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Risk of research waste in COVID-19 drug trials conducted in Europe

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TranspariMED, 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

Executive summary

This report assesses the risk of research waste across 118 clinical trials of possible COVID-19 drug treatments currently being conducted in Europe.

Researchers run clinical trials to determine which medical interventions work, and which do not. An effective medical response to the COVID-19 pandemic is only possible if scientists and clinicians have access to the complete evidence base on potential treatments. However, around half of all clinical trials worldwide become research waste because their results are never made public. In the past, ineffective drugs have entered the market and numerous patients have died because information about drug benefits and harms detected during clinical trials remained hidden from view.

Companies and universities running drug trials in Europe are obliged to make trial results public on the European trial registry EudraCT within a maximum of 12 months of trial completion. However, many universities and smaller companies violate this mandatory transparency requirement.

Key findings:

- A majority of COVID-19 drug trials in Europe (79/118) are run by universities and companies that have no experience of uploading clinical trial results onto EudraCT. Of these, 39 trials are being run by sponsors that have in the past violated their transparency obligations to upload results, with zero results uploaded so far. A further 40 trials are being run by sponsors who are unfamiliar with the uploading process because they have not completed any applicable drug trials to date.

- Of the remaining 39 COVID-19 drug trials, only 8 are being run by sponsors that are fully compliant with EU clinical trial transparency rules.

- Across Europe, national regulators in 14 countries are responsible for overseeing COVID-19 drug trials.

- The large number of COVID-19 trials run by non-compliant and inexperienced trial sponsors poses a threat to the accuracy and utility of data on EudraCT, creating a high risk of research waste. This undermines the global search for safe and effective COVID-19 drugs.

Policy recommendations:

- ***National regulators should closely monitor the COVID-19 drug trials they are responsible for and proactively engage with trial sponsors.*** Regulators should work with companies and universities to make them aware of their obligation to provide accurate data to the registry and keep it up to date (including, but not limited to, trial status). Regulators should actively monitor compliance, while supporting sponsors with guidance and training materials.

- ***National regulators should encourage COVID-19 trial sponsors to voluntarily upload summary results onto the registry as soon as possible after trial completion,*** on a voluntary basis, rather than 12 months after trial completion as required by current rules.

- ***National policy makers in EU Member States should follow the positive example of Denmark and introduce sanctions*** for sponsors that fail to make the results of clinical trials public.

Why this matters

Clinical trials are essential to determine which drugs and treatments genuinely help patients, and which do more harm than good. However, the outcomes of around half of all clinical trials are never made public. Globally, an estimated $85 billion in medical research funding is wasted every year because the results of medical research never see the light of day. Since the 1980s, thousands of patients have died because clinical trial results that contained early warning signs were not made public. Clinical trials whose results remain hidden waste precious medical research funding, endanger patients and public health, and slow down the development of effective treatments.

Since 2014, European Union rules have required companies and universities running drug trials (so-called CTIMPs) to make trial results public on the European trial registry EudraCT within a maximum of 12 months of trial completion. However, over 4,000 completed drug trials are currently verifiably missing results on the registry. Universities and smaller companies in particular tend to have low compliance rates.

Worldwide, hundreds of clinical trials are currently underway to find drugs that could help to end the COVID-19 pandemic. This poses significant challenges for the medical research community – challenges that are exacerbated by the underfunding and weak management of trial registries:

- Information on who is currently researching what is crucial to research funders so that they can avoid duplication of efforts and identify gaps where further research is required. However, many trials that have been suspended, terminated early or completed are falsely listed as ongoing on EudraCT, providing a ***misleading picture of current research activity***. Because national regulators are not updating the status of clinical trials as required by EU rules, funders cannot determine how many – let alone which – COVID-19 trials in Europe are currently in progress.

- In many European countries, the 'first wave' of infections was less severe than originally feared, so many trials will not succeed in recruiting the originally planned number of patients. Some of these trials will therefore be ***terminated early***, after treating only a small number of patients. Medical journals may not be interested in publishing the results of these trials, especially if they found that the drug in question did not benefit patients, even though such trials can make a valuable contribution to the overall evidence base. Posting these results onto EudraCT in line with existing rules would ensure that the data from terminated trials is made public and does not become research waste.

- Many COVID-19 trials are too small to be able to conclusively prove (or disprove) that the drug being tested helps patients to recover. Accurately assessing the efficacy and safety of some drugs may thus require ***combining the results of multiple trials***. However, a recent study showed that that the results of over a quarter of all trials run by German universities remain completely unknown. The EU requirement to upload results onto the registry aims to overcome this problem of 'publication bias', but the national regulators responsible for enforcing the rules have so far failed to impose any sanctions, resulting in low compliance.

