BIH Berlin Institute of Health @Charité

BIH Lecture Series: Frontiers in Translational Medicine - Scientific and Structural Challenges

Maximizing the Impact of Medical Journal Requirements for Clinical Trial Data-Sharing

Florian Naudet (ORCID: 0000-0003-3760-3801)

CHU Rennes

UNIVERSITÉ DE RENNES 1

Twitter : @NaudetFlorian

e-mails : florian.naudet@chu-rennes.fr / floriannaudet@gmail.com

BIH Lecture Series: Frontiers in Translational Medicine - Scientific and Structural Challenges

Maximizing the Impact of Medical Journal Requirements for Clinical Trial Data-Sharing

Florian Naudet (ORCID: 0000-0003-3760-3801), Maximilian Siebert† (ORCID: 0000-0003-4385-5773), Claude Pellen† (ORCID: 0000-0001-8712-0766), Jeanne Gaba† (ORCID: 0000-0002-1440-0895), Cathrine Axfors (ORCID: 0000-0002-2706-1730), Ioana Cristea (ORCID: 0000-0002-9854-7076), Valentin Danchev (ORCID: 0000-0002-7563-0168), Ulrich Mansmann (ORCID: 0000-0002-9955-8906), Christian Ohmann (0000-0002-5919-1003), Joshua D. Wallach (ORCID: 0000-0002-2816-6905), David Moher (ORCID: 0000-0003-2434-4206), John P.A. Ioannidis (ORCID: 0000-0003-3118-6859)

Twitter : @NaudetFlorian

e-mails : florian.naudet@chu-rennes.fr / floriannaudet@gmail.com

Apetizer

THE LANCET

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia

Denis Y Logunov, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatulin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg*

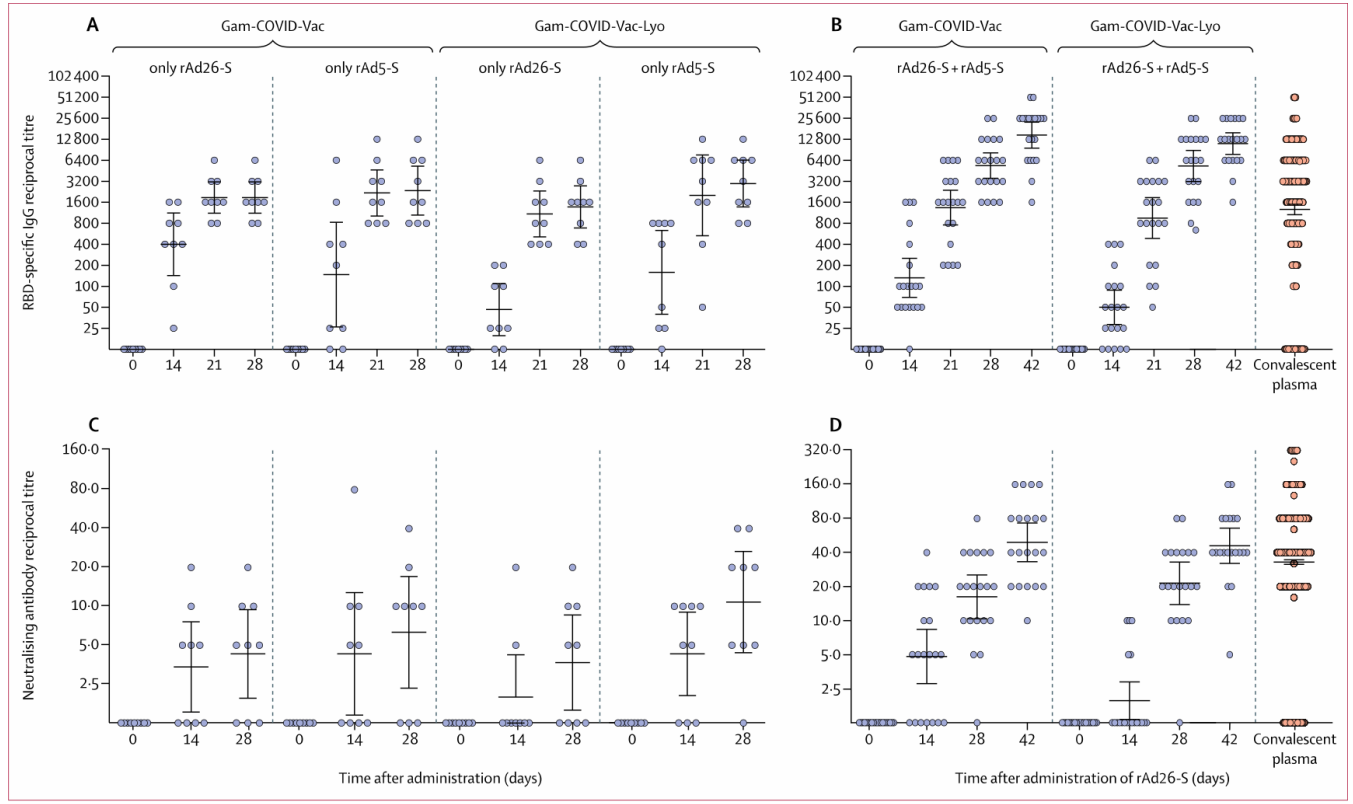


Figure 2: **Humoral immune response**
Data are geometric mean titres and 95% CIs. (A) RBD-specific antibodies on days 0, 14, 21, and 28, as measured by ELISA, in participants vaccinated with rAd26-S or rAd5-S only. (B) RBD-specific antibodies on days 0, 14, 21, 28, and 42, as measured by ELISA, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. (C) Neutralising antibodies on days 0, 14, and 28, as measured by neutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S or rAd5-S only. (D) Neutralising antibodies on days 0, 14, 28, and 42, as measured by microneutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. RBD-specific IgGs and neutralising antibodies of in convalescent plasma are also shown in (B) and (D). Gam-COVID-Vac=frozen vaccine formulation. Gam-COVID-Vac-Lyo=lyophilised vaccine formulation. rAd26-S=recombinant adenovirus type 26 carrying the gene for SARS-CoV-2 full-length glycoprotein S. rAd5-S=recombinant adenovirus type 5 carrying the gene for SARS-CoV-2 full-length glycoprotein S. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. RBD=receptor-binding domain. TCID50=50% tissue culture infective dose.

THE LANCET

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia

Denis Y Logunov, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatulin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg*

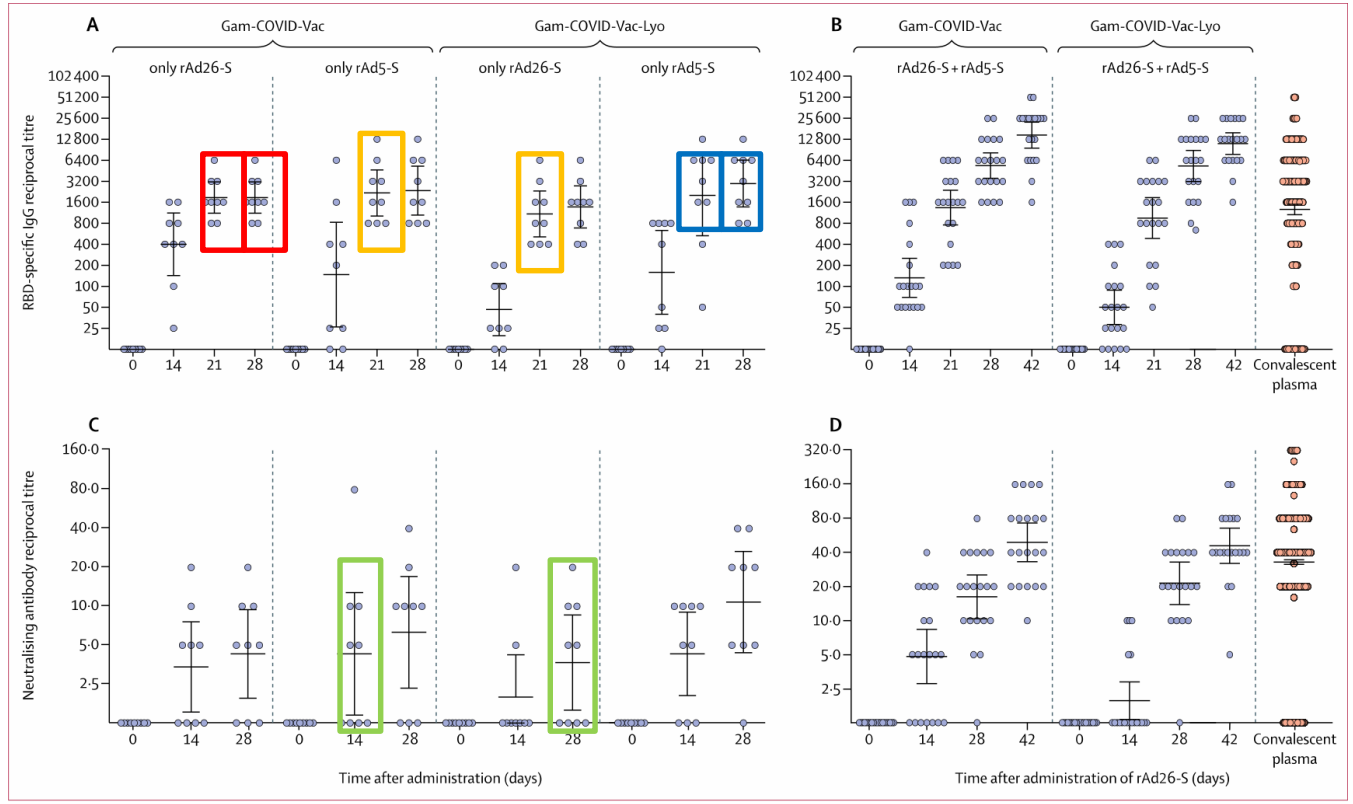


Figure 2: **Humoral immune response**
Data are geometric mean titres and 95% CIs. (A) RBD-specific antibodies on days 0, 14, 21, and 28, as measured by ELISA, in participants vaccinated with rAd26-S or rAd5-S only. (B) RBD-specific antibodies on days 0, 14, 21, 28, and 42, as measured by ELISA, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. (C) Neutralising antibodies on days 0, 14, and 28, as measured by neutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S or rAd5-S only. (D) Neutralising antibodies on days 0, 14, 28, and 42, as measured by microneutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. RBD-specific IgGs and neutralising antibodies of in convalescent plasma are also shown in (B) and (D). Gam-COVID-Vac=frozen vaccine formulation. Gam-COVID-Vac-Lyo=lyophilised vaccine formulation. rAd26-S=recombinant adenovirus type 26 carrying the gene for SARS-CoV-2 full-length glycoprotein S. rAd5-S=recombinant adenovirus type 5 carrying the gene for SARS-CoV-2 full-length glycoprotein S. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. RBD=receptor-binding domain. TCID50=50% tissue culture infective dose.

Safety and efficacy of the Russian COVID-19 vaccine: more information needed

**Enrico Bucci, Konstantin Andreev, Anders Björkman, Raffaele Adolfo Calogero, Ernesto Carafoli, Piero Carninci, Paola Castagnoli, Andrea Cossarizza, Cristina Mussini, Philippe Guerin, Brian Lipworth, Gianluca Sbardella, Teresa Stocki, Loretta Tuosto, Christoffer van Tulleken, Antonella Viola*
enrico.bucci@resis-srl.com

We feel that a detailed answer and rendering the actual data available would considerably strengthen the significance of the study findings.

THE LANCET

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia

Denis Y Logunov, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatulin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg*

Data sharing

Individual participant data will be made available on request, directed to the corresponding author (DYL). After approval of a proposal, data can be shared through a secure online platform.

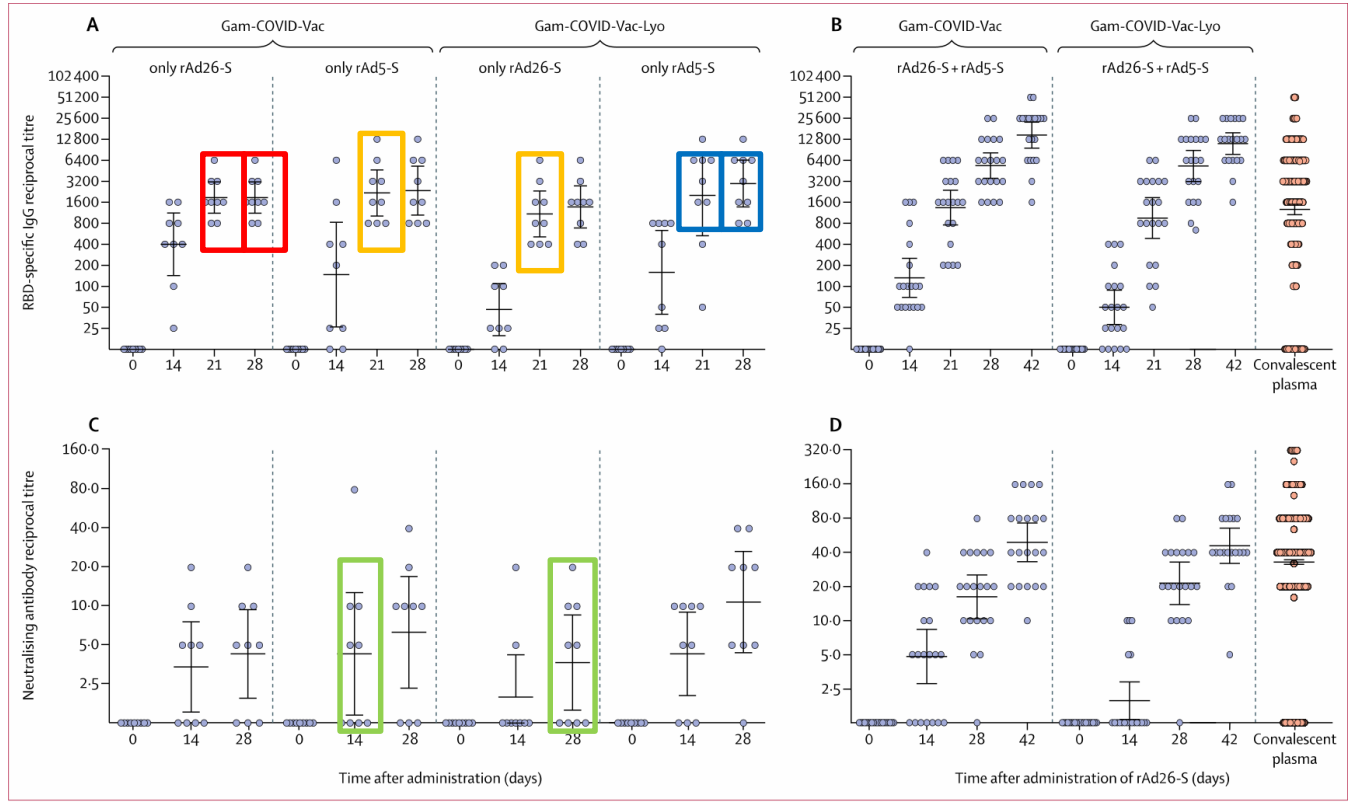


Figure 2: **Humoral immune response**

Data are geometric mean titres and 95% CIs. (A) RBD-specific antibodies on days 0, 14, 21, and 28, as measured by ELISA, in participants vaccinated with rAd26-S or rAd5-S only. (B) RBD-specific antibodies on days 0, 14, 21, 28, and 42, as measured by ELISA, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. (C) Neutralising antibodies on days 0, 14, and 28, as measured by neutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S or rAd5-S only. (D) Neutralising antibodies on days 0, 14, 28, and 42, as measured by microneutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. RBD-specific IgGs and neutralising antibodies of in convalescent plasma are also shown in (B) and (D). Gam-COVID-Vac=frozen vaccine formulation. Gam-COVID-Vac-Lyo=lyophilised vaccine formulation. rAd26-S=recombinant adenovirus type 26 carrying the gene for SARS-CoV-2 full-length glycoprotein S. rAd5-S=recombinant adenovirus type 5 carrying the gene for SARS-CoV-2 full-length glycoprotein S. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. RBD=receptor-binding domain. TCID50=50% tissue culture infective dose.

THE LANCET

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia

Denis Y Logunov, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatulin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg*

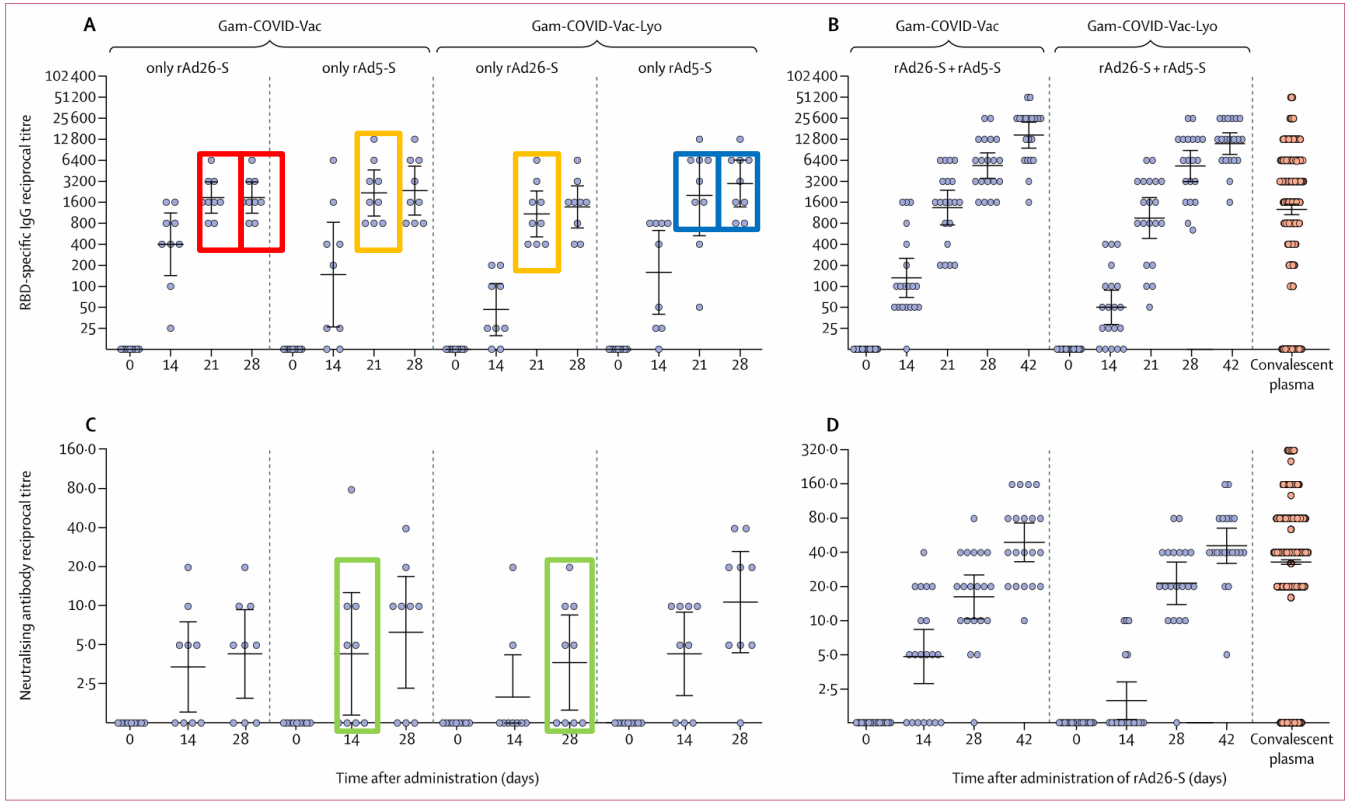


Figure 2: **Humoral immune response**
Data are geometric mean titres and 95% CIs. (A) RBD-specific antibodies on days 0, 14, 21, and 28, as measured by ELISA, in participants vaccinated with rAd26-S or rAd5-S only. (B) RBD-specific antibodies on days 0, 14, 21, 28, and 42, as measured by ELISA, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. (C) Neutralising antibodies on days 0, 14, and 28, as measured by neutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S or rAd5-S only. (D) Neutralising antibodies on days 0, 14, 28, and 42, as measured by microneutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. RBD-specific IgGs and neutralising antibodies of in convalescent plasma are also shown in (B) and (D). Gam-COVID-Vac=frozen vaccine formulation. Gam-COVID-Vac-Lyo=lyophilised vaccine formulation. rAd26-S=recombinant adenovirus type 26 carrying the gene for SARS-CoV-2 full-length glycoprotein S. rAd5-S=recombinant adenovirus type 5 carrying the gene for SARS-CoV-2 full-length glycoprotein S. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. RBD=receptor-binding domain. TCID50=50% tissue culture infective dose.

