Adherence to legislation and recommendations to publicly post protocols and results of post-authorisation studies registered with European Medicines Agency: cross sectional study

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Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2026;392:e086693
http://dx.doi.org/10.1136/bmj-2025-086693

Accepted: 02 February 2026

ABSTRACT

OBJECTIVE

To assess whether post-authorisation studies registered with the European Medicines Agency (EMA) adhere to legislation and recommendations to publicly post study protocols and results.

DESIGN

Cross sectional study.

SETTING

Data extracted from the EMA Catalogue of real-world data studies in February 2024, including post-authorisation studies registered since November 2010. EU legislation requires EU risk management plan (RMP) category 1 and 2 studies to upload the protocol and results to the catalogue. The EMA also recommends uploading the protocol and results for all other registered post-authorisation studies, including EU RMP category 3 studies, non-EU RMP-only studies, and those not included in an RMP.

INCLUDED STUDIES

2300 (1484 finalised; 816 ongoing) post-authorisation studies for protocol availability and 1482 finalised post-authorisation studies (excluding two recently finalised post-authorisation studies) for results availability.

MAIN OUTCOME MEASURES

Public availability of protocols for ongoing and finalised post-authorisation studies and results (abstract and/or final report) for finalised post-authorisation studies.

RESULTS

Overall, protocols were available for 1370 (59.6%) of 2300 ongoing and finalised post-authorisation studies and results were available for 1014 (68.4%) of 1482 finalised post-authorisation studies. For ongoing and finalised post-authorisation studies according to RMP requirements, protocols were available for 76 (68%) of 112 EU RMP category 1 studies, 21 (64%) of 33 EU RMP category 2 studies, 419 (67.0%) of 625 EU RMP category 3 studies, 87 (67%) of 129 non-EU RMP-only studies, and 715 (55.3%) of 1292 post-authorisation studies not included in an RMP. For finalised post-authorisation studies, results were available for 61 (90%) of 68 EU RMP category 1 studies, 17 (90%) of 19 EU RMP category 2 studies, 304 (75.8%) of 401 EU RMP category 3 studies, 56 (69%) of 81 non-EU RMP-only studies, and 547 (64.1%) of 853 post-authorisation studies not included in an RMP.

CONCLUSIONS

Adherence to legislation and recommendations to publicly post protocols and results of post-authorisation studies registered with the EMA is insufficient: only 6 of every 10 finalised and ongoing post-authorisation studies had uploaded a protocol and less than 7 of every 10 finalised post-authorisation studies had uploaded results to the EMA Catalogue of real-world data studies. Adherence was particularly poor among post-authorisation studies not included in an RMP subject to recommendations (but no legal obligation) to post the protocol and results. Assessing data on the upload status of the protocols and results of EMA registered post-authorisation studies is feasible and helps to scrutinise whether post-authorisation studies adhere to legislation and recommendations. Better adherence is needed for greater research transparency.

WHAT IS ALREADY KNOWN ON THIS TOPIC

A previous survey showed that post-authorisation studies requested by regulators and registered with the European Medicines Agency often fail to make public the protocol

Data have so far been lacking on the extent to which EMA registered post-authorisation studies make their results public

WHAT THIS STUDY ADDS

Post-authorisation studies registered with the EMA insufficiently adhere to legislation and recommendations to upload the protocol and results to the Catalogue of real-world data studies

Post-authorisation studies not included in a risk management plan were less likely to have posted the protocol and results than studies required by a risk management plan

Adherence varied considerably between sponsors; a web application was developed to investigate aggregate and individual post-authorisation studies by sponsor

Introduction

Post-authorisation studies aim to close, mostly through observational designs, any gaps in knowledge on the benefits and risks of medicines that remain at the time of marketing authorisation. Regulatory authorities grant the authorisation to market medicines to drug companies, known as marketing authorisation holders. When doing so on the basis of less comprehensive data than would normally be required, regulators often require that marketing authorisation holders conduct post-authorisation studies in view of emerging concerns on drug safety once the drug is placed on the market or to assess the effectiveness of additional risk minimisation measures.[1] However, marketing authorisation holders also conduct post-authorisation studies on their own initiative. In the EU, the European Medicines Agency

Box 1: Post-authorisation studies by EU risk management plan (RMP) categories 1-3

