 2020. As completion of data also depends on the availability of Principal Investigators, it may be difficult to reach 100% coverage, though.

The Medical University of Graz is not only committed to improving its study reporting but is also highly interested in a wider discussion of possible improvements that might foster the use of EudraCT (both as a reporting platform and a useful source for further research).

Response by Innsbruck Medical University

The reproducibility of clinical trial data as well as providing reliable and validated results of clinical trials to the stakeholders are important missions of the Medical University Innsbruck. We take best efforts to comply with the requirements of *Good Clinical Practice* to protect patients' rights and to guarantee data integrity. In the past, in particular in close cooperation of Ethics Committees, clinical trial support centers and the BASG (the Austrian Medical Agency), a number of initiatives have been implemented to improve the reporting compliance of clinical trial data. Nevertheless, we acknowledge that further initiatives are necessary to raise awareness as well as to provide additional support structures to fulfill legal and ethical standards.

Unfortunately, many of our study teams who have already posted or currently try to post the results in EudraCT face various difficulties. Complaints include that EudraCT is not very user friendly, especially in an academic setting where investigators normally not amass extensive experience in using this system. The user interface is not intuitive, as the data requested for database upload are not necessarily congruent with a scientific/research question or the structure of data reports in scientific journals. Although numerous concerns were raised by investigators regarding necessary improvements to use the EudraCT database, none of the problems have yet been addressed or overcome. Thus, doubts on the usefulness of data uploaded in the database hampers the motivation of researchers to add data onto EudraCT, although we fully acknowledge this legal requirement. We have already forwarded these concerns to the BASG last year to raise awareness to these issues.

[Note by TranspariMED: It is true that EudraCT is not user friendly. [See this report for more details](#). The European Medicine Agency has recently taken steps to facilitate results reporting on EudraCT, notably by improving the EMA helpdesk for trial sponsors.]

[Regarding trials incorrectly listed as still “ongoing” on the registry:] This is in the responsibility of the designated coordinating investigator (sponsor representative). We do not assume that BASG did not update the status.

We provide centralized support to our coordinating investigators to fulfil all reporting obligations and to upload the results.

Coordinating investigators who submitted a clinical trial application (on medicinal products or medical device) to the Ethics Committee of the Medical University of Innsbruck after March 03, 2017 are automatically contacted in case the planned duration of the study is extended and no End of Trial information is sent to the Ethic Committee to verify the status of the respective project.

In case a study is completed, the investigator will be informed of the reporting obligation and the possibility to obtain assistance.

Coordinating investigators of studies submitted to the Ethic Committee before March 03, 2017 are reminded of their legal obligations. This is still work in progress.

We will make all efforts to meet the reporting obligations as quickly as possible, but are aware to face problems, as for instance some coordinating investigators are no longer at our university. Nevertheless, we expect a substantial increase within this year.

ANNEX III: RESPONSE BY BASG

TranspariMED invited the Austrian regulator BASG to explain its current efforts and future plans to improve results reporting and improve data quality on the registry. A draft of this report and the full data set were attached to the email to enable BASG to flag possible errors and misinterpretations prior to publication.

Response by BASG

General comments

The Austrian Federal Office for Safety in Health Care (BASG) supports the importance of completeness and accuracy of data on trials and trial results in the EudraCT Database and its public module, the EU Clinical Trials Register. The position taken by the authors on these matters in Chapter 8 is considered in public interest.

BASG welcomes this article as an important contribution to the mission of the European Commission, the European Medical Agency (EMA) and the European Health Authorities to guarantee the safety of participants in clinical trials, the validity and reproducibility of data generated and the transparency of trials and trial results.

Ever since the transparency regulations came into force in 2014, the BASG has been actively engaging stakeholders to fulfil their obligations. To emphasize the importance clinical trial submission guidance on the BASG website contains the rules for publication of results and the recent joint letter by the European Commission, the EMA and the heads of the European medicines agencies. Presentations of BASG to stakeholders on responsibilities of sponsors of clinical trials include transparency requirements as a standard topic.

BASG responds to chapters 2 to 7 of the publication:

Reporting compliance

It is correct that a large number of trials in Austria did not post results via the EudraCT results module in time. Chapter 3 correctly shows that the problem mainly concerns the three universities of Vienna, Graz and Innsbruck. BASG is in constant and close collaboration with these sponsors and their respective Ethics Committees to increase data quality and completeness in EudraCT.