- Articles published in medical journals often do not give a complete and accurate account of clinical trial outcomes because their authors use a variety of scientifically unsound tricks (such as outcome switching, post hoc subgroup analyses, p-hacking and spin) to make their findings look more exciting. Results uploaded onto trial registries do not suffer from these ***evidence distortions***, and often provide better data on drug harms and secondary outcomes in particular.

Risk of research waste

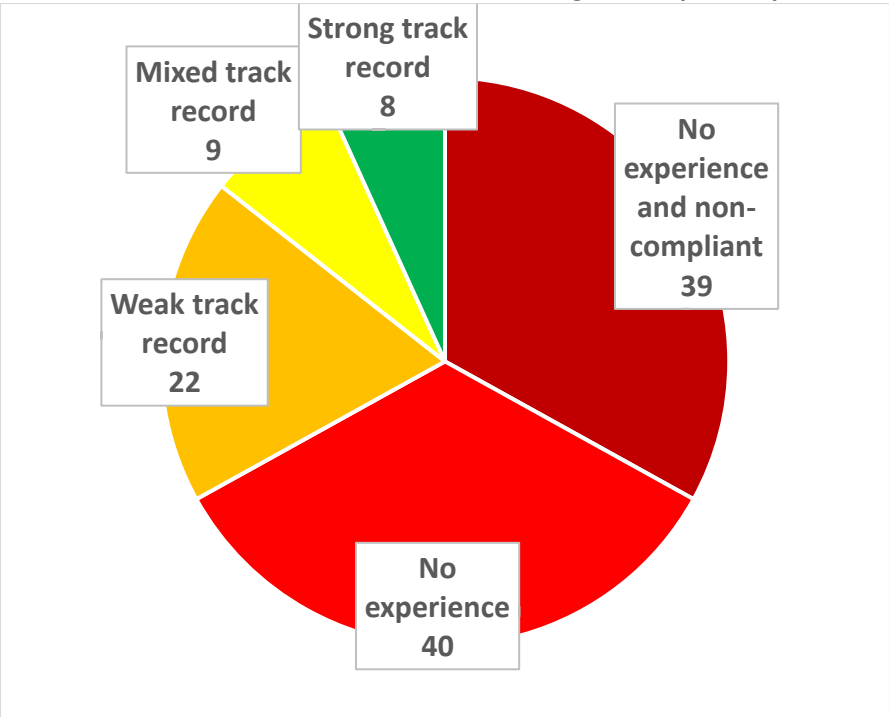
A review of the companies and universities sponsoring[1] the 118 COVID-19 drug trials in Europe shows that most have no experience in uploading clinical trial results onto the European trial registry EudraCT. A total of 79 COVID-19 trials are at high risk of research waste because their sponsors have never uploaded a result onto EudraCT:

- Out of these, the 39 trials run by sponsors that are currently in violation of EU reporting rules are of particular concern, as these sponsors combine a track record of disregarding transparency requirements with a lack of experience.
- The 40 trials run by sponsors that have no track record are also at high risk. Many of these sponsors have never before conducted a drug trial of this type ('CTIMP'), and studies consistently show that such low-volume trial sponsors tend to perform especially weakly on trial reporting. These sponsors may be unaware of their obligations, and/or may struggle to manage the complex reporting process without external guidance and support.

A further 22 trials are run by sponsors with a weak track record (less than 50% of results uploaded). The sponsors of 9 trials have a mixed compliance record (52-88% of results uploaded).

Only 8 COVID-19 drug trials are being run by sponsors that are fully (or nearly fully) compliant with EU clinical trial transparency rules, providing confidence that their results will be made public.[2]

Chart 1: Research waste risk for 118 COVID drug trials: sponsor performance and experience



[1] Note: A trial 'sponsor' is the entity running the trial, not the entity that finances the trial. Under EU rules, it is the trial sponsor – not the trial funder – that is responsible for making trial results public.

[2] COVID-19 trial sponsors with a perfect or near perfect compliance record are: Chelsea and Westminster Hospital NHS Foundation Trust (UK), CHU d'Angers (France), Guy's and St Thomas' NHS Foundation Trust (UK), Institute of Tropical Medicine Antwerp (Belgium), Novartis Pharmaceuticals (Switzerland), Sanofi (France), Synairgen Research Limited (UK), and University of Dundee (UK). Note: CHU d'Angers (France) appears fully compliant on the Tracker, but its actual performance is likely to be weaker as many of its trials that are listed as 'ongoing' were probably completed long ago.