Safety and efficacy of the Russian COVID-19 vaccine: more information needed

Authors' reply

**Denis Y Logunov, Inna V Dolzhikova, Amir I Tukhvatullin, Dmitry V Shcheblyakov*
ldenisy@gmail.com

We confirm that individual participant data will be made available on request to DYL and that after approval of a proposal, data can be shared through a secure online platform.

THE LANCET

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia

Denis Y Logunov, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatulin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg*

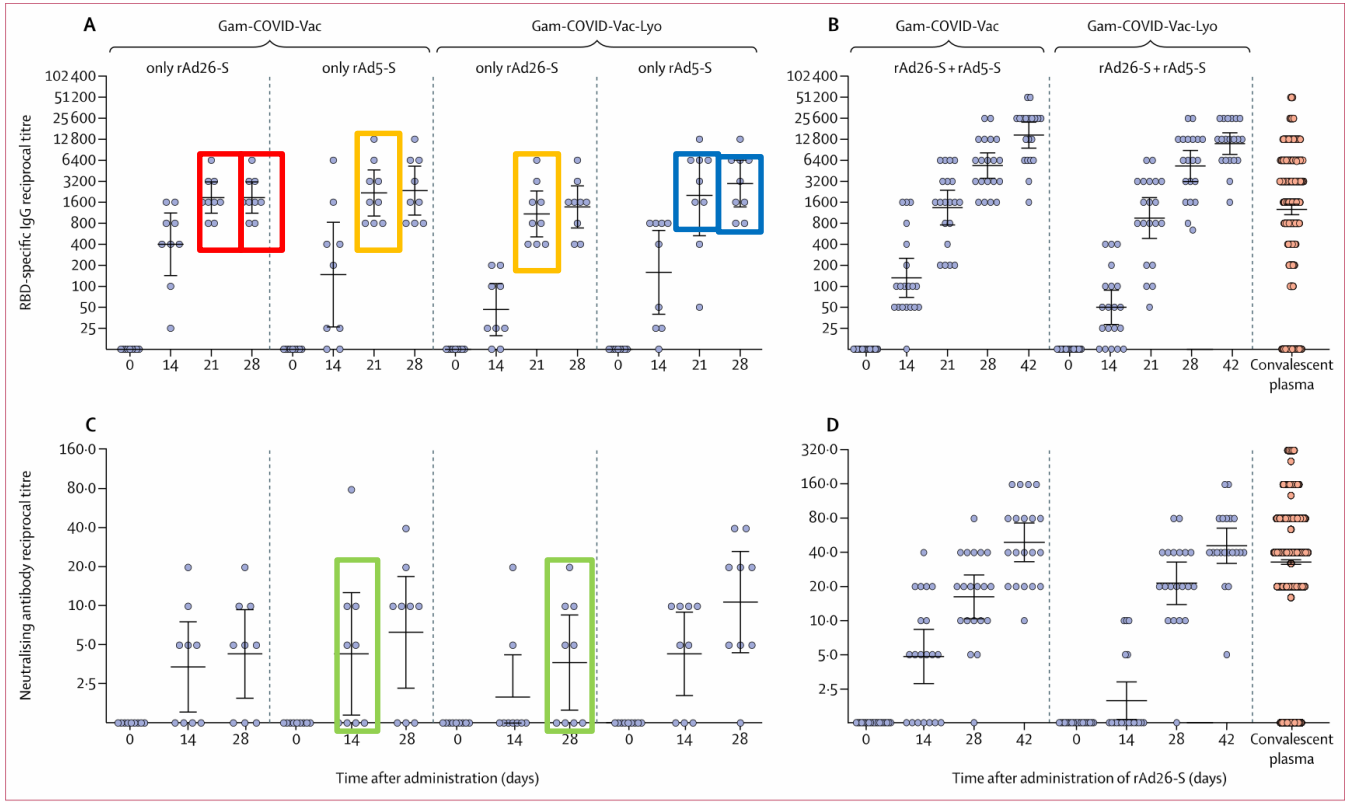


Figure 2: **Humoral immune response**
Data are geometric mean titres and 95% CIs. (A) RBD-specific antibodies on days 0, 14, 21, and 28, as measured by ELISA, in participants vaccinated with rAd26-S or rAd5-S only. (B) RBD-specific antibodies on days 0, 14, 21, 28, and 42, as measured by ELISA, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. (C) Neutralising antibodies on days 0, 14, and 28, as measured by neutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S or rAd5-S only. (D) Neutralising antibodies on days 0, 14, 28, and 42, as measured by microneutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. RBD-specific IgGs and neutralising antibodies of in convalescent plasma are also shown in (B) and (D). Gam-COVID-Vac=frozen vaccine formulation. Gam-COVID-Vac-Lyo=lyophilised vaccine formulation. rAd26-S=recombinant adenovirus type 26 carrying the gene for SARS-CoV-2 full-length glycoprotein S. rAd5-S=recombinant adenovirus type 5 carrying the gene for SARS-CoV-2 full-length glycoprotein S. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. RBD=receptor-binding domain. TCID50=50% tissue culture infective dose.

Accessing to anonymous data referring to your paper on Lancet 2021.pdf

Requesting data access Lancet paper Logunov et a 2020_1.pdf

Requesting data access Lancet paper Logunov et a 2020_2.pdf

Requesting data access Lancet paper Logunov et a 2020_3.pdf

Requesting data access Lancet paper Logunov et a 2020_4.pdf

GILLIBERT data sharing 1.pdf

GILLIBERT data sharing 2.pdf

NO RESPONSE

disproportionately higher numbers than have other groups in the United States. The panel determined that these groups are vulnerable chiefly for socio-economic reasons tied to systemic racism — for example, they have high-risk jobs and live in high-risk areas — and therefore addressed the request through this lens, without singling out the groups because of their identities.

"We really are trying to make sure that people of colour, who have been disproportionately impacted, will also have priority — but for the factors that put them at risk, not highlighting just their racial and ethnic make-up," says Helene Gayle, president and chief executive of the Chicago Community Trust in Illinois and a co-chair of the NASEM committee that drafted the proposal.

Faden says the recommendations acknowledge the current focus on racial injustice in the United States. "I was reading to see: does this report speak to the cultural moment in the United States, does it speak to racism and other forms of structural inequality? And it does," she says.

The WHO's strategic advisory group will continue to update its guidance, first to assign rankings to its priority groups, and then to include real data from vaccine trials, such as how effective a given vaccine is in older people. In the United States, the NASEM committee is due to issue a final plan in October. Ultimately, the CDC will consider these recommendations, among others, while developing its own vaccine-allocation plan for the country, expected later this year.

That will be the guidance that public-health departments, doctors and pharmacies throughout the United States should follow when handing out vaccines — assuming that one has been proved safe and people are willing to take it.

"We really are trying to make sure that people of colour will have priority."

Trump has been rooting for a vaccine to be ready by November, in time for the US presidential election — but a perception that the vaccine has been rushed could erode trust in it, says Sandra Crouse Quinn, a behavioural scientist at the Center for Health Equity at the University of Maryland in College Park. This could make vaccine-allocation plans less effective.

RESEARCHERS QUESTION RUSSIAN COVID VACCINE TRIAL RESULTS

Scientists flag trial findings that seem to be duplicated and call for access to the underlying data.

By Alison Abbott

A group of researchers have expressed concern about repetitive patterns of data in a paper describing early-phase clinical trials of Russia's coronavirus vaccine — the first jab worldwide to be approved for widespread use.

In an open letter to the study authors, who published the trial results[1] this month, the researchers highlight values that seem to be duplicated, and warn that the paper presents its results only as box plots, without providing a detailed breakdown of the data on which they are based. "While the research described in this study is potentially significant, the presentation of the data raises several concerns which require access to the original data to fully investigate", the letter says. It has been signed by almost 40 scientists (see go.nature.com/3kqvsqv).

The trials tested two slightly different viral-vector vaccines — which use genetically engineered adenoviruses to produce coronavirus proteins in the body — on 76 volunteers. The results indicated that the vaccine produced a strong immune response, and that side effects were limited to mild, short-term effects, such as irritation at injection sites or headaches, in a few people. In August, the Russian authorities approved the vaccine, called Sputnik V, for widespread use, and have said that it could be available to the general public within months. This fast-track approval caused consternation among researchers, who argued that the decision to roll out the vaccine before larger safety and efficacy trials had been completed was dangerously rushed.

Possible duplications

The open letter was posted on a blog run by molecular biologist Enrico Bucci, who heads a science-integrity company called Resis in Samone, Italy. Bucci says that he noticed irregularities in the paper soon after it was published (D. Y. Logunov *et al. Lancet* https://doi.org/gg96hq; 2020). For example, in one figure, in which the authors report their measurements of markers of a type of immune cell in the blood, many members of two groups of nine volunteers tested with different formulations of the vaccine seem to have the same levels. "The odds of this arising by coincidence are extremely small," Bucci says.

"To see such similar data patterns between unrelated measurements is really not likely," says Konstantin Andreev, who studies viral respiratory infections at Northwestern University at Evanston, Illinois. "These discrepancies are not minor." Andreev had been independently concerned about aspects of the clinical trial, and signed the open letter shortly after it was made public.

"We are not alleging scientific misconduct, but asking for clarification about how these apparently similar data points came about," says Bucci. "When we read reports that Russia had started to inject the vaccine into people outside clinical trials, we felt we had to speak out immediately." Late-phase clinical trials of the vaccine, which will involve tens of thousands of people, began on 26 August.

The paper's underlying data should be made available, says epidemiologist Michael Favorov, president of DiaPrep Systems, a diagnostics company in Atlanta, Georgia. "We have a lot of questionable data — in terms of its presentation," he says. "Maybe the data are good — we can't judge." He adds that the decision to publish the reports without the underlying data seems unusual. By contrast, when clinical studies involving a coronavirus vaccine that was developed by the pharmaceutical company AstraZeneca and the University of Oxford, UK, were published in the same journal, they were accompanied by a large amount of supplementary data that other researchers were able to scrutinize (P. M. Folegatti *et al. Lancet* **396**, 467–478; 2020).

The Russian paper's lead author, Denis Logunov at the Gamaleya National Research Centre for Epidemiology and Microbiology in Moscow, did not respond to requests for comment from *Nature*'s news team. But he told the Russian news outlet Meduza that he did not intend to respond to the open letter. He denied that there were errors in the publication, and stated that measured antibody levels were "exactly as they were presented" in the figures. He added that he was in contact with *The Lancet* and "was ready to clarify any issues".

The Lancet declined to comment on its policy for providing data in support of clinical trials that it publishes, but said that it "has invited the authors of the Russian vaccine study to respond to the questions raised in the open letter by Enrico Bucci", and that it would continue to follow the situation closely.

nature

disproportionately higher numbers than have other groups in the United States. The panel determined that these groups are vulnerable chiefly for socio-economic reasons tied to systemic racism — for example, they have high-risk jobs and live in high-risk areas — and therefore addressed the request through this lens, without singling out the groups because of their identities.

"We really are trying to make sure that people of colour, who have been disproportionately impacted, will also have priority — but for the factors that put them at risk, not highlighting just their racial and ethnic make-up," says Helene Gayle, president and chief executive of the Chicago Community Trust in Illinois and a co-chair of the NASEM committee that drafted

how effective a given vaccine is in older people. In the United States, the NASEM committee is due to issue a final plan in October. Ultimately, the CDC will consider these recommendations, among others, while developing its own vaccine-allocation plan for the country, expected later this year.

That will be the guidance that public-health departments, doctors and pharmacies throughout the United States should follow

"We really are trying to make sure that people of colour will have priority."

in Samone, Italy. Bucci says that he noticed irregularities in the paper soon after it was published (D. Y. Logunov *et al. Lancet* https://doi.org/gg96hq; 2020). For example, in one figure, in which the authors report their measurements of markers of a type of immune cell in the blood, many members of two groups of nine volunteers tested with different formulations of the vaccine seem to have the same levels. "The odds of this arising by coincidence are extremely small," Bucci says.

"To see such similar data patterns between unrelated measurements is really not likely," says Konstantin Andreev, who studies viral respiratory infections at Northwestern University at Evanston, Illinois. "These discrep-

The Lancet declined to comment on its policy for providing data in support of clinical trials that it publishes, but said that it "has invited the authors of the Russian vaccine study to respond to the questions raised in the open letter by Enrico Bucci", and that it would continue to follow the situation closely.

A clinical trials of Russia's coronavirus vaccine — the first jab worldwide to be approved for widespread use.

In an open letter to the study authors, who published the trial results[1] this month, the researchers highlight values that seem to be duplicated, and warn that the paper presents its results only as box plots, without providing a detailed breakdown of the data on which they are based. "While the research described in this study is potentially significant, the presentation of the data raises several concerns which require access to the original data to fully investigate", the letter says. It has been signed by almost 40 scientists (see go.nature.com/3kqvsqv).

The trials tested two slightly different

side effects were limited to mild, short-term effects, such as irritation at injection sites or headaches, in a few people. In August, the Russian authorities approved the vaccine, called Sputnik V, for widespread use, and have said that it could be available to the general public within months. This fast-track approval caused consternation among researche who argued that the decision to roll out vaccine before larger safety and efficacy tr had been completed was dangerously rush

Possible duplications

The open letter was posted on a blog run molecular biologist Enrico Bucci, who he a science-integrity company called Re

in Moscow, and ... spond to requests for comment from M...'s news team. But he told the Russian ne... utlet Meduza that he did not intend to res... d to the open letter. He denied that there w... rors in the publication, and stated that m... ed antibody levels were "exactly as they w... resented" in the

The Lancet and "was ready to clarify any issues".

The Lancet declined to comment on its policy for providing data in support of clinical trials that it publishes, but said that it "has invited the authors of the Russian vaccine study to respond to the questions raised in the open letter by Enrico Bucci", and that it would continue to follow the situation closely.

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

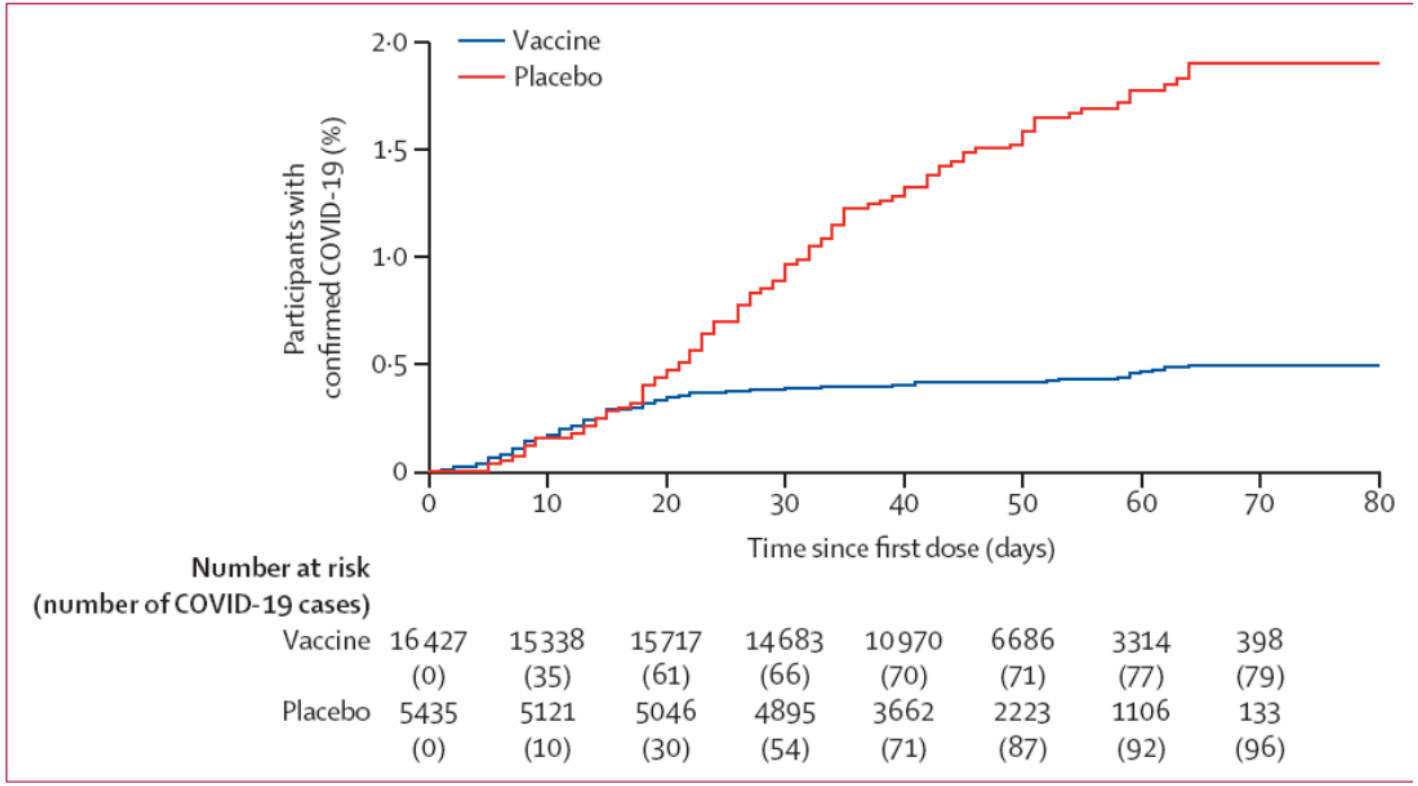
Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

We describe the first immunogenicity results of the trial, including receptor-binding domain-specific IgG titres, virus neutralising antibody titres, and IFN-γ response. The heterologous prime-boost regimen of vaccination provides robust humoral and cellular immune responses, with 91·6% (95% CI 85·6–95·2) efficacy against COVID-19. The vaccine is stored and distributed at –18°C, but storage at 2–8°C, a favourable temperature profile for global distribution, has also been approved by the Ministry of Health of the Russian Federation.