One explanation as to why posting of results may seem delayed in Austria compared to other countries might be attributed to efforts of BASG, Ethics Committees and universities to correctly reflect the status of trials. Therefore a higher proportion of trials might have the status “completed” as in other countries. The authors correctly recognise this as limitation of the system (p.16).

It should also be noted that publishing results in EudraCT is not an easy task and neither intuitive nor particularly user-friendly. It therefore poses a particular challenge for sponsors with few trials and therefore little experience. Where a “fast-track” upload of a publication is foreseen, it is often legally not possible, because the necessary rights for publication (that have to be confirmed during the upload) lie with the journals and not the researchers themselves. In addition, transparency requirements were retrospectively introduced in 2014 for all clinical trials, some dating back to 2006 or earlier. Due to academic fluctuation, the longer completion predates this requirement, the more challenging it is to post results.

What is currently not adequately reflected in the article is the time factor. BASG is definitely seeing an improvement in data quality and completeness in EudraCT over time. It would be beneficial to analyse if this positive trend can be confirmed.

[Note: The draft report sent to BASG for review did not include data on recent improvements. A paragraph describing that additional trial results were uploaded by Vienna and Graz universities during 2019 was subsequently added to the report.]

Ghost Trials

BASG strongly disagrees with the notion of weak oversight when it comes to so-called “ghost trials”. All sponsors are identifiable to BASG by the combination of institution and address, though this information is not made public. It is currently not required that the sponsor is a university or that affiliation to a university is clear from the sponsor's name in EudraCT.

Per definition an academic (i.e. investigator-initiated) trial is a trial performed by the individual researcher. There is no legal basis to prohibit individual researchers to act as sponsors as the article is correctly pointing out. The proposal for universities to take oversight over their studies as sponsors is valid and, in fact, the current practice in Austria. Trials sponsored by individual researchers are the minority and mostly older trials (before 2010).

Examples of data quality issues

BASG would welcome to receive the EudraCT numbers for the mentioned trials with inconsistent data for further review and correction. At the moment we can only assume that these few trials (less than 2% of all trials) are old trials that were already reviewed. Where BASG found that contact with the researcher is no longer possible, the trial status cannot be updated. Eventually, these trials will be suspended by Regulation 536/2014 when Directive 2001/20/EC is no longer applicable.

Although English is the encouraged language for the EudraCT form (and is recommended in the BASG submission guidance), there has never been a legal requirement to use the English language as German is the official language in Austria.

Recommendations to Austrian universities

Austrian universities, Ethics Committees and BASG share the same interest in striving for completeness and accuracy of data entries in EudraCT. BASG considers the proposals made in the publication as appropriate, many of which are already implemented by Universities in Austria.

Policy recommendations

Policy decisions and changes to the legal basis such as sanctions and fines are solely within the competency of the Ministry of Health as being responsible for the Austrian Medicinal Products Act. BASG has already communicated the issue of compliance to result reporting to the Ministry of Health and will continue to do so in order to support changes of the legal framework.

Regarding the regular systematic review of ongoing trials, it is to be noted that only the estimated duration of a trial is reported and changes do not need to be notified. Most trials take much longer than planned. Therefore, BASG has to rely on information by sponsors when a trial has ended. In addition to our information campaign BASG evaluated the option of regularly contacting sponsors of trials that “should have ended” and found it unfeasible, because most of them were still ongoing.

ANNEX IV: METHODOLOGY AND LIMITATIONS

Authorship

Report author: [Dr Till Bruckner](#) (Founder, TranspariMED) tillbruckner@gmail.com
Data extraction: [Nicholas DeVito](#) (EBM Data Lab, University of Oxford)

The author would like to thank Nicholas DeVito for volunteering his time and expertise for extracting the data used to inform this report. EBM Data Lab as an institution was not involved in developing this report. Any errors in this report are exclusively the responsibility of TranspariMED.

Transparency International-Austria Chapter and Cochrane Austria endorse the report but have not been part of the analyses.

Potential Conflicts of Interest:

None of the authors has any potential conflicts of interest

Methodology

- **Data extraction**

The EU Clinical Trial Register (EUCTR) was scraped and processed using [EU TrialsTracker](#) code and the standard methodology to determine the reporting status of each trial. As part of the process, free-text sponsor names are normalised for display on the website. Alongside the standard EUCTR scraper, a second scraper was run to obtain detailed sponsor info from section B of each EUCTR country level protocol (specifically the sponsor name, country, and sponsor status). This detailed sponsor information was then combined with the processed EU TrialsTracker data for January 2020, and normalisation data, to extract all trials with an Austrian sponsor.