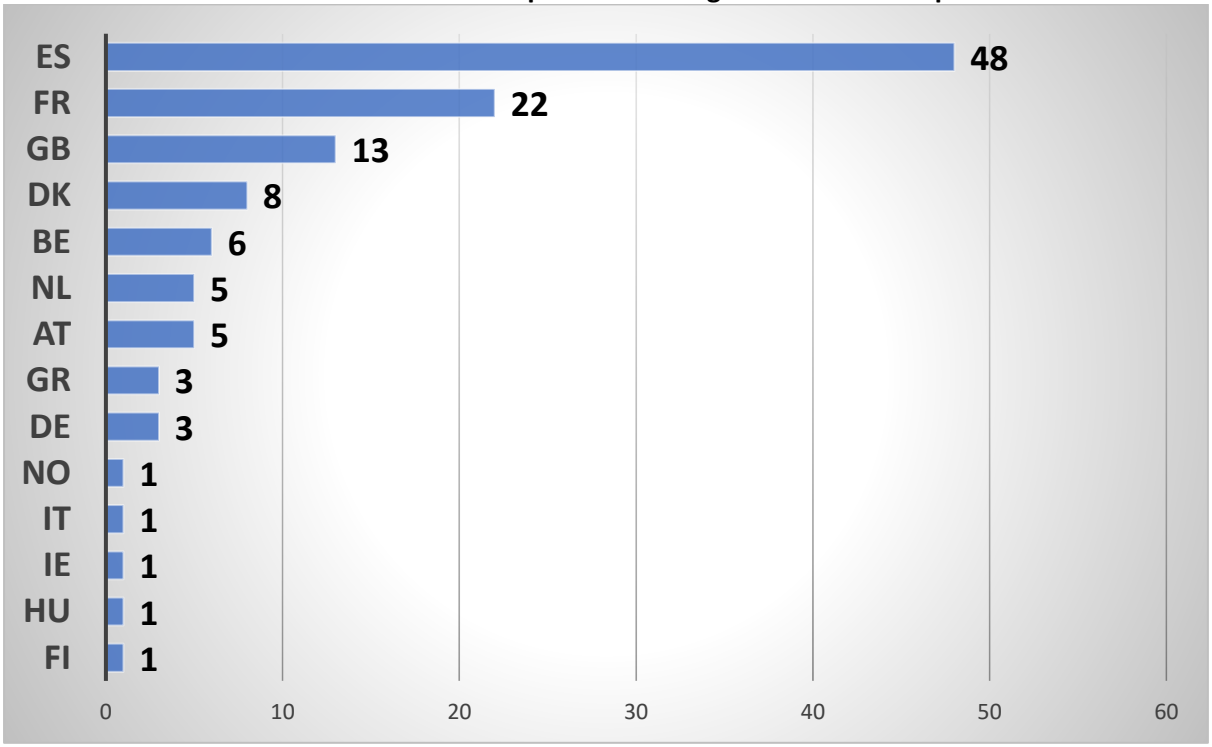
National regulator portfolios

According to European Union transparency rules, clinical trial sponsors are obliged to make the results of their trials public on the European database EudraCT within a maximum of 12 months of trial completion. National regulators are responsible for enforcing these rules, but to date, only the Danish regulator has announced sanctions. In addition, many national regulators provide little guidance or support to help trial sponsors to navigate the EudraCT system. As a result, over 4,000 completed clinical trials are verifiably missing results on the database, in clear violation of disclosure requirements.

In addition, national regulators are (following notification by the trial sponsor) responsible for updating the status of a trial once is has been suspended, terminated or completed. Keep registry records up to date is vital because registry users can then determine which trials are really going ahead and when they are likely to complete. Access to this information helps to prevent needless (and costly) duplication of efforts, and helps to identify gaps in research that require further trials to be launched. Past research by TranspariMED has shown that many – but not all – national regulators fail to perform the required updates. For example, as of late 2019, the Dutch regulator had only marked 25 out of 1,160 clinical trials run by Dutch universities as completed, an implausibly low number.

National regulators should proactively reach out to the sponsors running COVID-19 trials to encourage and support rapid results reporting and regular status updates. The data below show that the workload required is very small. Only the regulators in Spain (48 trials), France (22) and UK (13) have more than ten COVID-19 drug trials in their portfolios.