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*



Number at risk (number of COVID-19 cases)

Vaccine	16 427 (0)	15 338 (35)	15 717 (61)	14 683 (66)	10 970 (70)	6686 (71)	3314 (77)	398 (79)
Placebo	5435 (0)	5121 (10)	5046 (30)	4895 (54)	3662 (71)	2223 (87)	1106 (92)	133 (96)

Figure 2: Kaplan-Meier cumulative incidence curves for the first symptomatic, PCR-positive COVID-19 after dose 1, in participants who received at least one dose of vaccine or placebo

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

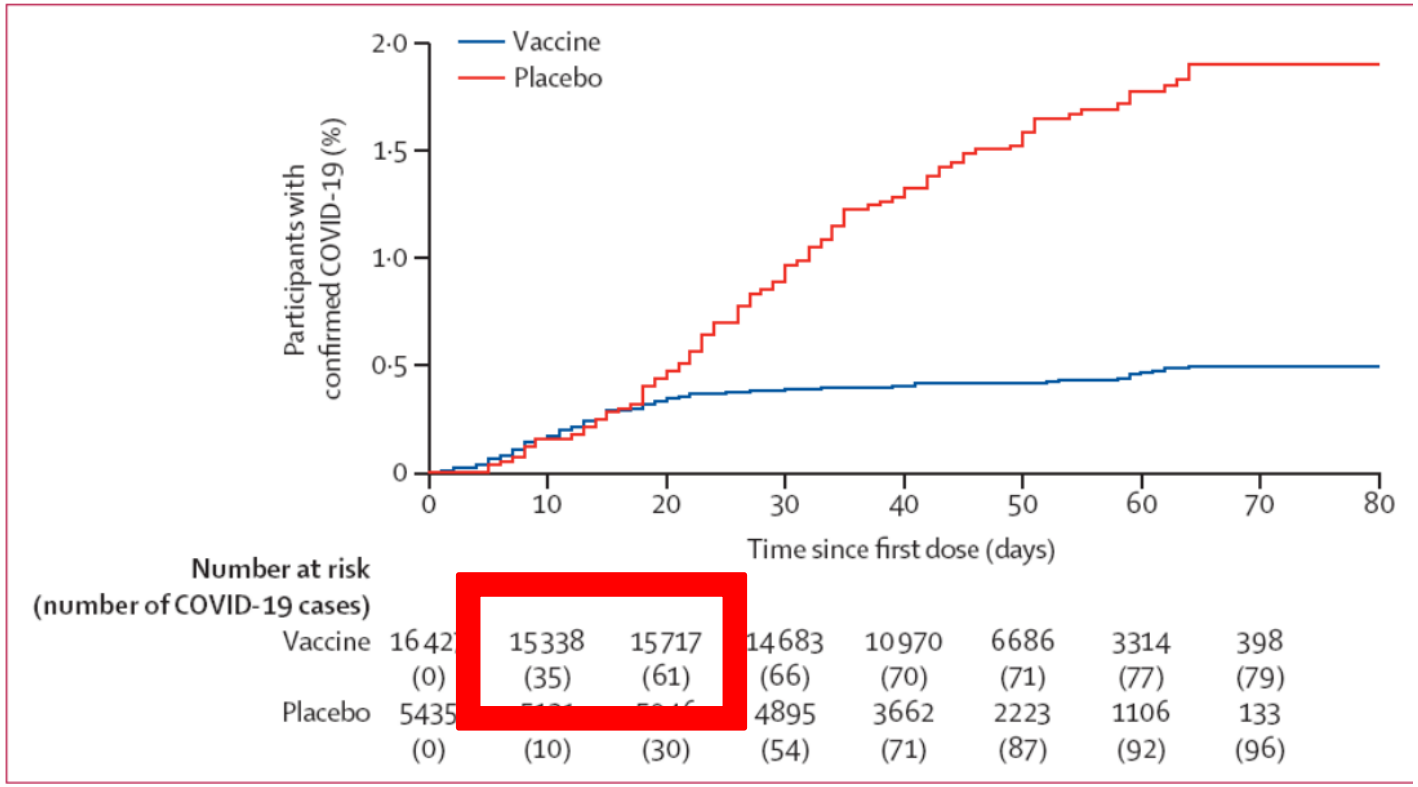


Figure 2: Kaplan-Meier cumulative incidence curves for the first symptomatic, PCR-positive COVID-19 after dose 1, in participants who received at least one dose of vaccine or placebo

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

	Total cases	Vaccine group	Placebo group	Vaccine efficacy (95% CI)	p value
First COVID-19 occurrence from 21 days after dose 1 (day of dose 2)*					
Overall	78	16/14 964 (0·1%)	62/4902 (1·3%)	91·6% (85·6–95·2)	<0·0001
Age group (years)					
18–30	5	1/1596 (0·1%)	4/521 (0·8%)	91·9% (51·2–99·3)	0·0146
31–40	17	4/3848 (0·1%)	13/1259 (1·0%)	90·0% (71·1–96·5)	<0·0001
41–50	19	4/4399 (0·1%)	15/1443 (1·0%)	91·3% (73·7–96·9)	<0·0001
51–60	27	5/3510 (0·1%)	22/1146 (1·9%)	92·7% (81·1–97·0)	<0·0001
>60	10	2/1611 (0·1%)	8/533 (1·5%)	91·8% (67·1–98·3)	0·0004
Sex					
Female	32	9/5821 (0·2%)	23/1887 (1·2%)	87·5% (73·4–94·2)	<0·0001
Male	46	7/9143 (0·1%)	39/3015 (1·3%)	94·2% (87·2–97·4)	<0·0001
Moderate or severe cases	20	0/14 964	20/4902 (0·4%)	100% (94·4–100·0)	<0·0001
First COVID-19 occurrence after dose 1†					
Any time after dose 1	175	79/16 427 (0·5%)	96/5435 (1·8%)	73·1% (63·7–80·1)	<0·0001
From 14 days after dose 1	109	30/14 999 (0·2%)	79/4950 (1·6%)	87·6% (81·1–91·8)	<0·0001
First COVID-19 occurrence after dose 2 (28 days after dose 1)*					
All	60	13/14 094 (0·1%)	47/4601 (1·0%)	91·1% (83·8–95·1)	<0·0001

Data are n/N (%), unless otherwise stated. *Includes those who received both doses. †Includes participants who received at least one dose.

Table 2: **Interim results on vaccine efficacy**

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

	Total cases	Vaccine group	Placebo group	Vaccine efficacy (95% CI)	p value
First COVID-19 occurrence from 21 days after dose 1 (day of dose 2)*					
Overall	78	16/14 964 (0·1%)	62/4902 (1·3%)	91·6% (85·6–95·2)	<0·0001
18–30	5	1/1596 (0·1%)	4/521 (0·8%)	91·9% (51·2–99·3)	0·0146
31–40	17	4/3848 (0·1%)	13/1259 (1·0%)	90·0% (71·1–96·5)	<0·0001
41–50	19	4/4399 (0·1%)	15/1443 (1·0%)	91·3% (73·7–96·9)	<0·0001
51–60	27	5/3510 (0·1%)	22/1146 (1·9%)	92·7% (81·1–97·0)	<0·0001
>60	10	2/1611 (0·1%)	8/533 (1·5%)	91·8% (67·1–98·3)	0·0004
Female	32	9/5821 (0·2%)	23/1887 (1·2%)	87·5% (73·4–94·2)	<0·0001
Male	46	7/9143 (0·1%)	39/3015 (1·3%)	94·2% (87·2–97·4)	<0·0001
Moderate or severe cases	20	0/14 964	20/4902 (0·4%)	100% (94·4–100·0)	<0·0001
First COVID-19 occurrence after dose 1†					
Any time after dose 1	175	79/16 427 (0·5%)	96/5435 (1·8%)	73·1% (63·7–80·1)	<0·0001
From 14 days after dose 1	109	30/14 999 (0·2%)	79/4950 (1·6%)	87·6% (81·1–91·8)	<0·0001
First COVID-19 occurrence after dose 2 (28 days after dose 1)*					
All	60	13/14 094 (0·1%)	47/4601 (1·0%)	91·1% (83·8–95·1)	<0·0001

Data are n/N (%), unless otherwise stated. *Includes those who received both doses. †Includes participants who received at least one dose.

Table 2: **Interim results on vaccine efficacy**

Data discrepancies and substandard reporting of interim data of Sputnik V phase 3 trial

**Enrico M Bucci, Johannes Berkhof, André Gillibert, Gowri Gopalakrishna, Raffaele A Calogero, Lex M Bouter, Konstantin Andreev, Florian Naudet, Vasiliy Vlassov*

A very peculiar result of the major subgroup analysis of the primary outcome caught our attention. The vaccine efficacy was said to be high for all age groups. The reported percentages were 91·9% in the 18–30-year age group, 90·0% in the 31–40-year age group, 91·3% in the 41–50-year age group, 92·7% in the 51–60-year age group, and 91·8% in participants older than 60 years. We checked the homogeneity of vaccine efficacy across age groups (interaction tests): the p value of the Tarone-adjusted Breslow-Day test was 0·9963, and the p value of a non-asymptotic test was 0·9956,[6] indicating a very low probability of observing a homogeneity this good if the actual homogeneity is perfect.

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

Source	Date	Rate of cases in vaccine group	Rate of cases in placebo group	Efficacy
Press release [9]	11/11/2020	4	16	92%
Press release [10]	11/24/2020	8/14,095	31/4,699	91,397%
Press release [11]	12/14/2020	16/17,032	62/5,682	91,391%
Lancet Article [1]	Database lock of 11/24/2020	16/14,964	62/4,902	91,546%

Table 1: efficacy of the vaccine in press releases and Lancet article [1]

Data discrepancies and substandard reporting of interim data of Sputnik V phase 3 trial

**Enrico M Bucci, Johannes Berkhof, André Gillibert, Gowri Gopalakrishna, Raffaele A Calogero, Lex M Bouter, Konstantin Andreev, Florian Naudet, Vasiliy Vlassov*

A very peculiar result of the major subgroup analysis of the primary outcome caught our attention. The vaccine efficacy was said to be high for all age groups. The reported percentages were 91·9% in the 18–30-year age group, 90·0% in the 31–40-year age group, 91·3% in the 41–50-year age group, 92·7% in the 51–60-year age group, and 91·8% in participants older than 60 years. We checked the homogeneity of vaccine efficacy across age groups (interaction tests): the p value of the Tarone-adjusted Breslow-Day test was 0·9963, and the p value of a non-asymptotic test was 0·9956,[6] indicating a very low probability of observing a homogeneity this good if the actual homogeneity is perfect.

Rapid Response:

Concerns with the Sputnik V vaccine data

06 April 2021
Florian Naudet
(Univ Rennes, CHU Rennes, Inserm, CIC 1414 (Centre d'Investigation Clinique de Rennes), France)
Enrico M. Bucci (Sbarro Institute - Temple University Department of Biology, USA), Johannes Berkhof (Amsterdam University Medical Centers, Department of Epidemiology and Data Science, Vrije Universiteit Amsterdam, Netherlands), André Gillibert (Department of Biostatistics, CHU Rouen, France), Gowri Gopalakrishna (Amsterdam University Medical Centers, Department of Epidemiology and Data Science, Vrije Universiteit Amsterdam, Netherlands), Raffaele A Calogero (Department of Molecular Biotechnology and Health Sciences, University of Torino, Italy), Anders Bjorkman (Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden), Lex M. Bouter (Amsterdam University Medical Centers, Department of Epidemiology and Data Science, Vrije Universiteit Amsterdam, Faculty of Humanities, Department of Philosophy, Netherlands), Konstantin Andreev (Howard Hughes Medical Institute, Department of Molecular Biosciences, Northwestern University, Evanston, USA), Florian Naudet (Univ Rennes, CHU Rennes, Inserm, CIC 1414 (Centre d'Investigation Clinique de Rennes), France), Vasiliy Vlassov (HSE University, Moscow, Russia)

.

Dear Editor

In a commissioned commentary, Chris Baraniuk reviews the "knowns and unknowns" about Russian vaccines against Covid-19, with a specific focus on Sputnik V [1]. While the commentary correctly emphasizes the inconsistencies identified in the phase 1/2 trial results published in the Lancet [2], it mainly discusses the more recently published phase 3 trial results [3].

Our previous concerns regarding the phase 1/2 trial included problematic data patterns with an excess homogeneity of vaccine efficacy across different time points [4]. The authors responded that the unusual data pattern was "a coincidence" due to the small sample size of their study and the discrete distributions of their outcomes [5].

Following such a reasoning, inconsistencies should not be expected in the subsequent larger phase 3 trial. However, we noticed an unexpected homogeneity of vaccine efficacy, this time between age groups. This analysis is central in the Lancet paper at issue because of the disproportionate disease burden in older people. Of course, implausible results can still be observed by chance. However, we have also identified a similar feature, i.e. an excessive homogeneity of the reported vaccine efficacy in the values reported in earlier interim analyses and the published article.

On 11 November 2020, a first press release announced a 92 % efficacy [6]. From this press release we can compute that there were four Covid cases in the vaccine group and 16 in the placebo group. On 24 November 2020, a second press release announced a 91% efficacy with 8/14,095 cases in the vaccine group and 31/4,699 in the placebo group [7]. On 14 December 2020 a third press release announced again a 91% efficacy with 16/17,032 cases in the vaccine group and 62/5,682 in the placebo group [8]. Much to

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

Data sharing

Anonymous participant data will be available upon completion of clinical trials and publication of the results of the completed study upon request to the corresponding author. Proposals will be reviewed and approved by the sponsor, security department, researcher, and staff on the basis of scientific merit and absence of competing interests. Once the proposal has been approved, data can be transferred through a secure online platform after the signing of a data access agreement and a confidentiality agreement.

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

Data sharing

Anonymous participant data will be available upon completion of clinical trials and publication of the results of the completed study upon request to the corresponding author. Proposals will be reviewed and approved by the sponsor's security department, researcher, and staff on the basis of scientific merit and absence of competing interests. Once the proposal has been approved, data can be transferred through a secure online platform after the signing of a data access agreement and a confidentiality agreement.

THE LANCET

Data discrepancies and substandard reporting of interim data of Sputnik V phase 3 trial

*Enrico M Bucci, Johannes Berkhof, André Gillibert, Gowri Gopalakrishna, Raffaele A Calogero, Lex M Bouter, Konstantin Andreev, Florian Naudet, Vasiliy Vlassov
enrico.bucci@temple.edu

Data discrepancies and substandard reporting of interim data of Sputnik V phase 3 trial

Authors' reply

*Denis Y Logunov, Inna V Dolzhikova, Dmitry V Shcheblyakov
ldenisy@gmail.com

Numerical inconsistencies were simple typing errors that were formally corrected.

The homogeneity of the values only confirms the fact that, as described in the Article, the effectiveness of the vaccine does not differ between age groups. In this case, the main parameter by which one can judge the difference in effectiveness is the confidence interval, the differences in which are quite significant due to the different sample sizes and the number of COVID-19 cases at the time of analysis.

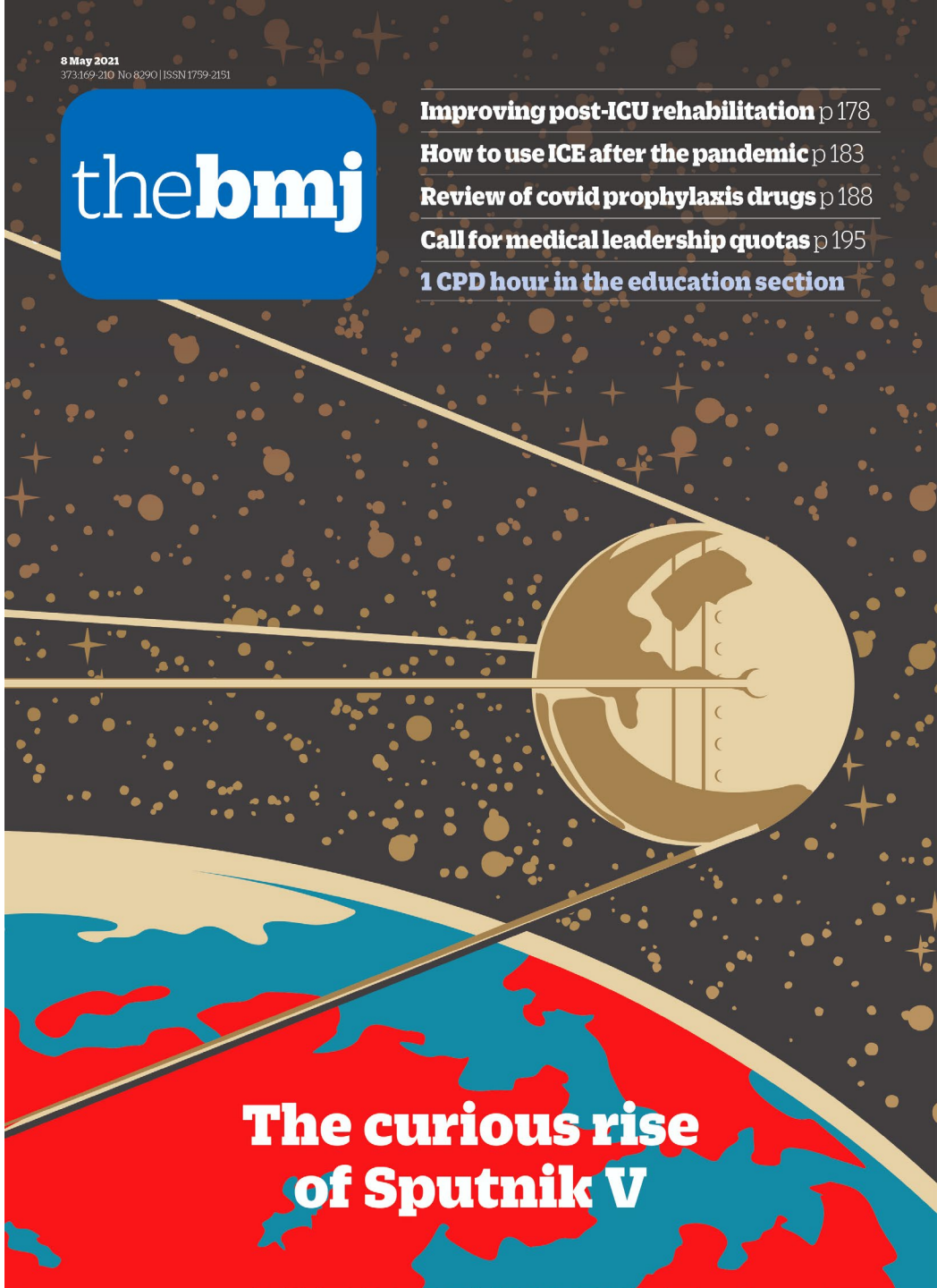
ESSAY

Covid-19: Sputnik vaccine rockets, thanks to Lancet boost

Journals risk being used in place of regulators when they publish studies of novel vaccines that have not yet been authorised by a major regulator. **Chris van Tulleken** argues that peer review is inadequate to decide the risk-benefit ratio of new drugs

Christoffer van Tulleken *honorary associate professor*

It is unclear exactly when the EMA will render its judgment on Sputnik V, especially considering the concerns about clotting problems that have since emerged with vaccines using similar adenovirus vector platforms. If it is authorised, Sputnik V will be a boost to global health, an idea which the *Lancet*, under Richard Horton, has championed with a radical approach. Perhaps their early endorsement of Sputnik is consistent with this, but, just as this episode raises questions about the *Lancet*'s commitment to open data, it also raises questions about the depth of the other commitments that they place under the banner "the best science for better lives."