The codes used are available on Github:

- [EU Trials Tracker code and data](#)
- [EUCTR Sponsor section scraper](#)
- The [code](#) for generating the dataset

[Click here to download the full data set as a CSV file.](#)

- **Cohort selection**

The main cohort for this study consists of all clinical trial sponsors headquartered in Austria that had sponsored 5 or more clinical trials on EUCTR as of year end 2019. The full data set listed 24 such sponsors. Based on a manual search of sponsor websites, 9 of these sponsors were excluded because they were subsidiaries or branches of institutions headquartered in other countries, and 1 'ghost' sponsor was excluded because its name ("department of clinical pharmacology") did not appear to relate to any clearly identifiable institution. [These 10 excluded sponsors are highlighted in yellow in the full data set.] This process yielded 14 identifiable sponsors headquartered in Austria with at least 5 trials listed on EUCTR.

In at least one case, the trial count for a sponsor in the full data set did not exactly match data on trials by that sponsor publicly available on the EU Trials Tracker. Such inconsistencies may appear due to missing data in the sponsor country field, incorrect data in that field, or sponsorship of trials through

affiliates located in multiple countries. In order to avoid confusion, on the cohort of 14 sponsors had been established, their trial reporting data was directly extracted from the EU Trials Tracker.

Thus, the data on the 14 sponsors presented in this report reflects EU Trials Tracker data as of January 2020, which in turn reflects EUCTR data as of year end 2019. Due to delays by the European Medicines Agency in making public trial results submitted by sponsors, trial results that were uploaded during December 2019 may not have been captured by the tracker.

The EU Trials Tracker was built by the EBM Data Lab, University of Oxford. The tracker is based exclusively on data that are publicly available on the EU Clinical Trial Register; the tracker is updated on a monthly basis. 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 based on registry records have been detected. 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.

- **Counting of ghost trials**

The full data set was reviewed to identify sponsors whose name did not appear to relate to any clearly identifiable institution. The full data set was also reviewed to identify sponsor names that appeared to be the name of an individual researcher rather than of an institution. [In the full data set, 'ghost' sponsors are highlighted in red, while 'individual' sponsors are highlighted in blue.] The data on ghost trials is only indicative (see limitations below).

Limitations

- **Undercounting of due trials**

The EU Trials Tracker significantly undercounts the number and proportion of trials due to post results because many trials are falsely marked as "ongoing" in the registry even though they were in fact completed long ago. As BASG correctly notes in its response (see above), the proportion of false "ongoing" trials in Austria is lower than in many other European countries, but the exact number of trials incorrectly marked as "ongoing" in Austria is impossible to determine based on registry data.

- **Undercounting of results posted**

Due to delays by the European Medicines Agency in making public trial results submitted by sponsors, trial results that were uploaded during December 2019 may not have been captured by the EU Trials Tracker. In consequence, some trials whose results were only recently made public on EUCTR may have been counted as unreported. In TranspariMED's experience, the number of such trials – if any – is likely to be very low in a cohort this size.

- **Identification of ghost trials**

The review of the full data set to identify sponsors whose name did not appear to relate to any clearly identifiable institution, or seemed to be the name of an individual academic. The review was performed by a single researcher, and only a sample of the corresponding registry entries for those trials was reviewed in depth, so the quantitative data on those 'ghost trials' may not be precise. Nonetheless, TranspariMED is confident that data quality is sufficient to support the claim that 'ghost trials' are a problem of sufficient scope to warrant the attention of sponsors and the regulator.

- **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 investigational medicinal products (CTIMPs) conducted in the European Union must be registered on the EU Clinical Trial Register, and must post their results there within 12 months of trial completion.

Non-drug trials, including trials of medical devices (e.g. pacemakers) and non-drug treatments (e.g. surgery or physiotherapy), cannot be registered on the EU Clinical Trial Register and are thus registered on other trial registries. Such trials can be of even greater medical importance than drug trials. Universities are required to make their results public under global ethics rules. However, assessing universities' trial reporting performance for these non-drug trials is beyond the scope of this report.



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