Chart 2: Number of COVID-19 clinical trials per national regulator in the European Union



Over the coming months, all EU Member States will incorporate the EU Clinical Trial Regulation into their national legislation. This process includes determining how violations of the regulation will be sanctioned. Policy makers should take advantage of this policy window to adopt detailed sanctions mechanisms to ensure that in future, all trial sponsors keep their registry entries up to date and make trial results public as required by law.

Example of COVID-19 trials at high risk of becoming research waste

This section briefly discusses two COVID-19 clinical trials in Spain to illustrate how weak institutional research governance, research funder complacency and national regulator inaction can combine to create a high risk of research waste. While these examples focus on only one sponsor, funder and regulator, the dynamics discussed below are common in many – though not all – European countries.

- **The COVID trials**

Clinical trial 2020-001409-21 aims to enrol 120 Spanish patients with COVID-19 to discover whether the drug defibrotide can help to prevent and treat respiratory distress and cytokine release syndrome. Trial 2020-001511-25 aims to enrol 102 Spanish patients with COVID-19 to find out whether the drug colchicine can prevent inflammations and improves clinical outcomes.

- **The trial sponsor**

Both trials are run by the Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS), a public sector non-profit foundation set up by the Spanish region of Murcia. As trial sponsor, the FFIS is responsible for keeping data about these trials on the European registry up to date, and for uploading their results within 12 months of trial completion.

- **Weak sponsor track record**

FFIS' past track record of disclosure and data management inspires little confidence. It currently has 17 drug trials in its portfolio. One of those trials was completed in 2015, but its results are still missing from the registry. A further 13 trials are still listed as 'ongoing' even though some of them seem likely to have been completed years ago. One trial is listed as 'completed,' but it appears that FFIS failed to provide a completion date.

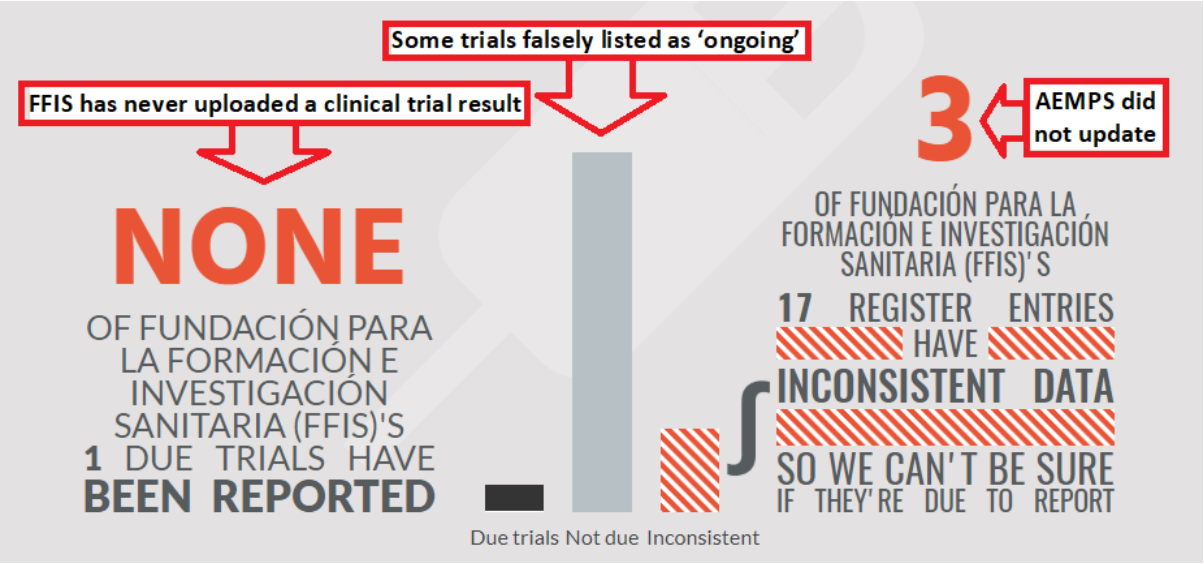


Image source: EU Trials Tracker

- **Lack of regulatory diligence**

The two remaining FFIS trials have obvious data inconsistencies that make it impossible to determine whether they are ongoing or have been completed.[3]

This suggests that the responsible Spanish national regulator, Agencia Española de Medicamentos y Productos Sanitarios (AEMPS), is not adequately monitoring data quality.