BMJ EBM

EBM analysis

Transparency of COVID-19 vaccine trials: decisions without data

Sarah Tanveer ,[1] Anisa Rowhani-Farid ,[1] Kyungwan Hong,[1] Tom Jefferson ,[2] Peter Doshi [1]

Trial ID; no enrolled; included ages	Pre-study documents	Post-study documents†					Total pages available§
		Press release	Pub	CSR	Other‡	IPD	
NCT04368728; n=43 998; 12–85 years	Protocol, SAP, Blank CRF	Press release 1, 2, 3	Pub 1,2,3	CSR	Other	No	3880
NCT04816643; n=4644; 6 months to 11 years	None	No	N/A: trial ongoing				0
NCT04470427; n=30 420; ≥18 years	Protocol, SAP	Press release	Pub	No	Other	No	3293
NCT04796896; n=6750; 6 months to 12 years	None	No	N/A: trial ongoing				0
ISRCTN89951424; n=10 300; ≥18 years	Protocol	Press release	Pub 1¶, 2¶	No	No	No	123
ISRCTN15638344; n=300; 6–17 years	None	No	N/A: trial ongoing				0
NCT04505722; n=44 325; ≥18 years	Protocol, SAP, Blank ICF	Press release	Pub	No	No	No	530
NCT04614948; n=30 000; ≥18 years	Protocol	No	N/A: trial ongoing				166
NCT04611802; n=30 000; ≥18 years	Protocol	No	N/A: trial ongoing				128
NCT04583995; n=15 187; 18–84 years	Protocol, SAP	Press release	Pub	No	No	No	128
NCT04530396; n=33 758; ≥18 years	None	Press release	Pub	No	No	No	11
NCT04642339; n=2000; ≥18 years	None	No	N/A: trial ongoing				0
ChiCTR2000032459; n=2128; ≥3 years	None	No	Pub	No	No	No	13
NCT04612972; n=12 000; ≥18 years	None	No	N/A: trial ongoing				0
NCT04456595; n=12 688; ≥18 years	Protocol	Press release	Pub	No	No	No	201
NCT04582344; n=13 000; 18–59 years	Protocol	Press release	No	No	No	No	57

Data current as of 27 June 2021.

*Pre-study documents include: protocol, statistical analysis plan, blank informed consent form, blank case report form, data monitoring board charter, event adjudication committee charter, investigational medicinal product dossier and investigator's brochure.

†Post-study documents include: press releases (that contain any results), journal publication (including pre-prints), clinical study report and individual participant data.

‡Other includes documents released by Health Canada and EMA other than the CSR.

§Total pages available excludes press releases. Access to the dataset used to determine page count for trials where additional data were available through Health Canada and the European Medicines Agency is available in the Zenodo repository (http://doi.org/10.5281/zenodo.4737417).

¶Pooled trial analysis publication listed if there were no individual trial publications.

CRF, case report form; CSR, clinical study report; EMA, European Medicines Agency; ICF, informed consent form; IPD, individual participant data; n, number enrolled in trial; N/A, not applicable; Pub, journal publication ; SAP, statistical analysis plan.

BMJ EBM

EBM analysis

Transparency of COVID-19 vaccine trials: decisions without data

Sarah Tanveer [1], Anisa Rowhani-Farid [1], Kyungwan Hong,[1] Tom Jefferson [2], Peter Doshi [1]

Trial ID; no enrolled; included ages	Pre-study documents	Post-study documents†					Total pages available§
		Press release	Pub	CSR	Other‡	IPD	
NCT04368728; n=43 998; 12–85 years	Protocol, SAP, Blank CRF	Press release 1, 2, 3	Pub 1,2,3	CSR	Other	No	3880
NCT04816643; n=4644; 6 months to 11 years	None	No	N/A: trial ongoing				0
NCT04470427; n=30 420; ≥18 years	Protocol, SAP	Press release	Pub	No	Other	No	3293
NCT04796896; n=6750; 6 months to 12 years	None	No	N/A: trial ongoing				0
ISRCTN89951424; n=10 300; ≥18 years	Protocol	Press release	Pub 1¶, 2¶	No	No	No	123
ISRCTN15638344; n=300; 6–17 years	None	No	N/A: trial ongoing				0
NCT04505722; n=44 325; ≥18 years	Protocol, SAP, Blank ICF	Press release	Pub	No	No	No	530
NCT04614948; n=30 000; ≥18 years	Protocol	No	N/A: trial ongoing				166
NCT04611802; n=30 000; ≥18 years	Protocol	No	N/A: trial ongoing				128
NCT04583995; n=15 187; 18–84 years	Protocol, SAP	Press release	Pub	No	No	No	128
NCT04530396; n=33 758; ≥18 years	None	Press release	Pub	No	No	No	11
NCT04642339; n=2000; ≥18 years	None	No	N/A: trial ongoing				0
ChiCTR2000032459; n=2128; ≥3 years	None	No	Pub	No	No	No	13
NCT04612972; n=12 000; ≥18 years	None	No	N/A: trial ongoing				0
NCT04456595; n=12 688; ≥18 years	Protocol	Press release	Pub	No	No	No	201
NCT04582344; n=13 000; 18–59 years	Protocol	Press release	No	No	No	No	57

Data current as of 27 June 2021.

*Pre-study documents include: protocol, statistical analysis plan, blank informed consent form, blank case report form, data monitoring board charter, event adjudication committee charter, investigational medicinal product dossier and investigator's brochure.

†Post-study documents include: press releases (that contain any results), journal publication (including pre-prints), clinical study report and individual participant data.

‡Other includes documents released by Health Canada and EMA other than the CSR.

§Total pages available excludes press releases. Access to the dataset used to determine page count for trials where additional data were available through Health Canada and the European Medicines Agency is available in the Zenodo repository (http://doi.org/10.5281/zenodo.4737417).

¶Pooled trial analysis publication listed if there were no individual trial publications.

CRF, case report form; CSR, clinical study report; EMA, European Medicines Agency; ICF, informed consent form; IPD, individual participant data; n, number enrolled in trial; N/A, not applicable; Pub, journal publication ; SAP, statistical analysis plan.

COIs

None in the past 3 years

Fundings

ReiTheR

Reproducibility in therapeutic research

- PROJET FINANCÉ PAR L'ANR - PROJECT FUNDED BY THE ANR
ANR
Fondation pour la Recherche Médicale
Région BRETAGNE
MINISTÈRE DES SOLIDARITÉS ET DE LA SANTÉ
Liberté Égalité Fraternité
MINISTÈRE DE L'ENSEIGNEMENT SUPÉRIEUR, DE LA RECHERCHE ET DE L'INNOVATION
Liberté Égalité Fraternité

COIs

None in the past 3 years

Fundings

ReiTheR

Reproducibility in therapeutic research

PROJET FINANCÉ PAR L'ANR - PROJECT FUNDED BY THE ANR

ANR

Fondation pour la Recherche Médicale

Région BRETAGNE

MINISTÈRE DES SOLIDARITÉS ET DE LA SANTÉ
Liberté Égalité Fraternité

MINISTÈRE DE L'ENSEIGNEMENT SUPÉRIEUR, DE LA RECHERCHE ET DE L'INNOVATION
Liberté Égalité Fraternité

ICMJE has a policy

« The ICMJE is a **small working group of general medical journal editors** whose participants meet annually and fund their own work on the **Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals**. The ICMJE invites comments on this document and suggestions for agenda items.

The current **members of the ICMJE** are Annals of Internal Medicine, British Medical Journal, Bulletin of the World Health Organization, Deutsches Ärzteblatt (German Medical Journal), Ethiopian Journal of Health Sciences, JAMA (Journal of the American Medical Association), Journal of Korean Medical Science, New England Journal of Medicine, New Zealand Medical Journal, The Lancet, Revista Médica de Chile (Medical Journal of Chile), Ugeskrift for Laeger (Danish Medical Journal), the U.S. National Library of Medicine, and the World Association of Medical Editors. »

5645 ICMJE-affiliated journals

ICMJE

INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

Annals of Internal Medicine

EDITORIAL

Sharing Clinical Trial Data: A Proposal From the International Committee of Medical Journal Editors

The International Committee of Medical Journal Editors (ICMJE) believes that there is **an ethical obligation** to responsibly share data generated by interventional clinical trials because participants have put themselves at risk.

In a growing consensus, many funders around the world—foundations, government agencies, and industry—now mandate data sharing. Here we outline ICMJE's proposed requirements to help meet this obligation. **We encourage feedback** on the proposed requirements. Anyone can provide feedback at www.icmje.org by 18 April 2016.

2016

Annals of Internal Medicine EDITORIAL

Sharing Clinical Trial Data: A Proposal From the International Committee of Medical Journal Editors

The International Committee of Medical Journal Editors (ICMJE) believes that there is **an ethical obligation** to responsibly share data generated by interventional clinical trials because participants have put themselves at risk.

In a growing consensus, many funders around the world—foundations, government agencies, and industry—now mandate data sharing. Here we outline ICMJE's proposed requirements to help meet this obligation. **We encourage feedback** on the proposed requirements. Anyone can provide feedback at www.icmje.org by 18 April 2016.

2016

Annals of Internal Medicine EDITORIAL

Data Sharing Statements for Clinical Trials: A Requirement of the International Committee of Medical Journal Editors

Data sharing statement in published papers

Can be « yes »
Can be « no »

Data sharing plan in registration

Can be « yes »
Can be « no »

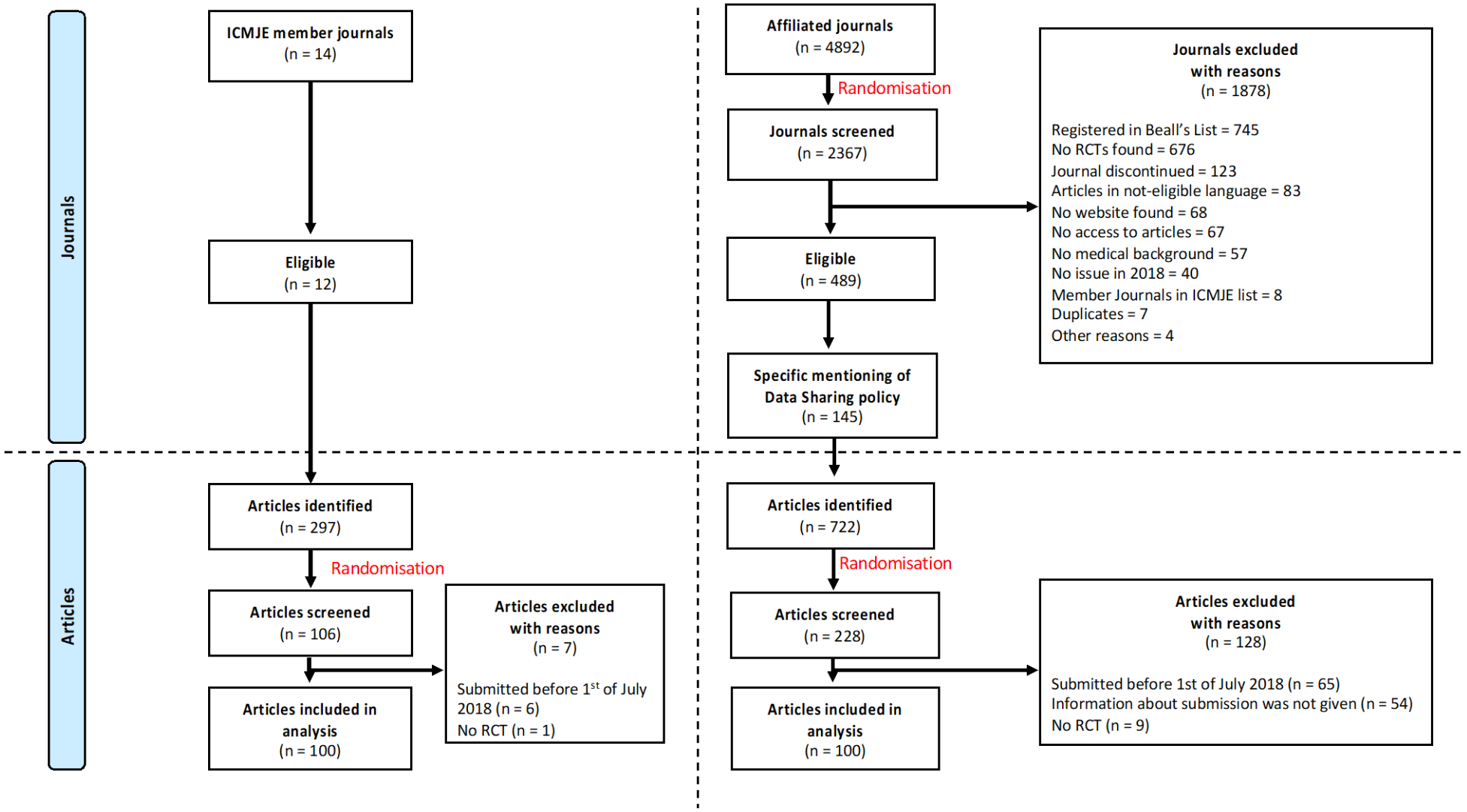
2017

Are these requirements implemented ?

BMJ Open

Data-sharing recommendations in biomedical journals and randomised controlled trials: an audit of journals following the ICMJE recommendations

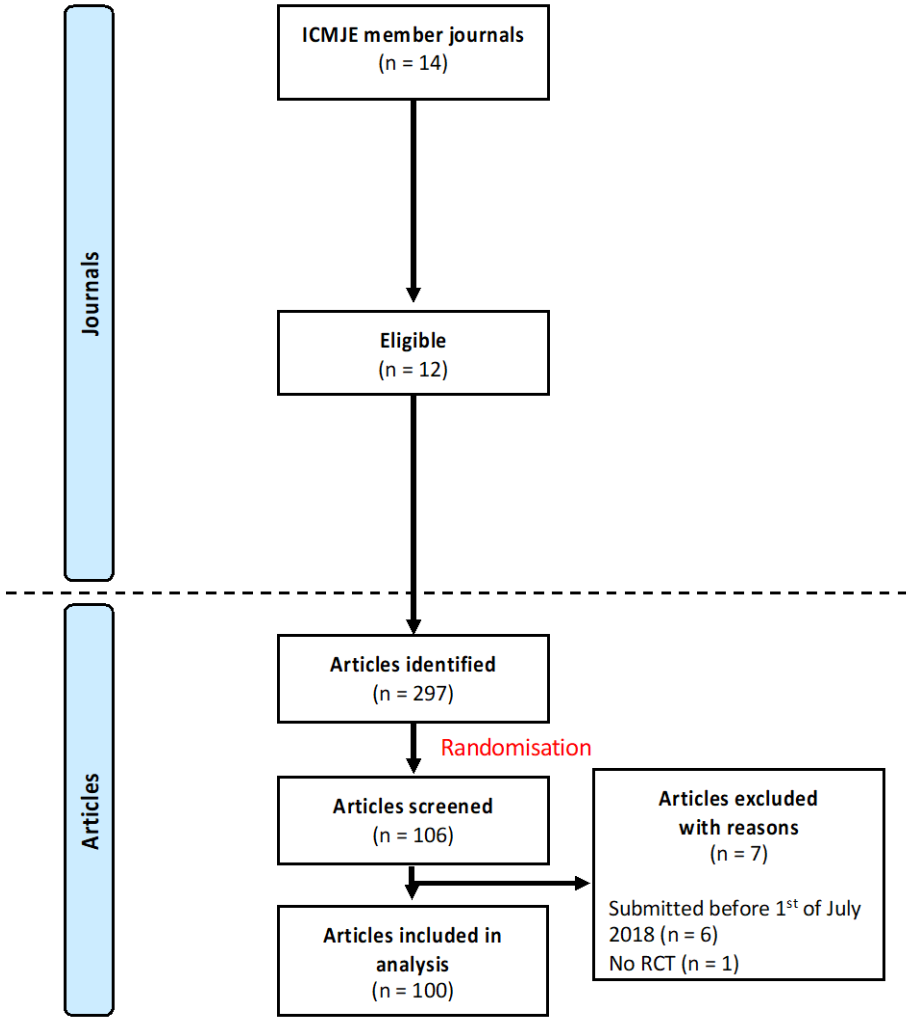
Maximilian Siebert ,[1,2] Jeanne Fabiola Gaba,[1,2] Laura Caquelin,[1] Henri Gouraud,[1] Alain Dupuy,[2] David Moher ,[3] Florian Naudet[1]



BMJ Open

Data-sharing recommendations in biomedical journals and randomised controlled trials: an audit of journals following the ICMJE recommendations

Maximilian Siebert ,[1,2] Jeanne Fabiola Gaba,[1,2] Laura Caquelin,[1] Henri Gouraud,[1] Alain Dupuy,[2] David Moher ,[3] Florian Naudet[1]



- **8/14** had an explicit data-sharing policy on their website:
  . 3 were more stringent than the ICMJE requirement,
  . 1 was less demanding,
  . 4 were compliant,
  - 5/14 stated that they followed ICMJE requirements,
  - 1/14 had no policy online.

12/14 had published RCTs

Data-sharing statements in **98/100** papers
Expressed intention to share individual patient data: **77/100** [77% - 67% to 85%].

BMJ Open

Data-sharing recommendations in biomedical journals and randomised controlled trials: an audit of journals following the ICMJE recommendations

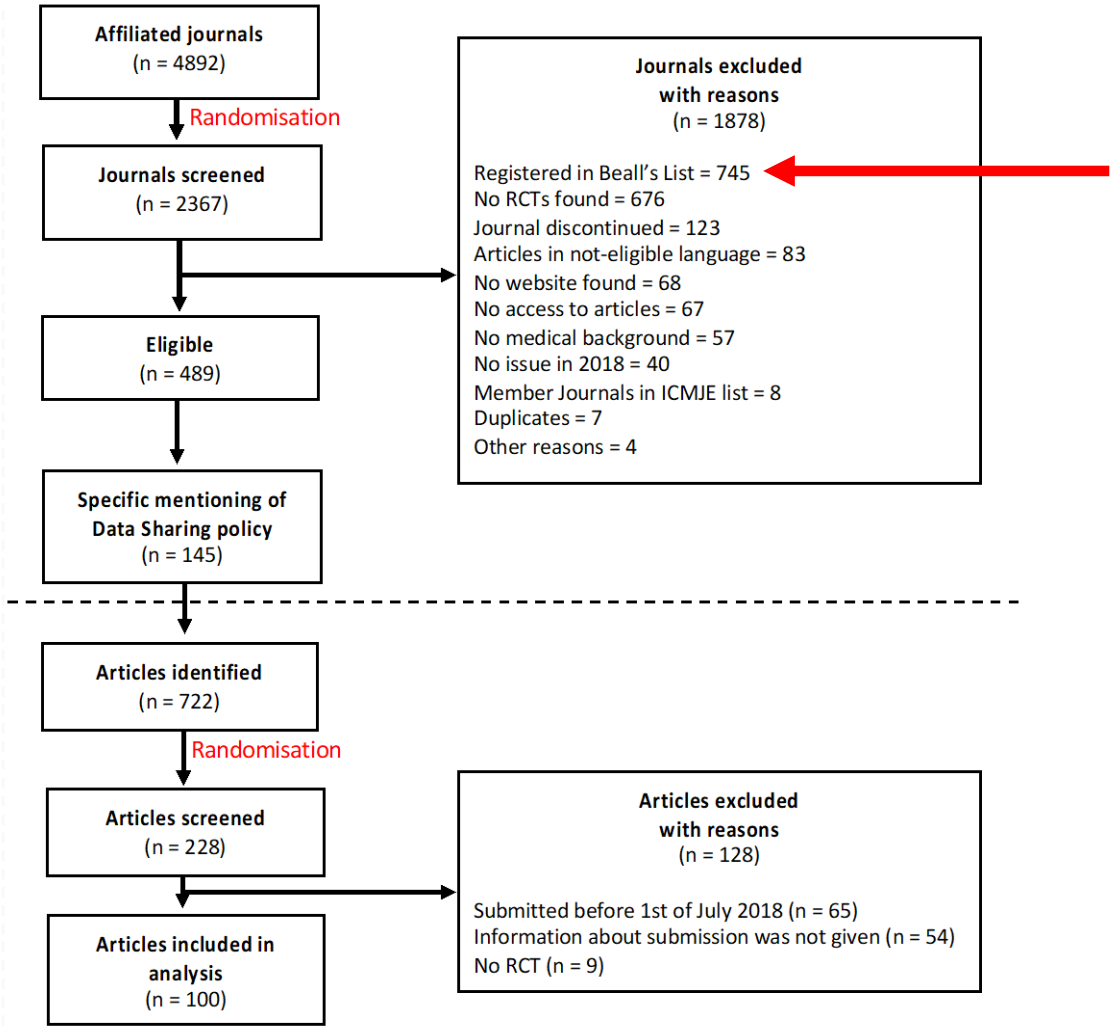
Maximilian Siebert ,[1,2] Jeanne Fabiola Gaba,[1,2] Laura Caquelin,[1] Henri Gouraud,[1] Alain Dupuy,[2] David Moher ,[3] Florian Naudet[1]

- 145/489 (**30 %** [26% to 34%]) had an explicit data-sharing policy
. 11 were more stringent than the ICMJE requirements
. 85 were less demanding
. 49 were compliant
- 276/489 (**56%** [52% to 61%]) merely referred to ICMJE requirements.