- EU RMP category 1 studies are "imposed as a condition" of the marketing authorisation
- EU RMP category 2 studies are "imposed as a specific obligation" for drugs approved under exceptional circumstances (eg, orphan drugs) or on conditional marketing authorisations (eg, drugs for life threatening diseases or unmet medical needs)
- EU RMP category 3 studies are "required" to investigate a safety concern

(EMA) is the regulatory body responsible for granting marketing authorisation and overseeing subsequent post-authorisation studies specified in any risk management plan (RMP) agreed on with the marketing authorisation holder.[2] Depending on the regulatory requirement, these post-authorisation studies fall into the EU RMP categories 1 to 3,[3] which are further described in box 1. They comprise post-authorisation safety studies, which investigate potential harms and the effectiveness of any risk minimisation measures, and post-authorisation efficacy studies, which further evaluate potential benefits of authorised medicines.[4] Additional pharmacovigilance activities include post-authorisation studies sponsored by the EMA and other competent authorities to support regulatory decision making, as well as those conducted voluntarily by marketing authorisation holders and other entities outside regulatory requirements.

Access to the protocols and results of post-authorisation studies is important to increase research transparency, reduce publication bias, and enable critical appraisal for improving research quality.[2 4] Accordingly, EU legislation adopted in 2010 and applicable since mid-2012 has required marketing authorisation holders to register any non-interventional imposed post-authorisation studies (that is, EU RMP category 1 and 2 studies) and to publish the protocol and abstract of results on an online portal run by the EMA,[5 6] and the EMA also strongly encourages public posting of the final study report of these post-authorisation studies.[7] Furthermore, the EMA recommends that the same study documents are also provided for all other post-authorisation studies as required for imposed post-authorisation studies.[4 7] Stemming from these legal provisions and regulatory guidelines, the EMA launched the EU PAS Register in November 2010 as a publicly accessible online database, allowing responsible entities to register post-authorisation studies and upload protocols and results.[8] The EMA has recommended that the study protocol should be uploaded before the start of data collection and a final study report should be entered in the register within two weeks of its finalisation.[4 7] In February 2024 the EMA launched the Catalogue of real-world data studies and transferred all post-authorisation studies previously included in the EU PAS Register to this new database.[9]

Adherence to public posting of protocols and study results of post-authorisation studies is crucial for scientific scrutiny and exchange to increase the value of post-marketing research but has been studied only to a limited extent. A research network coordinated by the EMA,[10] examining post-authorisation studies included in the EU PAS Register from 2010 to 2018, showed that a protocol was publicly available for less than two thirds of non-interventional post-authorisation studies requested by competent authorities.[11] However, the study did not consider RMP requirements that define whether post-authorisation studies are subject to legislation as opposed to recommendations and also refrained from reporting on registered post-authorisation studies that were not requested by regulators. Furthermore, to the best of our knowledge, no previous study has investigated whether results of post-authorisation studies registered with the EMA have been made publicly available. The objective of this study was therefore to assess the adherence to legislation and recommendations to publicly post the protocols and results of all post-authorisation studies registered with the EMA.

Methods

This study was preregistered in the Open Science Framework on 24 December 2023 specifying the design, sampling plan, variables, and analysis plan.[12] Our study follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guidelines. Please see the completed STROBE checklist in the supplementary material.

Study design and data

This is a cross sectional study based on data from the EMA Catalogue of real-world data studies.[9] In this repository, responsible entities can register post-authorisation studies, enter metadata, and upload study documents. The EMA provides a list of metadata describing all data items and documents to be included in the catalogue.[13] Specifically, entering the "actual date of study start" and "actual date of final study report" automatically updates the study status to "ongoing" and "finalised," setting the timelines for protocol and results upload, respectively.[13] Once uploaded in the catalogue, a document cannot be replaced, preventing any post hoc changes to uploaded protocols and reports (personal communication, EMA ServiceDesk, 2 June 2024).

Data extraction

To assess the data for our study, we extracted the metadata from the catalogue on 21 February 2024 in two different ways: firstly, we exported the data by using the integrated export function; secondly, we scraped data from the websites by using Python version 3.11.6 (code available on GitHub).[14] Whereas the exported dataset includes the names of uploaded documents for post-authorisation studies, the scraped dataset includes the web addresses of these documents. Using the web addresses in the scraped dataset, we

doi: 10.1136/bmj-2025-086693 | *BMJ* 2026;392:e086693 | the bmj

downloaded all documents for post-authorisation studies from the catalogue on 7 July 2024.