Status	Trial ID	Title	Completion date
Listed as ongoing, but also has a completion date	2015-005180-16	Early vaginal progesterone for the prevention of spontaneous preterm birth in twins: A randomised, placebo controlled, double-blinded trial.	2019-12-01
Listed as ongoing, but also has a completion date	2015-005130-22	Randomised Controlled Trial with Pravastatin versus Placebo for Prevention of Pre-eclampsia	2016-12-20

Image source: EU Trials Tracker

- **Weak funder safeguards**

Both COVID-19 trials are funded by the Instituto de Salud Carlos III, a large Spanish public health research institute. A 2017 assessment of the institute's policies found significant gaps in its research waste safeguards.

The institute has so far not signed up to the WHO Joint Statement, which would commit it to addressing these gaps, and does not appear to audit whether its grantees make the results of their clinical trials public.

[3] Trial 2015-005180-16 is listed as 'completed' in Bulgaria with a "Global end of trial date" but is still listed as 'ongoing' in Spain, Italy, and Belgium.
Trial 2015-005130-22 is listed as 'prematurely ended' in Spain, but it also provides a "Global end of trial date," and it is still listed as 'ongoing' in Belgium and the UK.
This means that the field "Global end of trial date," which is supposed to state the date on which a trial has been completed in all countries, is being applied inconsistently. Either incorrect data was entered into the field by the Bulgarian/Spanish national regulators, or trials that have actually been completed are incorrectly listed as 'ongoing'.

List of COVID drug trials in Europe

The table below shows which national regulators are responsible for the 118 COVID drug trials that were registered on the European trial registry as of 19 May 2020, plus the identification number of each trial, the company or institution sponsoring each trial, and trial sponsors' current level of compliance with European trial reporting rules.

Out of the 118 COVID trials, 79 are at high risk of research waste because their sponsors have never uploaded a result onto EudraCT, either due to complete disregard for disclosure rules (sponsors of 39 trials, marked as "0"), or because their research portfolios are very small and none of their trials have yet become due to report results (sponsors of 40 trials, marked as "n/a").

Only eight sponsors have a perfect or near perfect (99-100%) track record of making the results of their clinical trials public on EudraCT as required by European transparency rules:

- Chelsea and Westminster Hospital NHS Foundation Trust (UK)
- CHU d'Angers (France)
- Guy's and St Thomas' NHS Foundation Trust (UK)
- Institute of Tropical Medicine Antwerp (Belgium)
- Novartis Pharmaceuticals (Switzerland)
- Sanofi (France)
- Synairgen Research Limited (UK)
- University of Dundee (UK)

Regulator	Trial number	Company or institution	Compliance
AT	EUCTR2020-001411-25-AT	Karyopharm Therapeutics Inc (USA)	0
AT	EUCTR2020-001244-26-AT	Medical University of Vienna	17
AT	EUCTR2020-001327-13-AT	Medical University of Vienna	17
AT	EUCTR2020-001206-35-AT	Medical University Innsbruck	19
AT	EUCTR2020-001329-30-AT	Massachusetts General Hospital (USA)	n/a
BE	EUCTR2020-001254-22-BE	University Hospital, Ghent	18
BE	EUCTR2020-001500-41-BE	University Hospital, Ghent	18
BE	EUCTR2020-001243-15-BE	UZLeuven	52
BE	EUCTR2020-001614-38-BE	UZLeuven	52
BE	EUCTR2020-001417-21-BE	Institute of Tropical Medicine	100
BE	EUCTR2020-001770-30-BE	CHU Ambroise Paré	n/a
DE	EUCTR2020-001408-41-DE	University Hospital, Freiburg	13
DE	EUCTR2020-001632-10-DE	University Hospital, Heidelberg	58
DE	EUCTR2020-001310-38-DE	DRK-Bluspendedienst Baden-Württemberg - Hessen gGmbH	n/a
DK	EUCTR2020-001198-55-DK	Chronic Obstructive Pulmonary Disease Trial Network	0
DK	EUCTR2020-001296-33-DK	Copenhagen University Hospital, Capital Region Blood Bank	0
DK	EUCTR2020-001888-90-DK	University of Southern Denmark	0
DK	EUCTR2020-001257-51-DK	Rigshospitalet, Denmark	13
DK	EUCTR2020-001363-85-DK	Odense University Hospital	15
DK	EUCTR2020-001275-32-DK	The Parker Institute (Bispebjerg and Frederiksberg Hospital)	20
DK	EUCTR2020-001459-42-DK	Zealand University Hospital	25
DK	EUCTR2020-001420-34-DK	Aarhus University	29