Publisher and wealth category of country of journal offices remained associated with the explicit mention of a data-sharing policy in multivariate analysis.

In RCTs published in affiliated journals with an explicit data-sharing policy:

- Data-sharing statements were rare (**25%**)
- Expressed intentions to share data were found in **22% [15% to 32%]** papers.



PLOS ONE

RESEARCH ARTICLE

Funders' data-sharing policies in therapeutic research: A survey of commercial and non-commercial funders

Jeanne Fabiola Gaba[1,2]*, Maximilian Siebert[1,2], Alain Dupuy[2], David Moher[3,4], Florian Naudet[1]

COMMERCIAL FUNDERS

Forty-one (of 100; 41%) had a data-sharing policy.

Among funders with a data-sharing policy, in a survey of 100 RCTs registered on clinicaltrials.gov:
. **Data-sharing statements** were present for eighty-one **(81% [72% - 88%])** registered RCTs.
. **Intention to share data** was expressed in **59% [49% – 69%]** of registered RCTs.

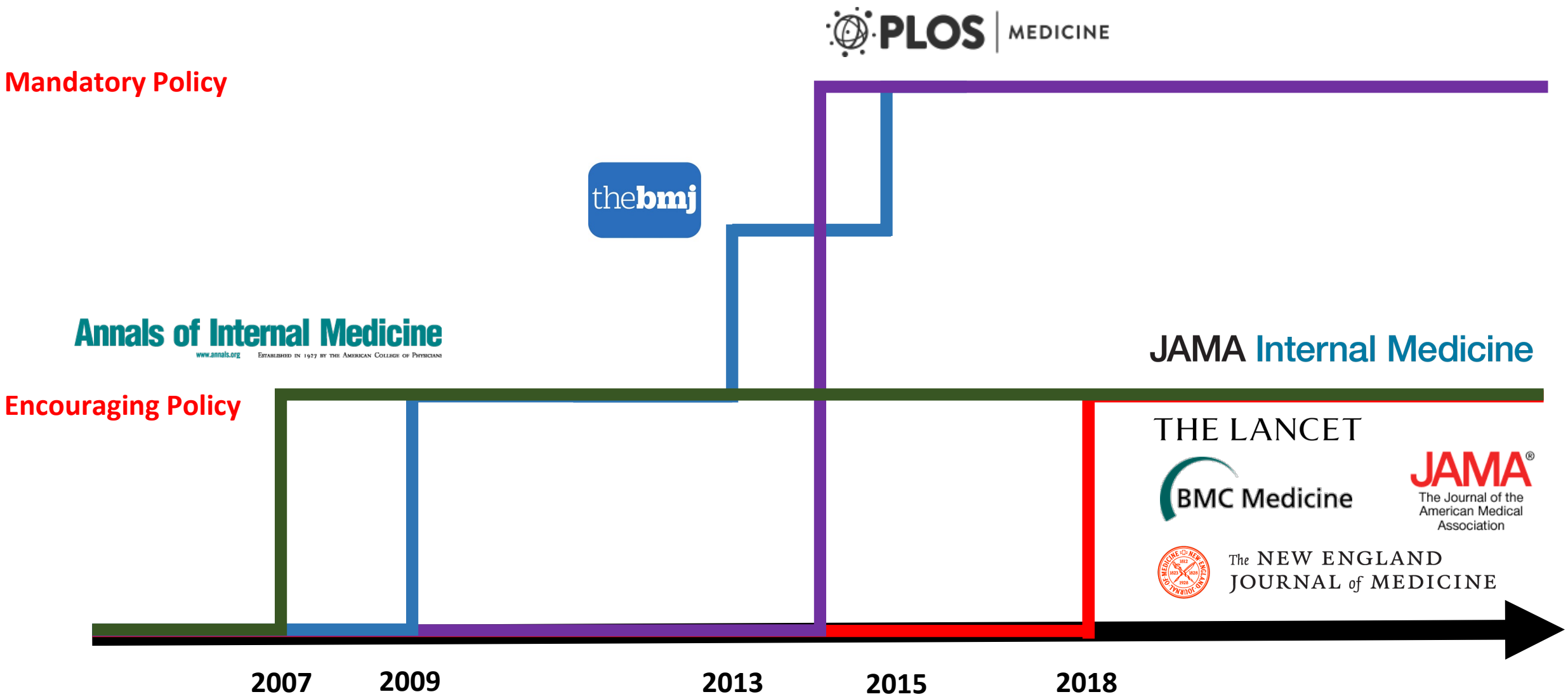
NON COMMERCIAL FUNDERS

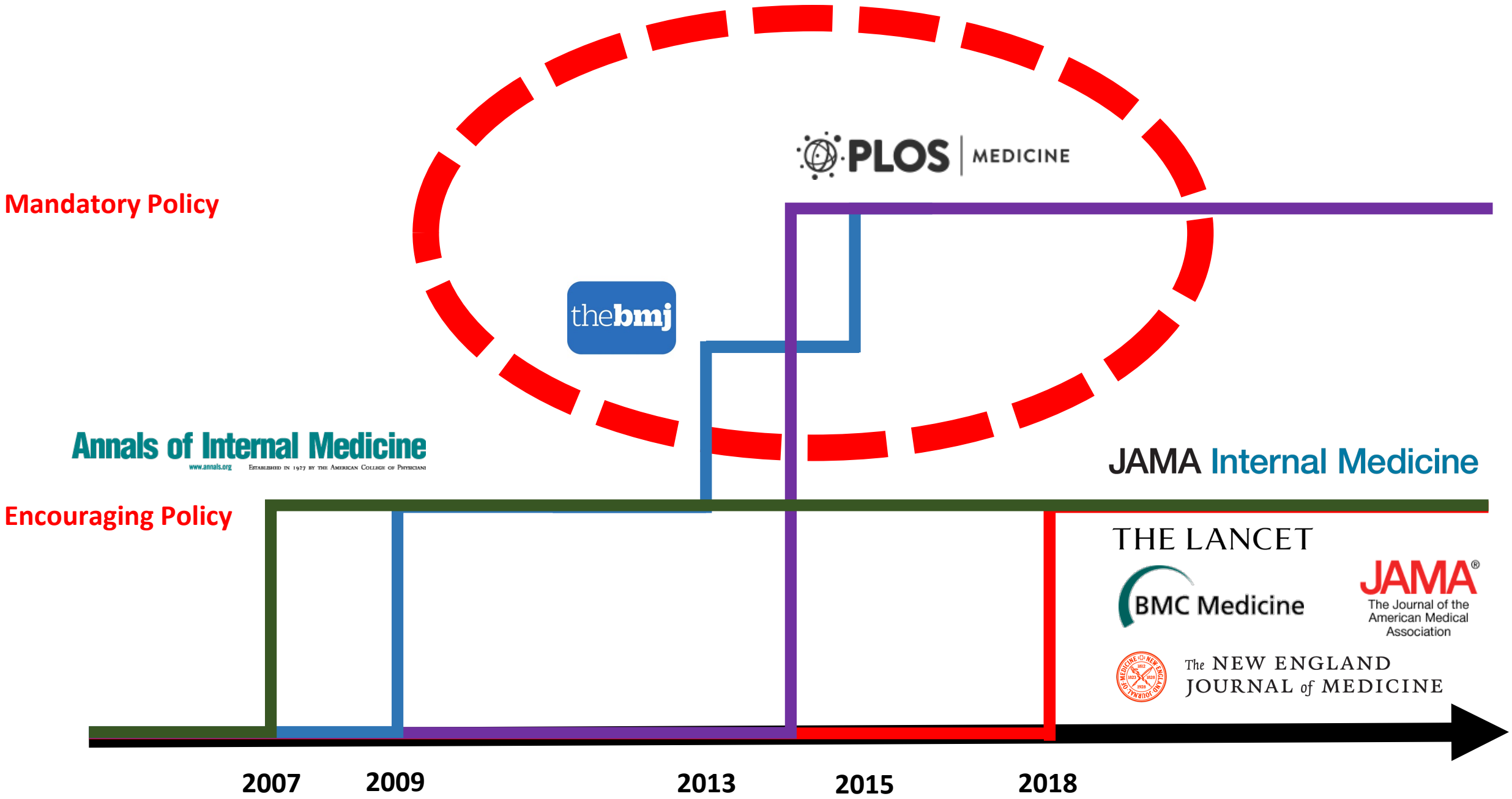
Thirty (of 78; **38%**) had a data-sharing policy with eighteen (of 30, **60%**) **making data-sharing mandatory** and twelve (**40%**) **encouraging data-sharing**.

Among funders with a data-sharing policy, in a survey of 100 RCTs registered on clinicaltrials.gov:
. **Data-sharing statements** were present for seventy-seven (**77%, 95% IC [67%-84%]**) registered RCTs.
. **Intention to share data** was expressed in **12% [7%-20%]** of registered RCTs.

What can we learn from previous experiences ?

UNIVERSITÉ DE RENNES 1


Mandatory Policy
Encouraging Policy
PLOS MEDICINE
thebmj
Annals of Internal Medicine
www.annals.org
Established in 1927 by the American College of Physicians
JAMA Internal Medicine
THE LANCET
BMC Medicine
JAMA
The Journal of the American Medical Association
The NEW ENGLAND JOURNAL of MEDICINE
2007
2009
2013
2015
2018


Mandatory Policy
PLOS | MEDICINE
thebmj
Annals of Internal Medicine
www.annals.org
Established in 1927 by the American College of Physicians
JAMA Internal Medicine
Encouraging Policy
THE LANCET
BMC Medicine
JAMA
The Journal of the American Medical Association
The NEW ENGLAND JOURNAL of MEDICINE
2007
2009
2013
2015
2018

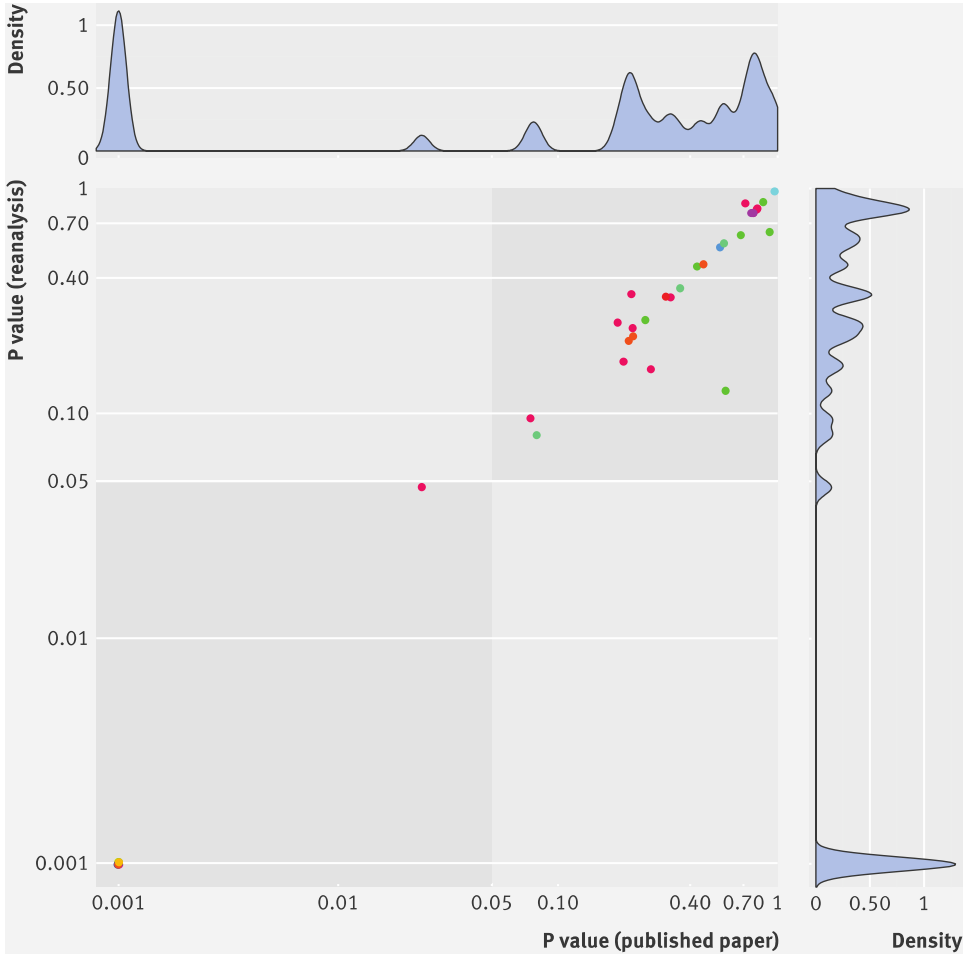


Fig 2 | P values in initial analyses and in reanalyses. Axes are on a log scale. Blue indicates identical conclusion between initial analysis and reanalysis. Dots of same colors indicate analyses from same study

Data availability: 46% (95% CI [30% to 62%])

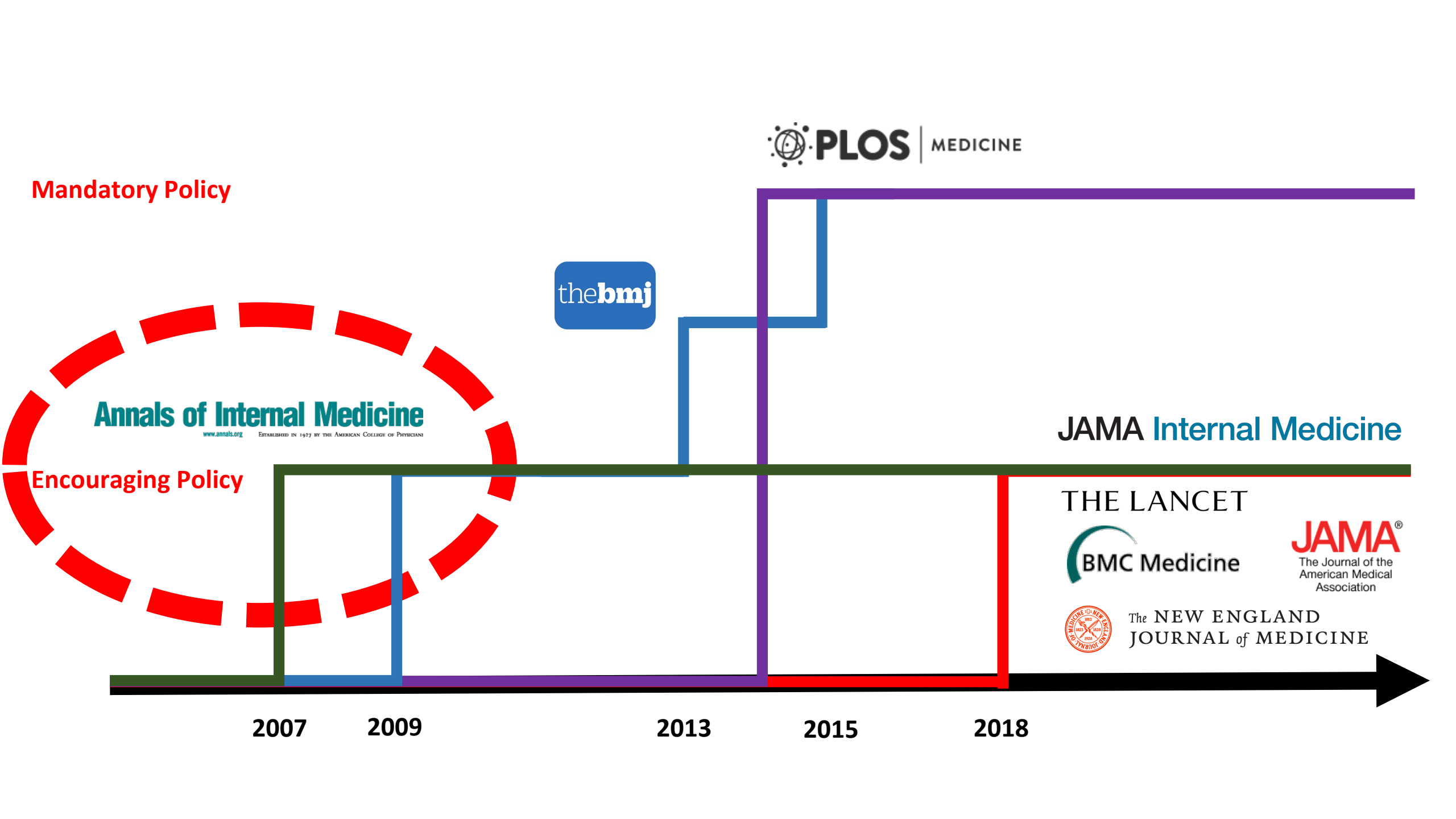
Analyses fully reproduced: 82%, 95% CI [59% to 94%])

Of the remaining RCTs, errors were identified in two but reached similar conclusions.