Data management

We merged the scraped and exported datasets by using the EU PAS number, a unique identifier assigned to each post-authorisation study registered, to associate downloaded documents with exported data. After this merging, we matched all overlapping dataset fields to confirm that the scraped and exported data were identical. We verified that the data were consistent with the EMA's metadata list. In particular, we verified that all categorical values aligned with the specifications and all numerical values were plausible. Furthermore, we assessed the number of unspecified and unique values in data fields for study variables (supplementary table S1). Finally, we manually matched the names of funding sources (sponsors) entered in free text data fields, harmonising labels and spellings.

Studies included and excluded

All post-authorisation studies registered in the Catalogue of real-world data studies at the time of the data extraction (21 February 2024) were eligible for inclusion in the study. We included studies with a status of "ongoing" or "finalised" in the sample examined for protocol availability, allowing a delay of five working days for approval of any protocol by the EMA. In addition, we included all post-authorisation studies with a study status of "finalised" in the sample examined for results availability, allowing a delay of 15 working days (10 days as conceded by the EMA guidelines, plus five more days for approval of any results by the EMA).[4] We chose a delay of five working days in line with previous research.[15] We considered a downtime of the catalogue from 21 January to 15 February 2024 in the delay calculations to account for the inability to upload during that time. We also explored the impact of extended delays. We excluded post-authorisation studies with a study status of "planned." We also excluded post-authorisation studies that had been cancelled according to the study description (EMA. FAQ – EU PAS Register. 2020). For this purpose, two authors (PR and CP) independently reviewed all descriptions of post-authorisation studies to classify studies as cancelled or not cancelled and subsequently discussed discrepancies to reach a consensus.

Review of study documents

In the Catalogue of real-world data studies, protocols had to be uploaded in the field "protocol document" and results in the fields "results tables" and "study report."[13] If protocol and results documents exceeded the 10 megabyte file size limit, they had to be split and uploaded in the field "study, other information" (EMA. FAQ – EU PAS Register. 2020). Thus, we considered all documents uploaded in the field "protocol document" to be protocols, and two authors (PR and CP) reviewed all documents uploaded in the fields "results tables," "study report," and "study, other information" (1469 documents) to identify further protocols as well as results—that is, abstracts and final reports—on the basis of document names, titles, and contents. As well as standalone abstracts, we also considered abstracts in uploaded result publications.

Study outcomes

Two main outcomes were pre-specified: protocol availability for finalised and ongoing post-authorisation studies; and results availability (defined as an abstract and/or final report) for finalised post-authorisation studies. As additional outcomes specified at the analysis stage, we examined posting of the abstract only and the final report as separate outcomes for finalised post-authorisation studies. We assessed these outcomes in the total samples of post-authorisation studies examined and by study characteristics and study sponsors.

Covariates

Most covariates were pre-specified in our protocol.[12] Using the metadata as given in the Catalogue of real-world data studies, we recorded each study's relation to an RMP (EU RMP category 1, 2, or 3, non-EU RMP-only, or not included in an RMP), whether the study was required by a regulatory body, the study type (clinical trial, non-interventional study, or not applicable), and study status (planned, ongoing, or finalised). On the basis of count data of funding sources and study countries listed, we determined whether a post-authorisation study had multiple funding sources and whether it was conducted in multiple countries versus a single country. We analysed the following age groups of the study population: <18 years, ≥18 years, and <18 years and ≥18 years. We calculated the planned study duration (quarters) using the planned start and end dates given and classified the estimated total study population (<100, 100-<500, 500-<1000, 1000-10 000, >10 000) by using the number specified. We defined medical condition(s) to be studied, outcome(s) specified, and collaboration of a research network (yes, no) on the basis of whether or not metadata were specified in corresponding data fields.

Following a previous study,[15] we specified two additional covariates at the analysis stage: type of funding source (commercial, non-commercial, mixed, or no funding) and the number of post-authorisation studies funded by the sponsor (quarters). For post-authorisation studies with multiple sponsors, to avoid double counting, we assigned that particular study to the sponsor funding the greatest number of post-authorisation studies; for sensitivity analysis, we divided the integer and assigned fractions of that particular post-authorisation study to sponsors (divide-and-assign approach).