Regulator	Trial number	Company or institution	Compliance
ES	EUCTR2020-001409-21-ES	Fundación para la Formación e Investigación Sanitarias Murcia	0
ES	EUCTR2020-001160-28-ES	Medica Scientia Innovation Research S.L. (MEDSIR)	0
ES	EUCTR2020-001437-12-ES	Vall d'Hebron Research Institute (VHIR)	0
ES	EUCTR2020-001413-20-ES	Fundació Clínic per a la Recerca Biomèdica	0
ES	EUCTR2020-001442-19-ES	Institut de Recerca Hospital de la Santa Creu i Sant Pau	0
ES	EUCTR2020-001290-74-ES	Consorci Parc de Salut Mar (PSMAR)	0
ES	EUCTR2020-001530-35-ES	Fundación Inv. Biomédica Hospital Universitario La Paz (FIBHU	0
ES	EUCTR2020-001511-25-ES	Fundación para la Formación e Investigación Sanitarias Murcia	0
ES	EUCTR2020-001440-26-ES	Fundación Pública Andaluza Sevilla (FISEVI)	0
ES	EUCTR2020-001827-15-ES	Navarrabiomed - Fundación Miguel Servet	0
ES	EUCTR2020-001722-66-ES	Fundació Clínic per a la Recerca Biomèdica	0
ES	EUCTR2020-001505-22-ES	Banc de Sang i Teixits	0
ES	EUCTR2020-001825-29-ES	Navarrabiomed - Fundación Miguel Servet	0
ES	EUCTR2020-001474-29-ES	Clínica Universidad de Navarra	0
ES	EUCTR2020-001156-18-ES	Fundación Inv. Biomédica Hospital Universitario La Paz (FIBHU	0
ES	EUCTR2020-001255-40-ES	Clínica Universidad de Navarra	0
ES	EUCTR2020-000705-86-ES	Vall d'Hebron University Hospital	0
ES	EUCTR2020-001696-32-ES	Instituto Grifols, S.A	88
ES	EUCTR2020-001953-36-ES	Instituto Grifols, S.A	88
ES	EUCTR2020-001194-69-ES	Félix Gutiérrez Rodero	n/a
ES	EUCTR2020-001565-37-ES	ISGlobal (Bercelona Institute for Global Health)	n/a
ES	EUCTR2020-001421-31-ES	Sociedad Espanola de Farmacia Hospitalaria	n/a
ES	EUCTR2020-001606-33-ES	Instituto Investigacin Sanitario Biocruces Bizkaia	n/a
ES	EUCTR2020-001262-11-ES	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	n/a
ES	EUCTR2020-001321-31-ES	Hospital Universitario de Fuenlabrada	n/a
ES	EUCTR2020-001682-36-ES	CITOSPIN S.L.	n/a
ES	EUCTR2020-001266-11-ES	Fundación Instituto de Inv. Sanitaria Fundación Jimenez Diaz	n/a
ES	EUCTR2020-001765-37-ES	Institut Català d'Oncologia	n/a
ES	EUCTR2020-001379-34-ES	Instituto de Investigación Sanitaria INCLIVA	n/a
ES	EUCTR2020-001385-11-ES	Plan Nacional sobre el Sida (PNS)	n/a
ES	EUCTR2020-001307-16-ES	Fundación para la Inv. Biomédica Hospital Ramón y Cajal	n/a
ES	EUCTR2020-001587-29-ES	ISGlobal (Bercelona Institute for Global Health)	n/a
ES	EUCTR2020-001634-36-ES	Rosario García de Vicuña	n/a
ES	EUCTR2020-001689-12-ES	Montreal Heart Institute (Canada)	n/a
ES	EUCTR2020-001622-64-ES	Dr. Ana Pueyo Bastida [individual investigator]	n/a
ES	EUCTR2020-001717-20-ES	Fundación para la Investigación Biomédica de Córdoba	n/a
ES	EUCTR2020-001541-39-ES	Fundación para la Investigación Biomédica de Córdoba	n/a
ES	EUCTR2020-001618-39-ES	Oryzon Genomics S. A.	n/a
ES	EUCTR2020-002032-69-ES	Fundación para la Inv. Biomédica Hospital Ramón y Cajal	n/a
ES	EUCTR2020-001994-66-ES	Fundació Assistencial Mútua Terrassa	n/a
ES	EUCTR2020-001891-14-ES	Fundación Neumosur	n/a
ES	EUCTR2020-001697-30-ES	Navarrabiomed - Fundación Miguel Servet	n/a
ES	EUCTR2020-001603-16-ES	Instituto de Investigación Marqués de Valdecilla (IDIVAL)	n/a
ES	EUCTR2020-001659-42-ES	Fundación para la Investigación Biomédica de Córdoba	n/a
ES	EUCTR2020-001536-98-ES	Mútua Terrassa University Hospital	n/a
ES	EUCTR2020-001364-29-ES	Red Andaluza de Diseño y Traslación de Terapias Avanzadas	n/a
ES	EUCTR2020-001934-37-ES	Instituto de Investigación Marqués de Valdecilla (IDIVAL)	n/a
ES	EUCTR2020-002123-11-ES	Tatiana Cobo Ibez [individual investigator]	n/a