One paper did not provide enough information in the Methods section to reproduce the analyses

Data sharing and reanalysis of randomized controlled trials in leading biomedical journals with a full data sharing policy: survey of studies published in *The BMJ* and *PLOS Medicine*

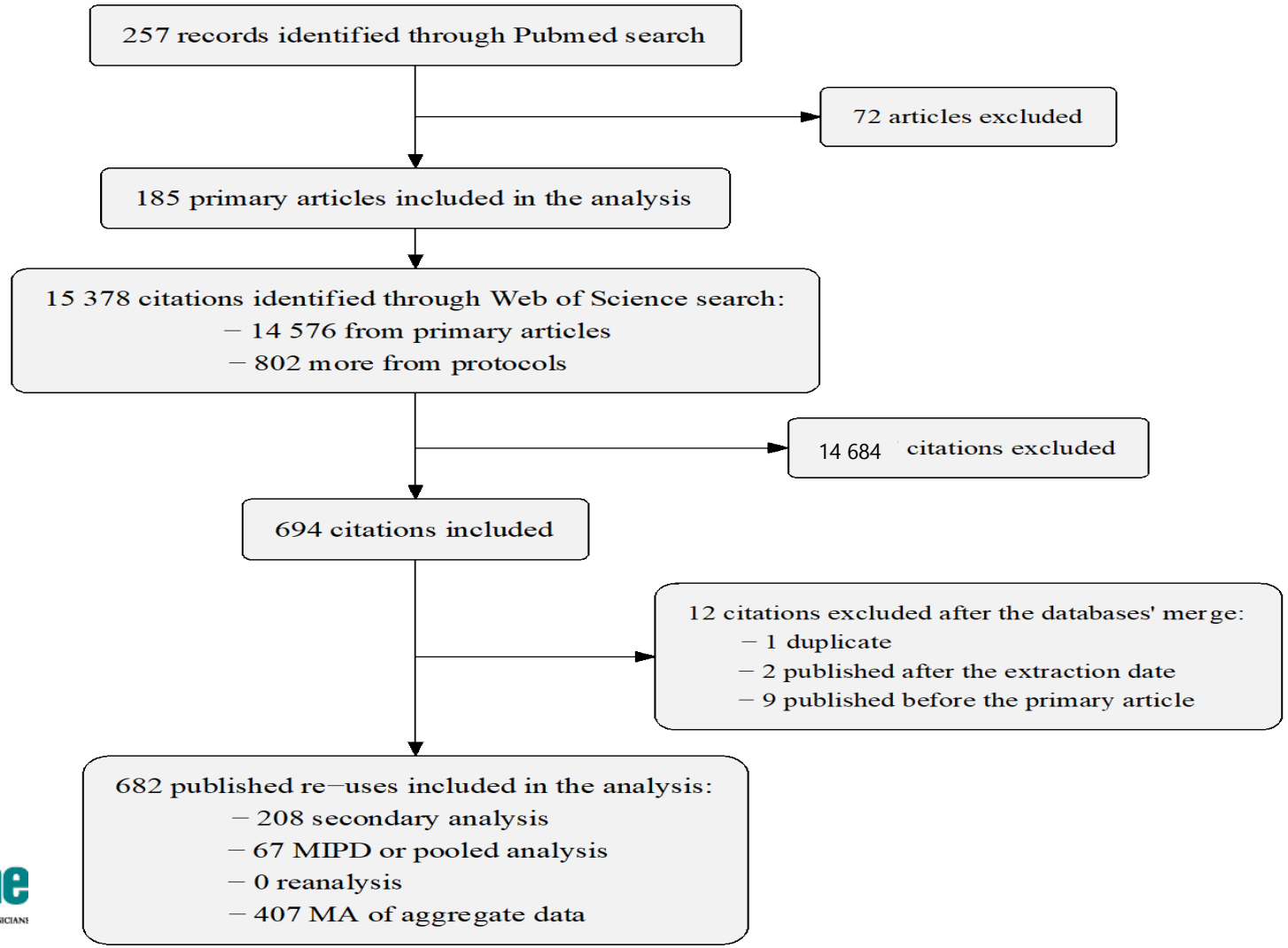
Florian Naudet,[1] Charlotte Sakarovitch,[2] Perrine Janiaud,[1] Ioana Cristea,[1,3] Daniele Fanelli,[1,4] David Moher,[1,5] John P A Ioannidis[1,6]


Mandatory Policy
Encouraging Policy
PLOS | MEDICINE
thebmj
Annals of Internal Medicine
www.annals.org
Established in 1927 by the American College of Physicians
JAMA Internal Medicine
THE LANCET
BMC Medicine
JAMA
The Journal of the American Medical Association
The NEW ENGLAND JOURNAL of MEDICINE
2007
2009
2013
2015
2018

Intent to share Annals of Internal Medicine's trial data was not associated with data re-use

Claude Pellen[a,*], Laura Caquelin[a], Alexia Jouvance-Le Bail[a], Jeanne Gaba[a], Mathilde Vérin[a], David Moher[b], John P.A. Ioannidis[c,d,e], Florian Naudet[a]

2007-2017
RCTs

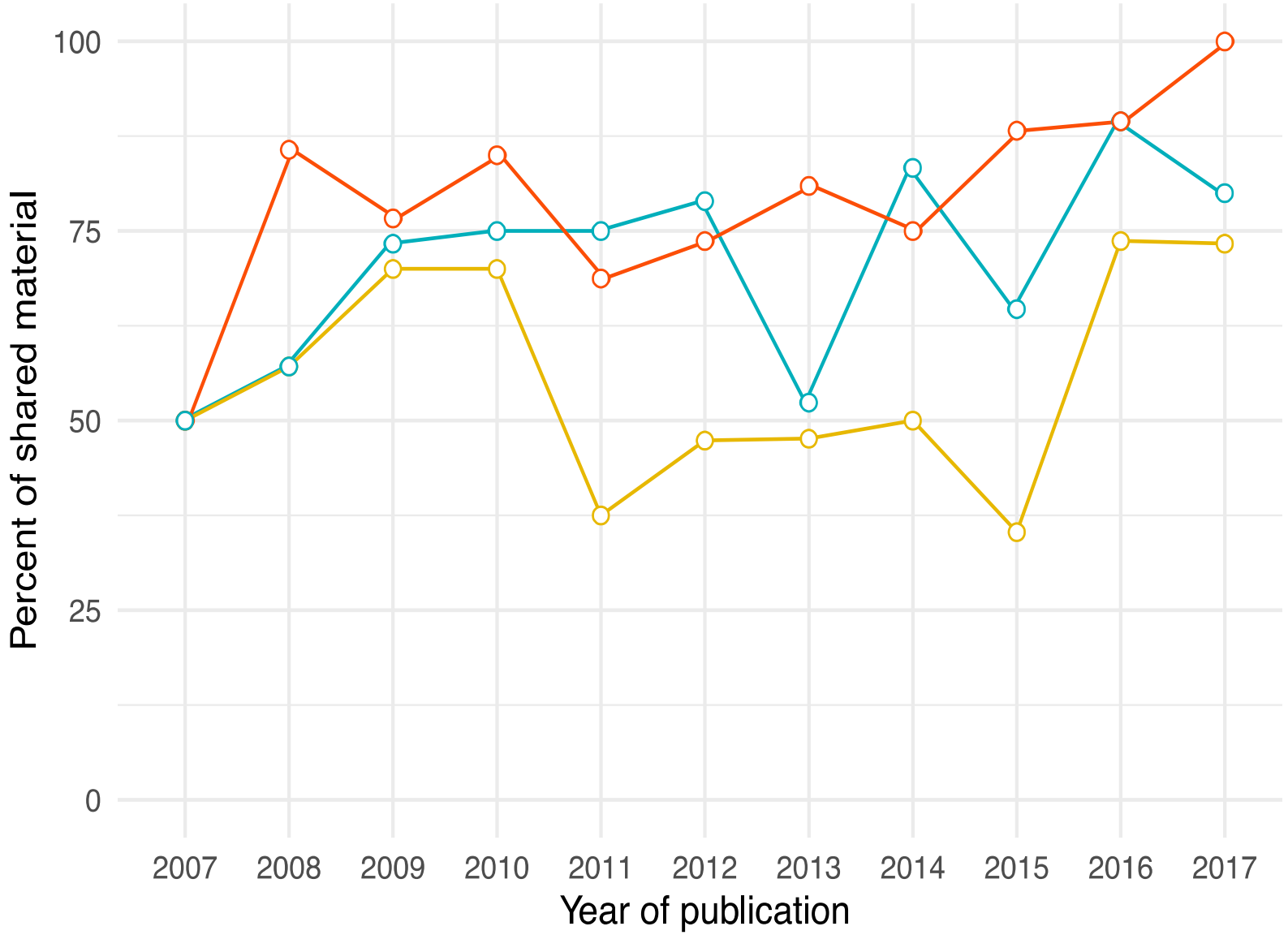


JCE JOURNAL OF CLINICAL EPIDEMIOLOGY

Annals of Internal Medicine
www.annals.org ESTABLISHED IN 1927 BY THE AMERICAN COLLEGE OF PHYSICIANS

Intent to share Annals of Internal Medicine's trial data was not associated with data re-use

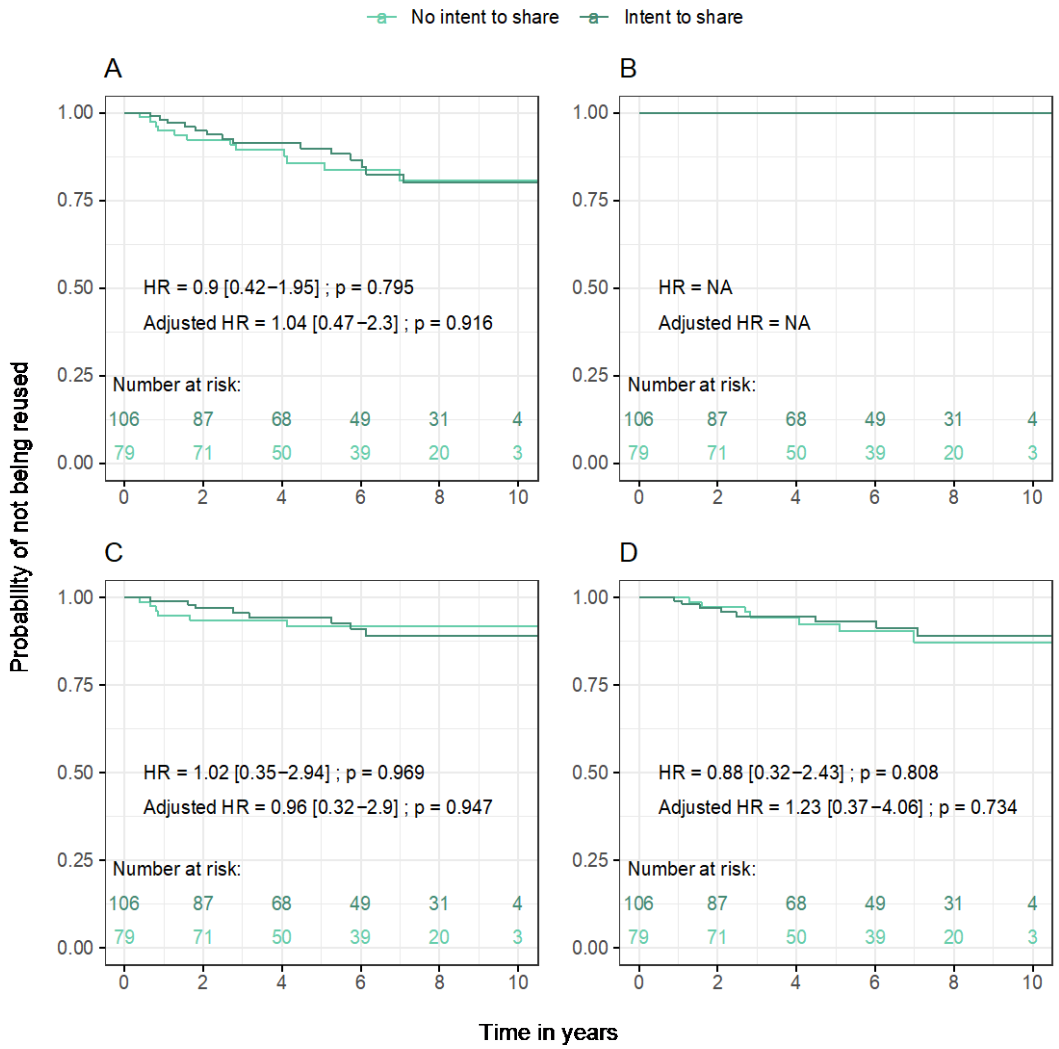
Claude Pellen[a,*], Laura Caquelin[a], Alexia Jouvance-Le Bail[a], Jeanne Gaba[a], Mathilde Vérin[a], David Moher[b], John P.A. Ioannidis[c,d,e], Florian Naudet[a]



JCE JOURNAL OF CLINICAL EPIDEMIOLOGY

Intent to share Annals of Internal Medicine's trial data was not associated with data re-use

Claude Pellen[a,*], Laura Caquelin[a], Alexia Jouvance-Le Bail[a], Jeanne Gaba[a], Mathilde Vérin[a], David Moher[b], John P.A. Ioannidis[c,d,e], Florian Naudet[a]



A: any type of published re-uses.

B: published re-analyses.

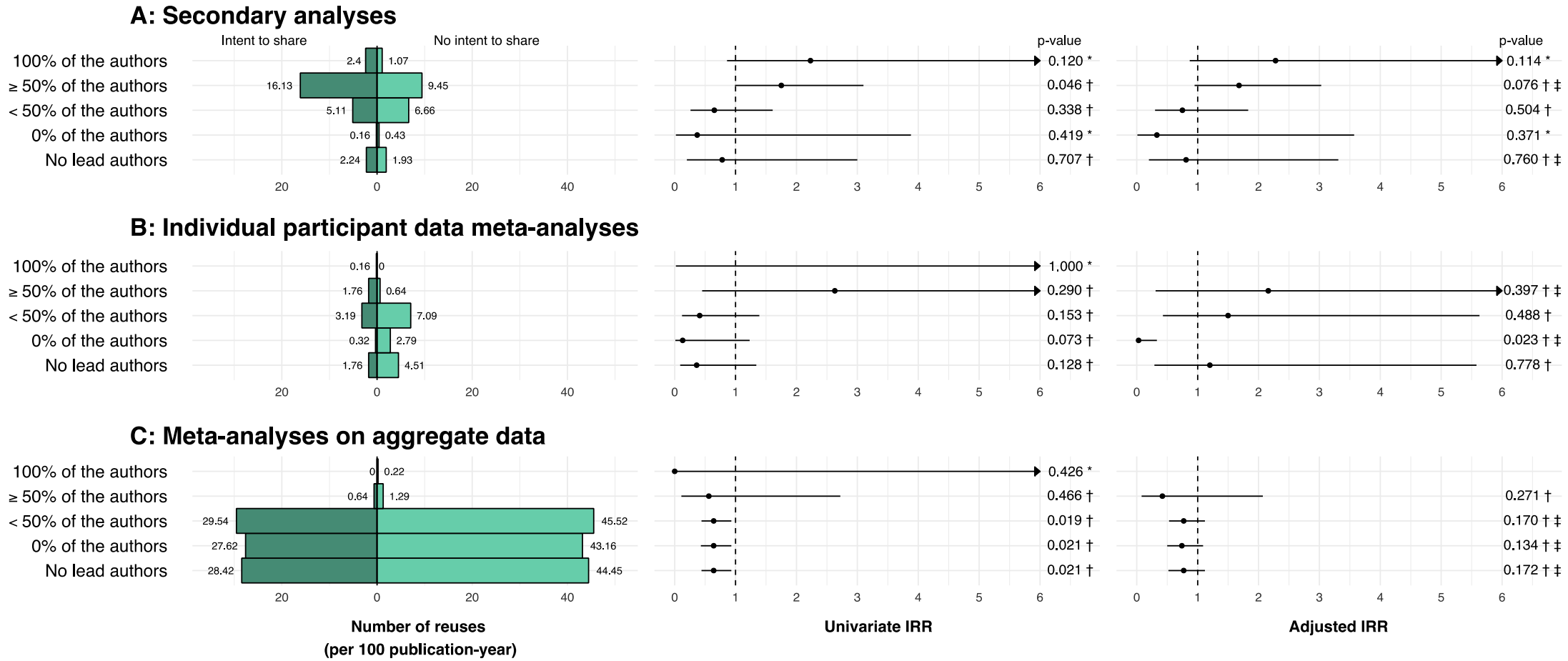
C: published secondary analyses.

D: published MIPD.

Intent to share Annals of Internal Medicine's trial data was not associated with data re-use

Claude Pellen[a,*], Laura Caquelin[a], Alexia Jouvance-Le Bail[a], Jeanne Gaba[a], Mathilde Vérin[a], David Moher[b], John P.A. Ioannidis[c,d,e], Florian Naudet[a]

JCE JOURNAL OF CLINICAL EPIDEMIOLOGY



What is the impact of sharing clinical trial data ?

UNIVERSITÉ DE RENNES 1

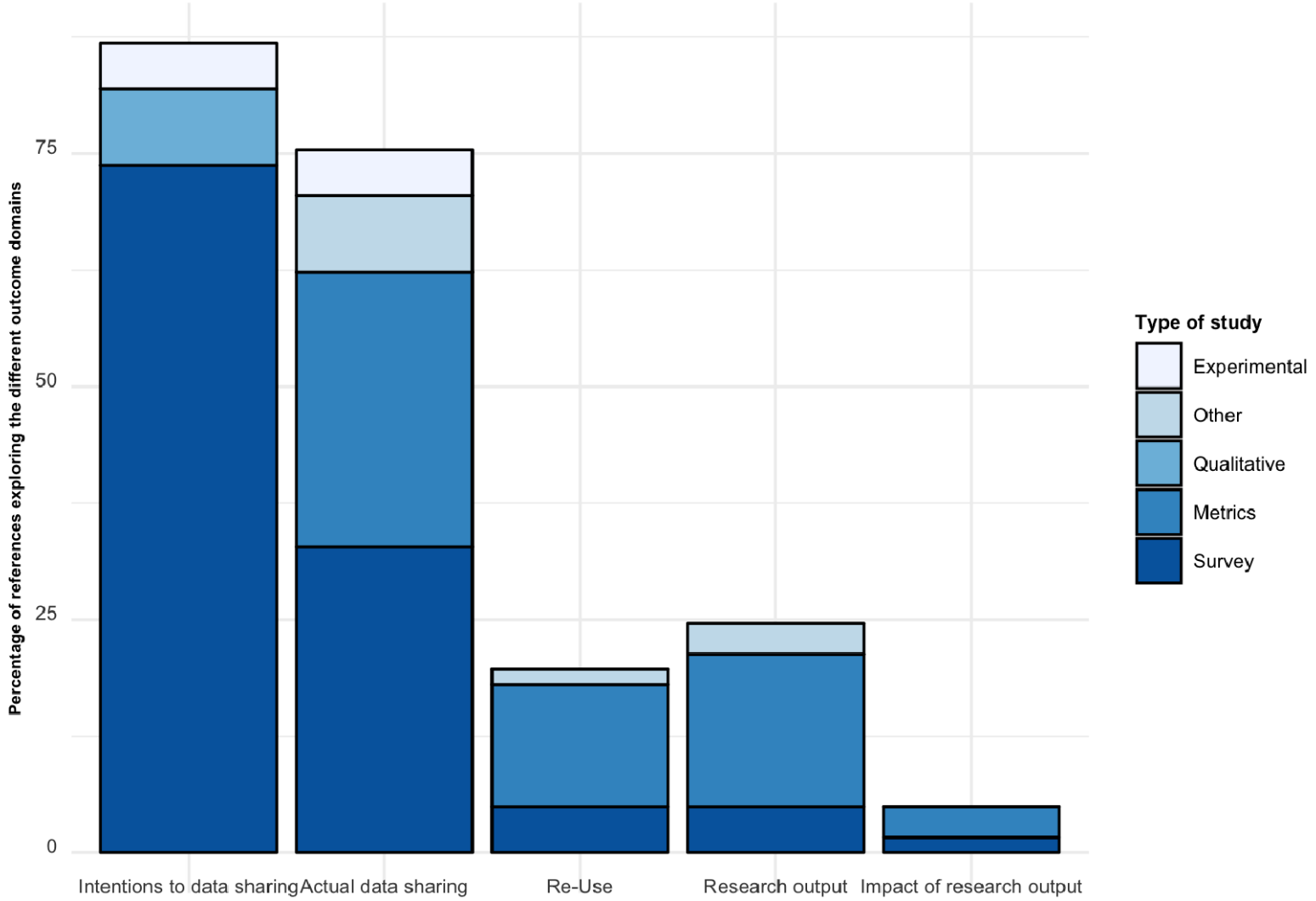
What is the impact of sharing clinical trial data ?