Data checks and updates

We checked data for plausibility, consistency, and validity where possible and updated them for the analysis if appropriate. Firstly, we replaced the implausible start date of a post-authorisation study

with study status "ongoing" by its registration date. Secondly, we checked whether the study status matched the specified study dates as detailed in the EMA's data descriptions—that is, ongoing post-authorisation studies have a study start date only, finalised post-authorisation studies have a final study report date, and all other post-authorisation studies are planned.[16] Contrary to this, we found 16 post-authorisation studies with study status unspecified but funding contract signed, for which we updated the status to "planned," and one post-authorisation study with study status "finalised" but study start date unspecified, for which we updated the status to "planned." Thirdly, we checked whether the study status matched the study documents. We excluded one post-authorisation study with study status "ongoing" and one with the status "finalised," as we found these to have been cancelled on the basis of the reviewed study documents. Furthermore, we detected an inconsistent study status in 15 post-authorisation studies with uploaded progress, interim, and final reports, for which we updated the status of three post-authorisation studies to "ongoing" and 12 to "finalised" as reported in the study documents. Finally, we observed inconsistencies when cross tabulating the variables "study required by an RMP" and "study required by a regulatory body" and a limited validity of the latter variable when reviewing selected post-authorisation study documents. We thus refrained from using the variable as a covariate in the main analysis.

Statistical analysis

The statistical analysis followed the pre-specified analysis plan. We calculated descriptive statistics including numbers (percentages) and medians (interquartile ranges). We estimated odds ratios with 95% confidence intervals for associations of covariates with the main outcomes by using logistic regression models. Multivariable models included all variables examined in the univariable models, and we additionally adjusted for time since study start date and date of final study report when analysing protocol and results availability, respectively. We checked models for multicollinearity by using generalised variance inflation factors (supplementary table S2). In sensitivity analyses, we assessed the robustness of estimates. Firstly, we excluded potentially influential outliers (Cook's distance >4/n; standardised residuals >2) comprising 25 and 28 post-authorisation studies examined for protocol and results availability, respectively. Secondly, we truncated the study start date and date of final study report at 6 November 2010 (that is, the earliest registration date after the launch of the registry) in 121 and seven post-authorisation studies started and finalised before that date, respectively. Thirdly, we excluded EU RMP category 1 and EU RMP category 2 studies with study start date before mid-2012 when the legislation became effective (that is, 14 and 11 post-authorisation studies from the protocol and results analysis, respectively). Fourthly, we included the variable study required by a regulatory body as an additional covariate. Fifthly, we used the covariate number of post-authorisation