FI	EUCTR2020-001784-88-FI	University of Helsinki	22
FR	EUCTR2020-001281-11-FR	CHU de Saint Etienne	0
FR	EUCTR2020-001435-27-FR	CHU de Bordeaux	0
FR	EUCTR2020-001406-27-FR	University Hospital, Montpellier	0
FR	EUCTR2020-001686-36-FR	Assistance Publique – Hôpitaux de Marseille	0
FR	EUCTR2020-001823-15-FR	CHU de Saint Etienne	0
FR	EUCTR2020-001768-27-FR	Centre Hospitalier de Versailles	0
FR	EUCTR2020-001734-36-FR	CHU de Tours	0
FR	EUCTR2020-001709-21-FR	CHU de Nancy	0
FR	EUCTR2020-001598-66-FR	Centre Hospitalier de Versailles	0
FR	EUCTR2020-001635-27-FR	AB Science	0
FR	EUCTR2020-001766-11-FR	Assistance Publique – Hôpitaux de Marseille	0
FR	EUCTR2020-001381-11-FR	Assistance Publique – Hôpitaux de Paris	6
FR	EUCTR2020-001301-23-FR	Assistance Publique – Hôpitaux de Paris	6
FR	EUCTR2020-001457-43-FR	Assistance Publique – Hôpitaux de Paris	6
FR	EUCTR2020-001678-31-FR	Assistance Publique – Hôpitaux de Paris	6
FR	EUCTR2020-001909-22-FR	Assistance Publique – Hôpitaux de Paris	6
FR	EUCTR2020-001700-42-FR	Assistance Publique – Hôpitaux de Paris	6
FR	EUCTR2020-001271-33-FR	CHU Angers	100
FR	EUCTR2020-000890-25-FR	Fondation Méditerranée Infection (FMI) - IHU	n/a
FR	EUCTR2020-001492-33-FR	L'Hôpital Fondation Adolphe de Rothschild	n/a
FR	EUCTR2020-001333-13-FR	Groupe Hospitalier Paris Saint-Joseph	n/a
FR	EUCTR2020-001723-13-FR	Groupe Hospitalier Paris Saint-Joseph	n/a
GB	EUCTR2020-001721-31-GB	Hampshire Hospitals NHS Foundation Trust	0
GB	EUCTR2020-001736-95-GB	University Hospital Southampton NHS Foundation Trust	18
GB	EUCTR2020-001448-24-GB	University of Birmingham	69
GB	EUCTR2020-001684-89-GB	University of Birmingham	69
GB	EUCTR2020-001228-32-GB	University of Oxford	84
GB	EUCTR2020-001740-26-GB	University of Oxford	84
GB	EUCTR2020-001270-29-GB	Sanofi (France)	99
GB	EUCTR2020-001023-14-GB	Synairgen Research Limited	100
GB	EUCTR2020-001643-13-GB	University of Dundee	100
GB	EUCTR2020-001449-38-GB	Chelsea and Westminster Hospital NHS Foundation Trust	100
GB	EUCTR2020-001777-71-GB	Guy's and St Thomas' NHS Foundation Trust	100
GB	EUCTR2020-001370-30-GB	Novartis Pharmaceuticals (Switzerland)	100
GB	EUCTR2020-001786-36-GB	Revimmune (France)	n/a
GR	EUCTR2020-001466-11-GR	Hellenic Institute for the Study of Sepsis	0
GR	EUCTR2020-001882-36-GR	Hellenic Institute for the Study of Sepsis	0
GR	EUCTR2020-001345-38-GR	Uni-Pharma Kleon Tsetis Pharmaceutical Laboratories S.A.	0
HU	EUCTR2020-001783-28-HU	National Kornyi Institute of Pulmonology	n/a
IE	EUCTR2020-001391-15-IE	Royal College of Surgeons Ireland	33
IT	EUCTR2020-001386-37-IT	Azienda Unit Sanitaria Locale Reggio Emilia	n/a
NL	EUCTR2020-001236-10-NL	UMC Amsterdam	0
NL	EUCTR2020-001335-28-NL	InflaRx GmbH (Germany)	0
NL	EUCTR2020-001375-32-NL	University Medical Center Groningen	0
NL	EUCTR2020-000919-69-NL	UMC Utrecht	11
NL	EUCTR2020-001527-14-NL	Erasmus MC	25
NO	EUCTR2020-001010-38-NO	Akershus University Hospital	n/a