UNIVERSITÉ DE RENNES 1

BMJ Open

Status, use and impact of sharing individual participant data from clinical trials: a scoping review

Christian Ohmann [1], David Moher [2], Maximilian Siebert [3], Edith Motschall [4], Florian Naudet [5]



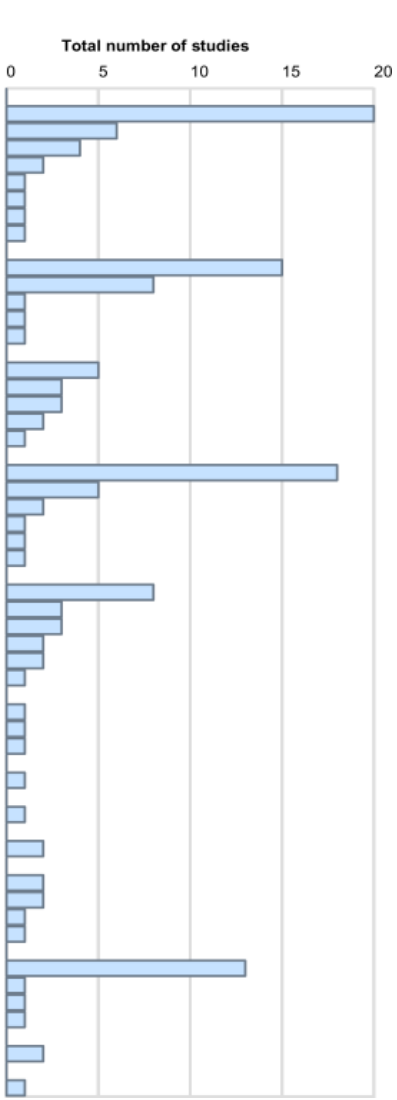
Proportion of the 93 references exploring each outcome domain

BMJ Open

Status, use and impact of sharing individual participant data from clinical trials: a scoping review

Christian Ohmann [1], David Moher [2], Maximilian Siebert [3], Edith Motschall [4], Florian Naudet [5]

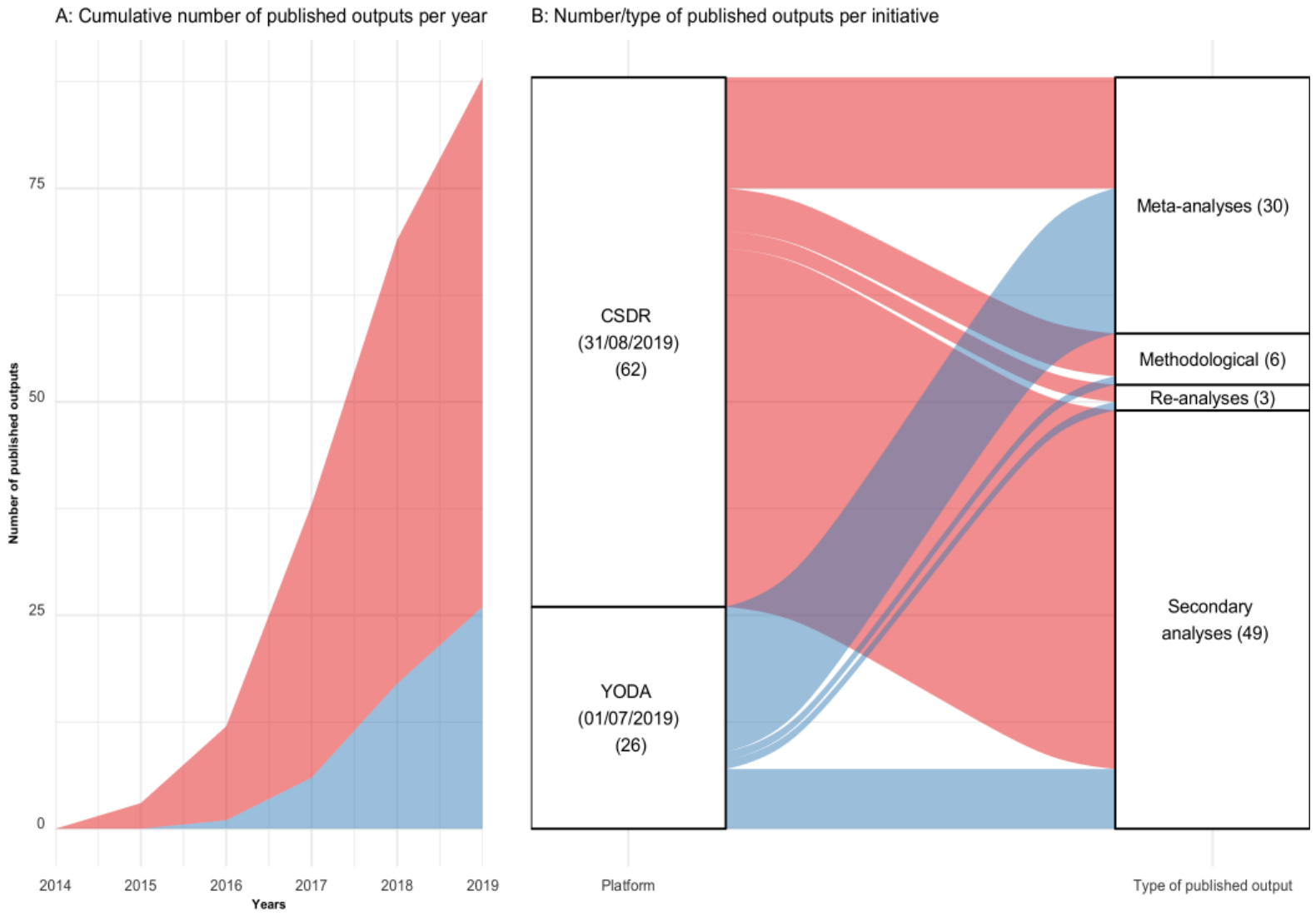
Outcome domains	Outcomes	Experimental	Survey	Metrics	Qualitative	Other
Intentions to data sharing	**For trialists**					
	Intentions to share data	2	18			
	Existence of a data sharing plan/data sharing statement		6			
	Type of data sharing plan		4			
	Support for data sharing		2			
	Willingness to store IPD in a central repository, conditions for storage		1			
	Most pressing ethical issues		1			
	Response to a request for data sharing and time to response	1				
	Preparedness for DS	1				
	For publishers/funders					
	Existence of a data sharing policy/intent to share		15			
	Type of data sharing policy		8			
	Journals requiring participant level data		1			
	Prohibiting data sharing in agreements with industry		1			
	Existence of a data sharing policy for clinical trial units		1			
	For trial participants					
	Willingness to share data		4		1	
	Barriers to share data		2		1	
	Patient Opinions on the Release of Deidentified Individual-Patient Data		3			
	Views, experience and attitudes towards DS				2	
	Information in consent forms		1			
Actual data sharing	**For re-users (e.g. IPD meta-analysts)**					
	Data availability (yes/no)	3	13			2
	Data release after a request		4	1		
	Data availability (time)	1		1		
	Data availability (completeness)	1				
	Rate of IPD meta-analyses / all requests			1		
	Reasons for request, research plan and experience of DS		1			
	For repositories/platforms					
	Data release after a request		2	5		1
	Approval of data release		2	1		
	Data availability		3			
	Number of downloads			2		
	Number of DS agreement, speed of data availability		1	1		
	Database access			1		
	For other stakeholders					
	Number of downloads and page hits for any public access			1		
	Re-use of data by independent data monitoring committees					1
	Cost of preparing the data for data generators					1
Re-use	**Further additional analyses**					
	Approved proposals by subject areas			1		
	IPD meta-analyses					
	Proposals for IPD-meta-analyses and one concrete example			1		
	Re-analyses					
	Reproducibility on primary outcomes		2			
	Any type of re-use					
	Type of re-use			2		
	Progression of the analysis			1		1
	Listing of type of studies performed			1		
	Project completion		1			
Output from data sharing	**Published re-use**					
	Publication of re-use (papers)		2	9		2
	Manuscripts in peer review			1		
	Request discontinued			1		
	Communication of re-use (oral presentation, posters)					1
Impact of research output	**Quantitative metrics for published articles**					
	Citation metrics		1	1		
	Identification of a new finding					
	Crowd voting		1			



BMJ Open

Status, use and impact of sharing individual participant data from clinical trials: a scoping review

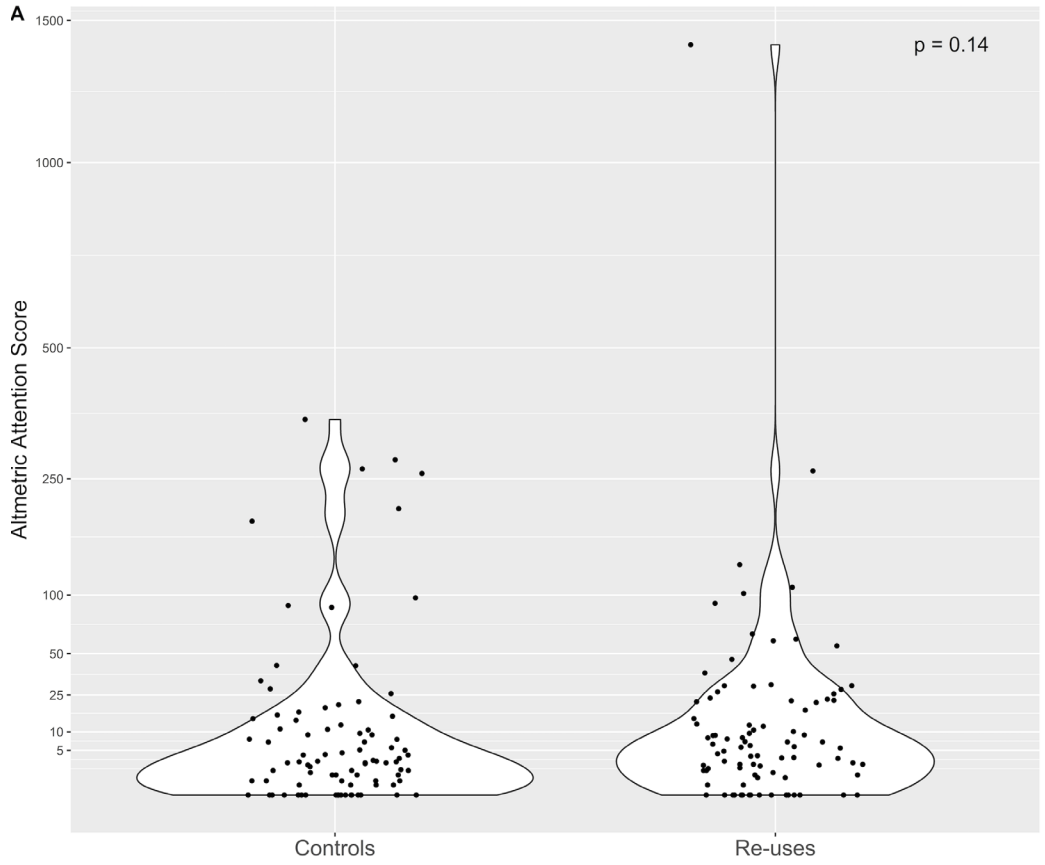
Christian Ohmann [1], David Moher [2], Maximilian Siebert [3], Edith Motschall [4], Florian Naudet [5]

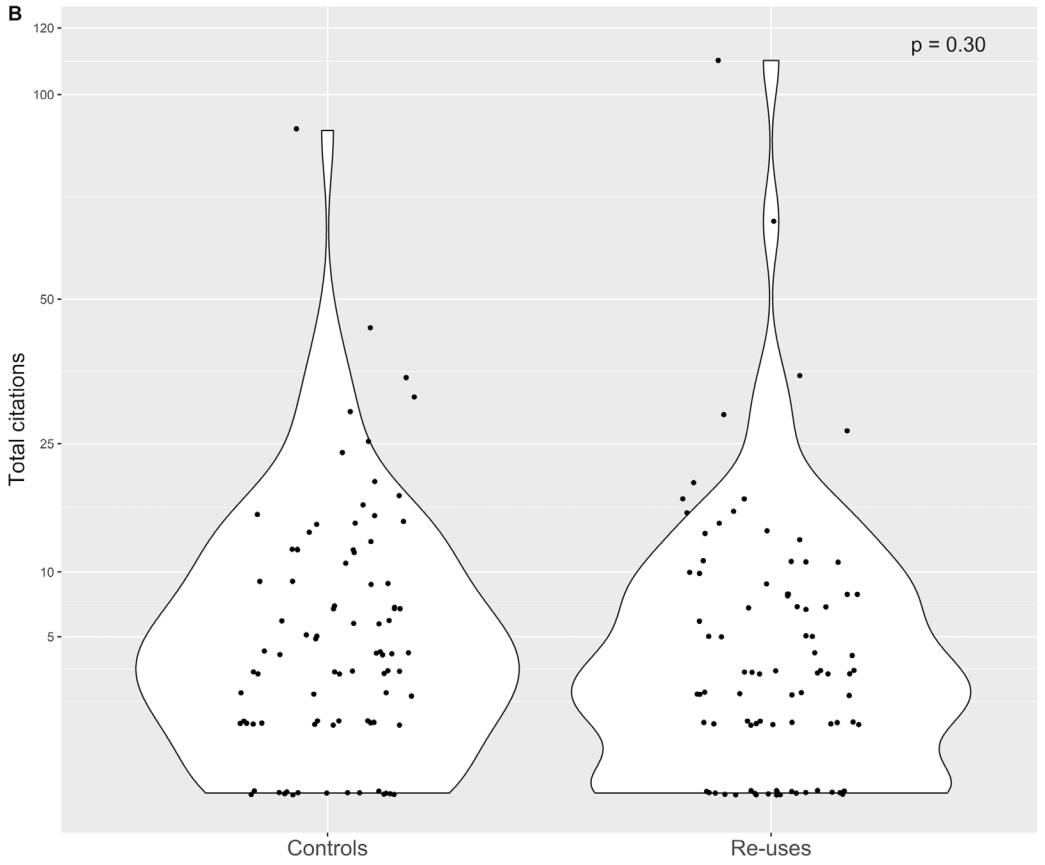


RESEARCH Open Access

Social media attention and citations of published outputs from re-use of clinical trial data: a matched comparison with articles published in the same journals

N. Anthony[1,2*], C. Pellen[2], C. Ohmann[3], D. Moher[4] and F. Naudet[2*]





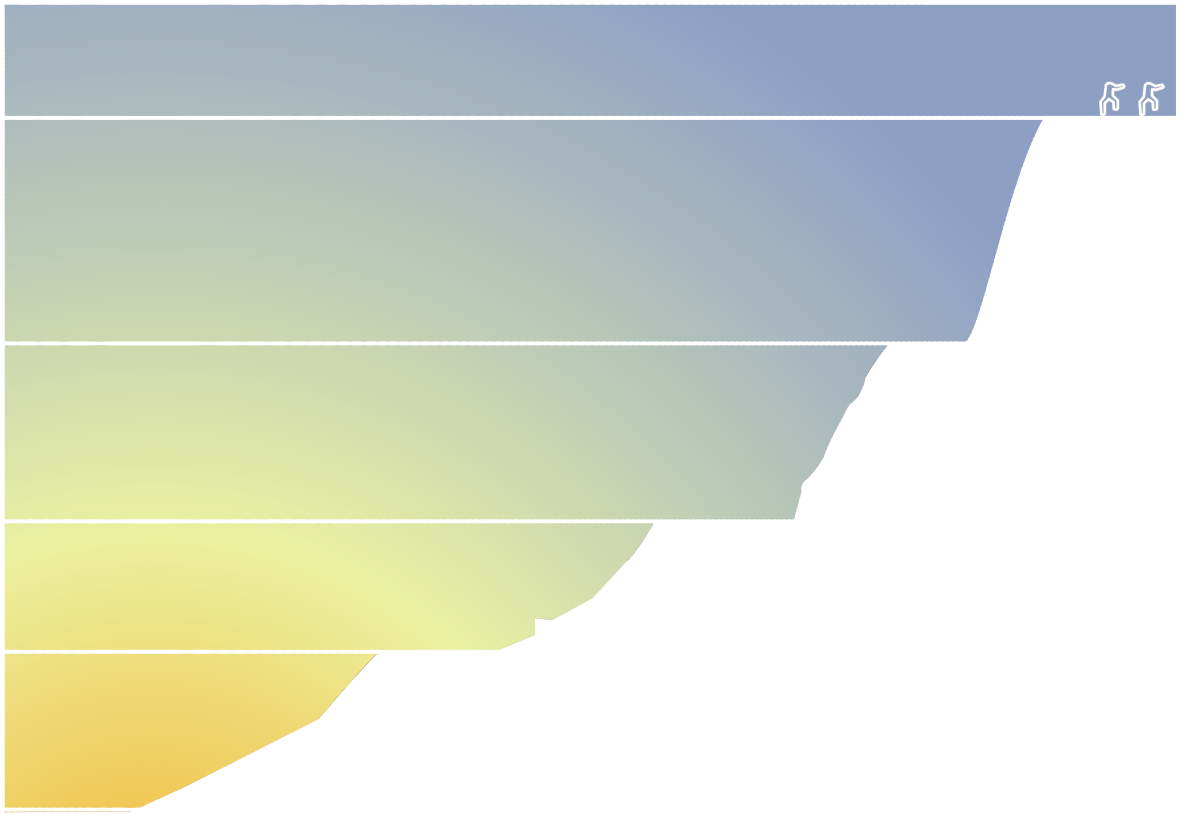
Altmetric

CITATIONS

The NEW ENGLAND JOURNAL of MEDICINE

Learning What We Didn't Know — The SPRINT Data Analysis Challenge

Nancy S. Burns and Pamela W. Miller



SPRINTing to the Finish.

A total of 279 groups requested data from BioLINCC, 218 individuals and teams entered the qualifying round, 200 qualified, and 143 of the entries to the Challenge round were judged.

Entries were judged on the basis of novelty, applicability to clinical practice, and soundness of methods. The judges were 15 recognized experts who represented the three primary constituencies — clinical trialists, data analysts, and patients. In addition to being reviewed by one representative from each constituency, all entries were opened to the public for voting.

- **Implementation of the policy leads to suboptimal Intention to share:**
  - In published RCTs
  - In registered RCTs
- **Intention to share does not imply effective data-sharing**
- **Intention to share does not imply more published re-uses**
- **To date few datasets were re-used from data-sharing platforms :**
  - A majority of secondary analyses
  - A large number of IPD
  - Very few re-analyses
- **Data re-use does not imply the impact of the re-use**

How can we move forward ?

Change the norms ?

Identified challenge	Suggested change to the ICMJE policy	Evaluation component
Poor implementation of the policy by ICMJE-affiliated journals	To certify ICMJE-affiliated journals based on their implementation of the policy. This could be facilitated if journals have a reproducibility research editor.	Developing software to monitor journals' implementation of ICMJE policy, e.g. in line with the TOP factor developed by the Center for Open Science.
Suboptimal intention to share data by RCTs published in ICMJE-journals with a data-sharing policy	Policies should require data-sharing unless major obstacles exist.	Monitoring ICMJE-affiliated journals' enforcement of the policy by implementing software to check whether papers offer data-sharing, similar to that proposed by the Berlin QUEST center.
Suboptimal intention to share data by RCTs in clinical trial registration on databases such as clinical trials.gov for funders with a data-sharing policy.	Policies should require the use of registries making intention to share data mandatory.	Monitoring compliance with funders/sponsors' policies by implementing software to check whether data-sharing plans offer data-sharing, and reporting of this information by funders/sponsors, e.g. Trial Tracker for clinical trial results, and the Good Pharma Scorecard (https://bioethicsinternational.org/good-pharma-scorecard/) for pharmaceutical firms.
"Data-sharing upon request" is not sufficient to ensure that data are shared	Policies should favor data deposition when it is ethically possible. Policies should also outline more clearly the procedures that data requesters should follow and how journals can reinforce data-sharing in case of non-compliance with promises.	Monitoring data availability by implementing practical tests of the policy. Performing interventional studies to evaluate mechanisms of sanction and incentives.
Impact of clinical trial data-sharing is still insufficiently documented.	State explicitly that policy aiming to reform medical science needs to be evidence-based. Policy should be continuously informed and revised via a strong evaluation component.	Defining and testing best practices in clinical trial data-sharing to maximize clinical trial value. Prospectively monitoring the impact of data-sharing policies on the progress of medical research, using observational and interventional designs. This implies developing a tool to identify clinical trial data re-use and then to track the impact of re-uses. Portals are needed that collect this type of data from a wide range of sources (journals, funders, repositories…) since currently, all this information is siloed.