Methodology

Authorship

This report was researched and authored by Till Bruckner, founder of TranspariMED. All errors are those of the author alone. Author contact: tillbruckner@gmail.com

Cohort selection

A list of all of COVID trials listed on the global ICTRP was obtained by downloading the dataset of the COVID Trials Tracker, which in turn aggregates data from the global WHO trial registry network. Out of that dataset, the author then extracted the 118 trials that had been registered on the European trial registry EudraCT. This registry exclusively contains drug trials, so-called CTIMPs.

The dataset was downloaded on 29 May 2020. At that point, the Tracker had last been updated on 19 May 2020.

Sponsor reporting performance

Using the search function of the EU Trials Tracker, the author then determined the clinical reporting performance of each trial's sponsoring institution. This performance data was manually extracted between 29 May and 01 June 2020. During that time period, the EU Trials Tracker displayed sponsor performance based on EudraCT data that had been scraped on 01 May 2020.

Some COVID trial sponsors had already registered one or more trials, but none of the trials in their portfolios were due to report results yet, so their reporting performance remains to be seen. Their reporting performance was coded as "n/a".

In the case of eight trials, the author was initially unable to determine sponsor performance using this methodology:

- Differences in the sponsor names listed by the two trackers made determining the sponsor performance of 3 trials by searching the EU Trials Tracker difficult. The names of the relevant sponsors used by the EU Trials Tracker were identified with the assistance of Nicholas DeVito, who manages both trackers. The author subsequently manually extracted their performance data. Trials: 2020-001010-38-NO, 2020-001417-21-BE, 2020-001345-38-GR.
- In 3 cases, the sponsoring institution had not previously registered any trials on EudraCT, and had only registered its new COVID trial in the time window 01-19 May 2020. A renewed search of the EU Trials Tracker following its monthly update on 01 June 2020 identified those sponsors, and their past trial reporting performance was coded as not applicable, or "n/a". Trials: 2020-001786-36-GB, 2020-001783-28-HU, 2020-001891-14-ES.
- In the case of one trial, 2020-001275-32-DK, the sponsor name given on EudraCT is "The Parker Institute (Bispebjerg and Frederiksberg Hospital)". Those two hospitals are separately listed by the EU Trials Tracker: Bispebjerg has posted 20% of its due results, while Frederiksberg has a reporting rate of 0%. This trial was coded using the higher 20% performance figure.
- A further trial, EUCTR 2020-002123-11-ES, appears to have been sponsored by an individual investigator with no previous track record on EudraCT. This was coded as "n/a" in keeping with the overall methodology.

Data quality

The data in this report includes all Covid trials registered on EudraCT as of 19 May 2020, and provides sponsor performance data that was accurate as of 01 May 2020.

The COVID Trials Tracker database and the EU Trials Tracker are both managed by EBM Data Lab (University of Oxford, UK). The COVID Trials Tracker database is publicly accessible and can be cross-checked against EudraCT data. The EU Trials Tracker has a strong and consistent track record of providing reliable data on clinical trial reporting; the performance data it provides can be cross-checked against EudraCT data. Thus, both the cohort selection and the performance data used in this report can be independently replicated by third parties.

Limitations

This report exclusively covers drug trials conducted in Europe, so-called CTIMPs, that were registered on EudraCT. Thus, it excludes trials of non-drug interventions such as medical devices (e.g. respirators), drug trials conducted wholly outside Europe, drug trials that were never registered in the first place, and observational studies. It also excludes CTIMPs registered after 19 May 2020.

Sponsor performance data generated by the EU Trials Tracker often overestimates sponsors' reporting performance because it exclusively draws on EudraCT registry data. Thus, if a trial was completed long ago but is still falsely listed as 'ongoing' in EudraCT, that trial is not flagged by the Tracker as overdue. The prevalence of such 'false ongoing' trials appears to vary strongly from one country to the next, but there is currently no comparative data on national regulators' performance in performing updates.

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