Some identified challenges, suggestions and evaluation components for the ICMJE data-sharing policy

Stakeholders	Proposed action
ICMJE	Should certify compliance, adopt more binding policies, and clarify when clinical trial data-sharing is required and ethically possible.
Journals	Should provide oversight with editorial screening (e.g. by a reproducible research editor) and software screening (e.g. by implementing an IT-infrastructure to verify data-sharing processes described in submitted data-sharing plans). Should postpone future publications from authors if they have not shared their data from previous manuscripts in their journal despite a promise to do so.
Funders/ institutions	Should monitor and reward data-sharing. Should provide technical/regulatory guidance for clinical trial data-sharing. Should implement Data Use and Access Committees (DUACs). Should withhold support from investigators not sharing data. Should support meta-research efforts that evaluate the impact of clinical trial data-sharing.
Researchers	Should commit to sharing data. **Should engage in evaluating the impact of clinical trial data-sharing and provide the necessary feedback to improve the policy.**

Proposed actions for various stakeholders to ensure that the ICMJE policy meets the mark

Clinical trial data sharing statement

- To ensure that no researcher or research sponsor is left without a solution to help draft a clinical trial data sharing statement (DSS).
- To promote responsible sharing of data from clinical trials.

MINISTÈRE
DE L'ENSEIGNEMENT
SUPÉRIEUR,
DE LA RECHERCHE
ET DE L'INNOVATION
Liberté
Égalité
Fraternité

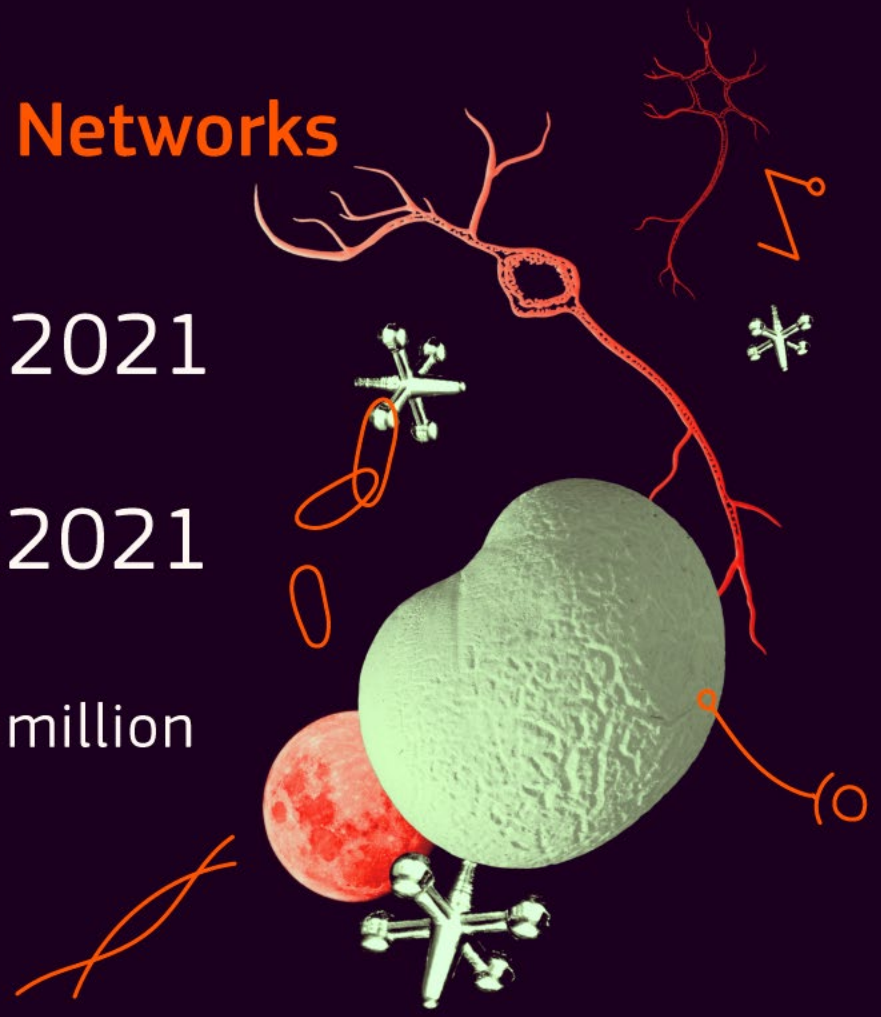
CALL

Doctoral Networks

opening:
22•06•2021

closing:
16•11•2021

budget:
402.95 € million



MSCA
Marie Skłodowska-Curie **Actions**
Developing talents, advancing research

European Commission

“To train a new generation of European experts in medical data science with a focus on clinical trial data sharing, transparency and related reproducible research practices”

WORK IN PROGRESS

Change the world !

The NEW ENGLAND JOURNAL of MEDICINE

A second concern held by some is that a new class of research person will emerge — people who had nothing to do with the design and execution of the study but use another group's data for their own ends, possibly stealing from the research productivity planned by the data gatherers, or even use the data to try to disprove what the original investigators had posited. There is concern among some front-line researchers that the system will be taken over by what some researchers have characterized as "research parasites."

Data Sharing

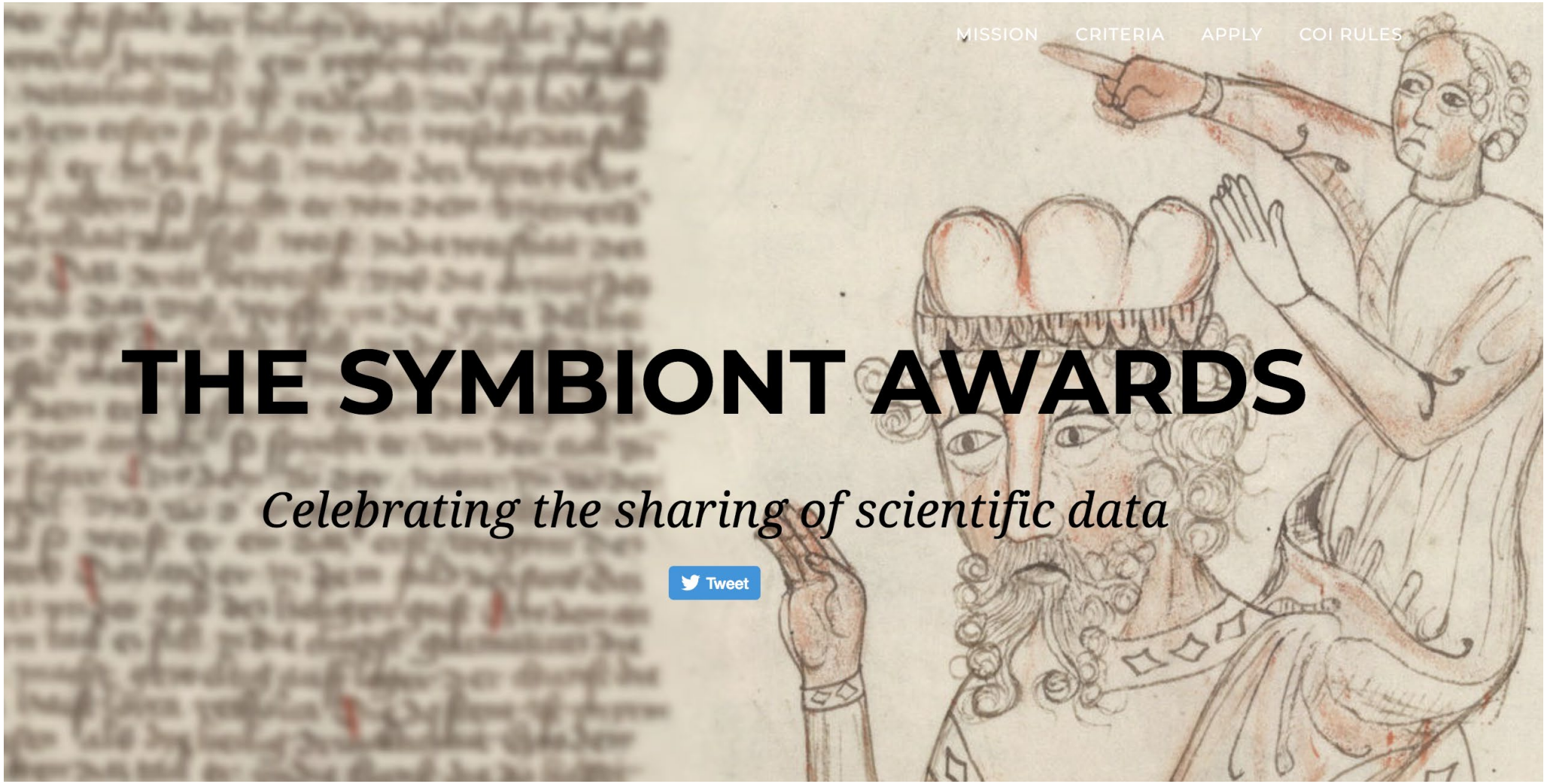
Dan L. Longo, M.D., and Jeffrey M. Drazen, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

Data Sharing

Dan L. Longo, M.D., and Jeffrey M. Drazen, M.D.

The NEW ENGLAND JOURNAL of MEDICINE



Data Sharing

Dan L. Longo, M.D., and Jeffrey M. Drazen, M.D.

PLOS BIOLOGY

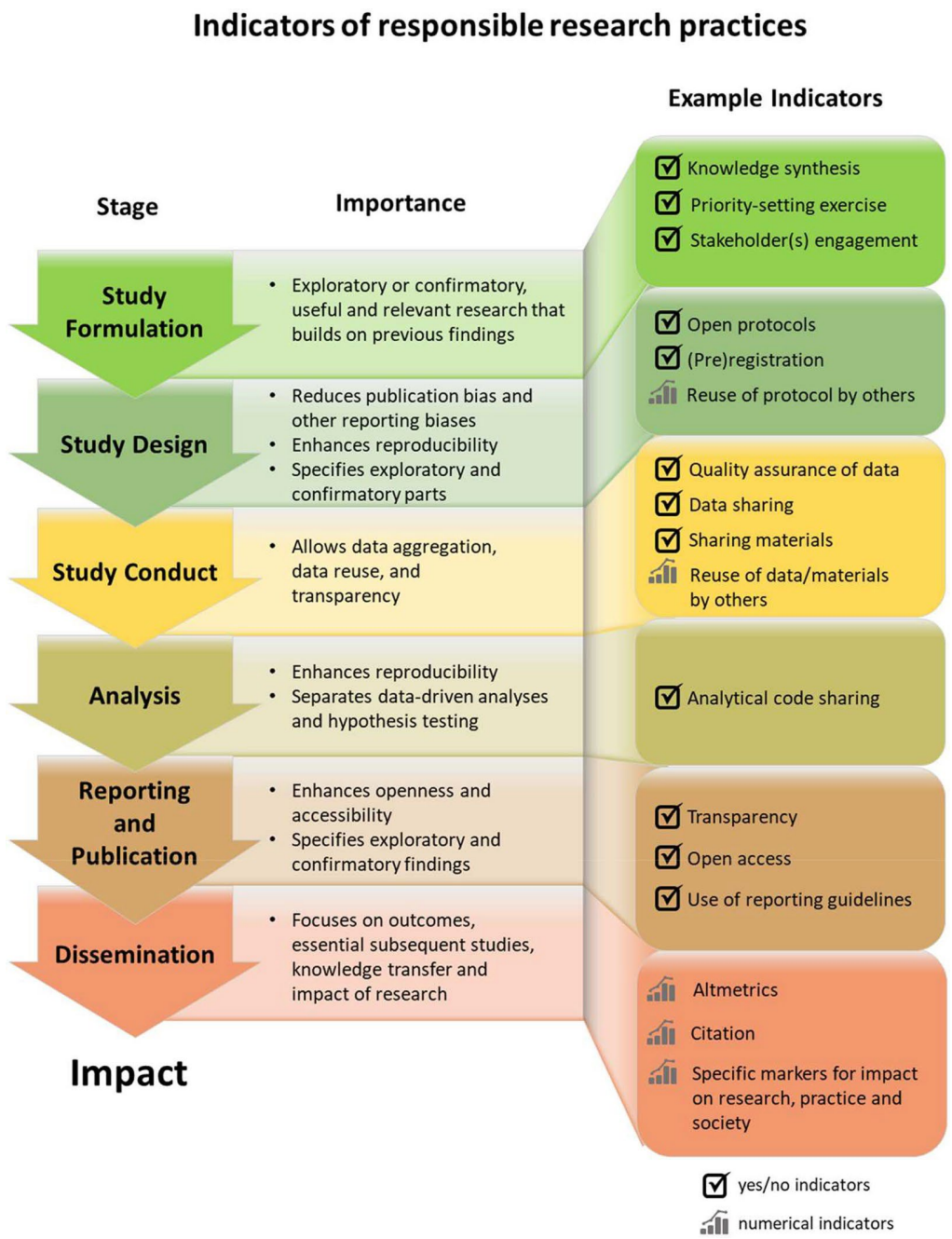


Fig 1. Indicators of responsible research practices.

https://doi.org/10.1371/journal.pbio.3000737.g001

ESSAY

The Hong Kong Principles for assessing researchers: Fostering research integrity

David Moher[1,2]*, Lex Bouter[3,4], Sabine Kleinert[5], Paul Glasziou[6], Mai Har Sham[7], Virginia Barbour[8], Anne-Marie Coriat[9], Nicole Foeger[10], Ulrich Dirnagl[11]

PLOS MEDICINE

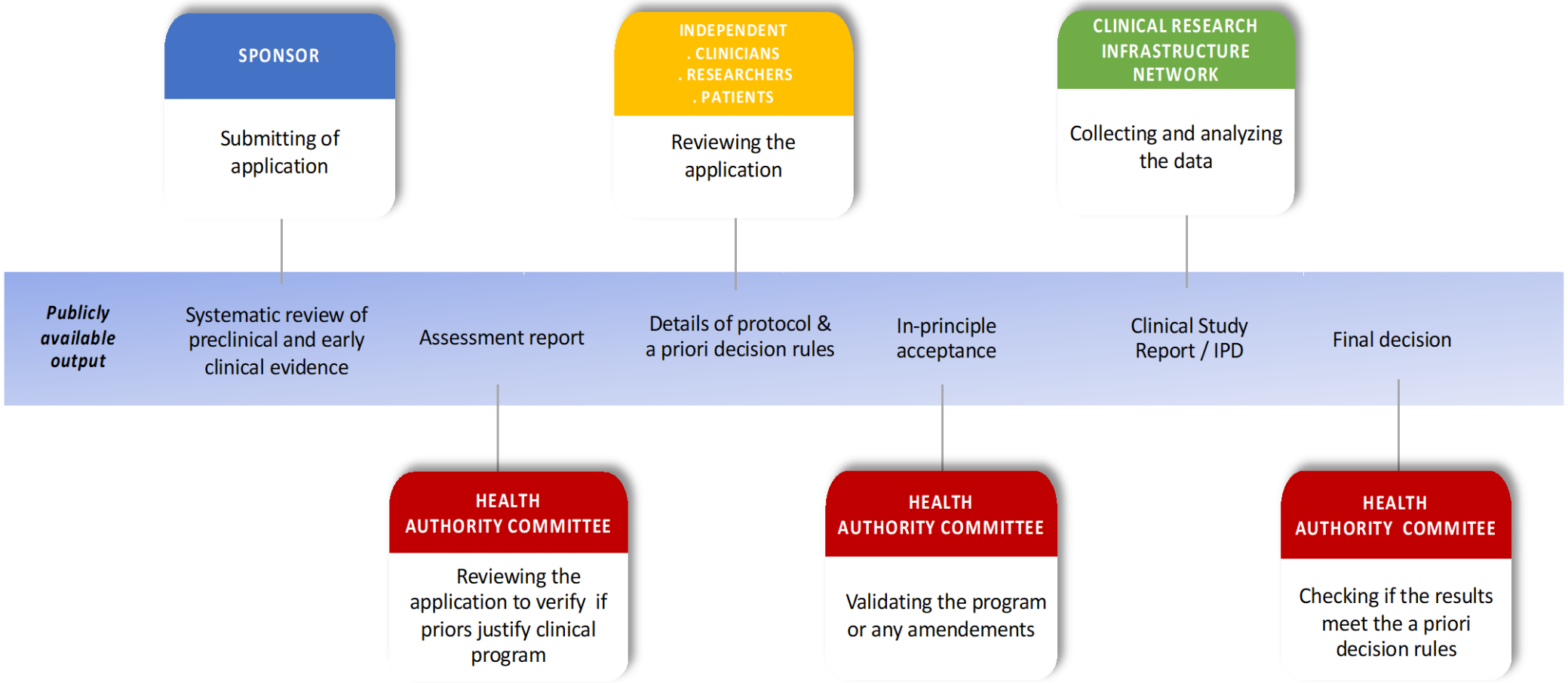
PERSPECTIVE

An open science pathway for drug marketing authorization—Registered drug approval

Florian Naudet[1]*, Maximilian Siebert[1], Rémy Boussageon[2], Ioana A. Cristea[3,4], Erick H. Turner[5,6]

1 Université de Rennes 1, CHU Rennes, Inserm, CIC 1414 (Centre d'Investigation Clinique de Rennes), Rennes, France, **2** Université Claude Bernard Lyon 1, CNRS, UMR 5558, LBBE, EMET, Lyon, France, **3** Department of Brain and Behavioral Sciences, University of Pavia, Italy, **4** IRCCS Mondino Foundation, Pavia, Italy, **5** Behavioral Health and Neurosciences Division, VA Portland Health Care System, Portland, Oregon, United States of America, **6** Department of Psychiatry, Oregon Health & Science University, Portland, Oregon, United States of America

* floriannaudet@gmail.com


SPONSOR
Submitting of application
INDEPENDENT
. CLINICIANS
. RESEARCHERS
. PATIENTS
Reviewing the application
CLINICAL RESEARCH INFRASTRUCTURE NETWORK
Collecting and analyzing the data
Publicly available output
Systematic review of preclinical and early clinical evidence
Assessment report
Details of protocol & a priori decision rules
In-principle acceptance
Clinical Study Report / IPD
Final decision
HEALTH AUTHORITY COMMITTEE
Reviewing the application to verify if priors justify clinical program
HEALTH AUTHORITY COMMITTEE
Validating the program or any amendements
HEALTH AUTHORITY COMMITEE
Checking if the results meet the a priori decision rules

Reproducibility in therapeutic research

ReiTheR

Jeanne Fabiola Gaba

Clara Locher

Maximilian Siebert

Damien Bergeat

Claude Pellen

Laura Caquelin

Norah Anthony

Pauline Rollando

David Moher

Ioana Cristea

Christian Ohmann

Ulrich Mansmann

John Ioannidis

THANK YOU

Maximizing the Impact of Medical Journal Requirements for Clinical Trial Data-Sharing

Florian Naudet[1*] (ORCID: 0000-0003-3760-3801), Maximilian Siebert[1†] (ORCID: 0000-0003-4385-5773), Claude Pellen[1†] (ORCID: 0000-0001-8712-0766), Jeanne Gaba[1†] (ORCID: 0000-0002-1440-0895), Cathrine Axfors[2/3] (ORCID: 0000-0002-2706-1730), Ioana Cristea[4] (ORCID: 0000-0002-9854-7076), Valentin Danchev[2,5] (ORCID: 0000-0002-7563-0168), Ulrich Mansmann[6/7] (ORCID: 0000-0002-9955-8906), Christian Ohmann[8] (0000-0002-5919-1003), Joshua D. Wallach[9] (ORCID: 0000-0002-2816-6905), David Moher[10] (ORCID: 0000-0003-2434-4206), John P.A. Ioannidis[2/11] (ORCID: 0000-0003-3118-6859)

UNDER REVIEW

Web-sites :
https://metrics.stanford.edu/about-us/bio/florian-naudet-0
https://www.reither.org/

Twitter : @NaudetFlorian

e-mails : florian.naudet@chu-rennes.fr / floriannaudet@gmail.com