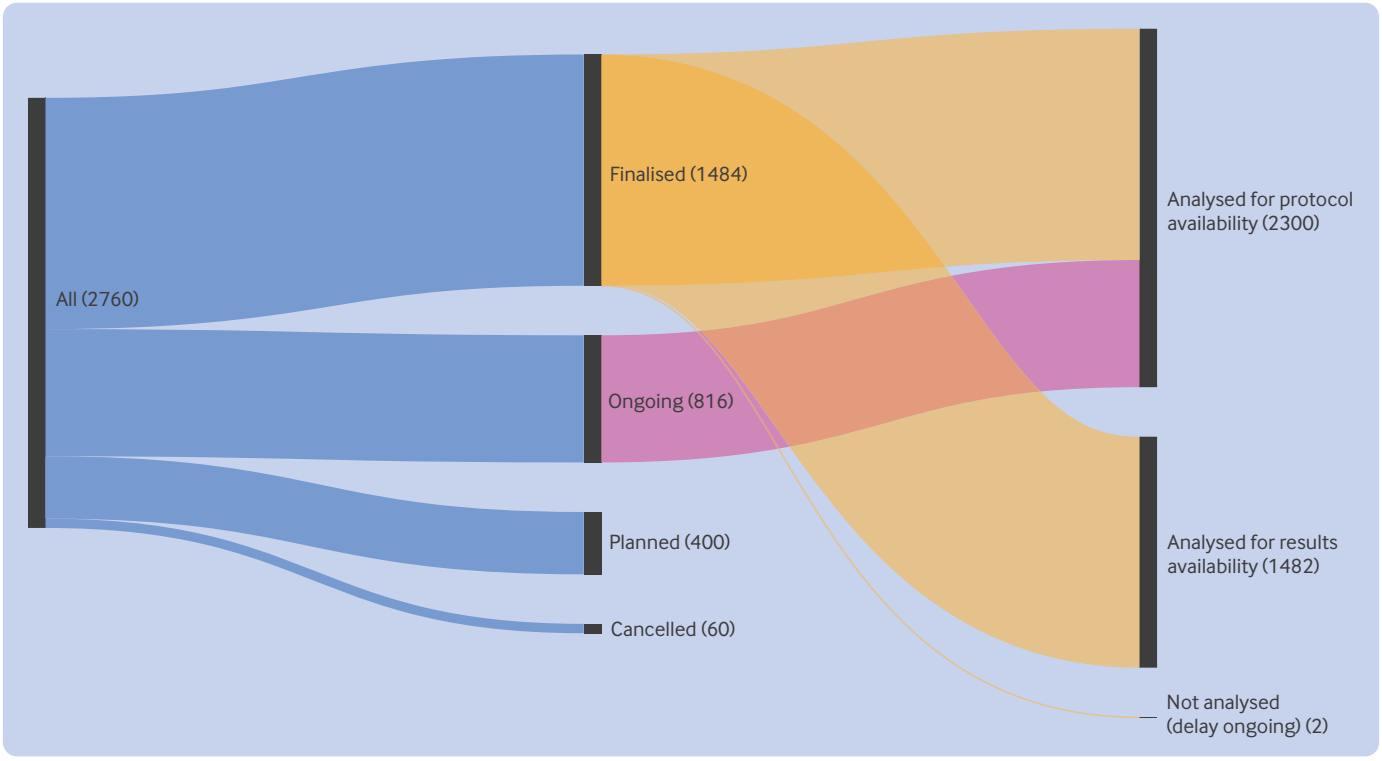

Fig 1 | Sankey diagram showing number of post-authorisation studies excluded from and included in study

doi: 10.1136/bmj-2025-086693 | *BMJ* 2026;392:e086693 | the bmj

Table 1 | Characteristics of ongoing and finalised post-authorisation studies (PAS) examined for protocol availability. Values are numbers (percentages)

Characteristic	All PAS (n=2300)	PAS according to study required by RMP					
		EU RMP category 1 (n=112)	EU RMP category 2 (n=33)	EU RMP category 3 (n=625)	Non-EU RMP-only (n=129)	Not included in RMP (n=1292)	Unspecified (n=109)
Study required by a regulatory body:							
Yes	1021 (44.4)	111 (99)	30 (91)	499 (79.8)	96 (74)	274 (21.2)	11 (10)
No	1255 (54.6)	1 (1)	3 (9)	124 (19.8)	33 (26)	999 (77.3)	95 (87)
Unspecified	24 (1.0)	0 (0)	0 (0)	2 (0.3)	0 (0)	19 (1.5)	3 (3)
Type of funding source:							
Commercial	1785 (77.6)	111 (99)	33 (100)	621 (99.4)	123 (95)	835 (64.6)	62 (57)
Non-commercial	391 (17.0)	0 (0)	0 (0)	2 (0.3)	4 (3)	359 (27.8)	26 (24)
Mixed	60 (2.6)	1 (1)	0 (0)	2 (0.3)	1 (1)	45 (3.5)	11 (10)
Unclear	36 (1.6)	0 (0)	0 (0)	0 (0.0)	0 (0)	27 (2.1)	9 (8)
No funding	28 (1.2)	0 (0)	0 (0)	0 (0.0)	1 (1)	26 (2.0)	1 (1)
Multiple funding sources:							
Yes	235 (10.2)	11 (10)	1 (3)	39 (6.2)	9 (7)	143 (11.1)	32 (29)
No	2065 (89.8)	101 (90)	32 (97)	586 (93.8)	120 (93)	1149 (88.9)	77 (71)
No of PAS funded by sponsor, quarters:							
1 (1-9 studies)	611 (26.6)	58 (52)	18 (55)	154 (24.6)	16 (12)	339 (26.2)	26 (24)
2 (10-58 studies)	604 (26.3)	24 (21)	6 (18)	215 (34.4)	43 (33)	290 (22.4)	26 (24)
3 (59-110 studies)	566 (24.6)	26 (23)	3 (9)	183 (29.3)	39 (30)	279 (21.6)	36 (33)
4 (111-176 studies)	519 (22.6)	4 (4)	6 (18)	73 (11.7)	31 (24)	384 (29.7)	21 (19)
Countries in which study is conducted:							
Multiple countries	945 (41.1)	85 (76)	25 (76)	388 (62.1)	18 (14)	399 (30.9)	30 (28)
Single country	1355 (58.9)	27 (24)	8 (24)	237 (37.9)	111 (86)	893 (69.1)	79 (72)
Study type:							
Clinical trial	32 (1.4)	0 (0)	0 (0)	8 (1.3)	2 (2)	15 (1.2)	7 (6)
Non-interventional	2224 (96.7)	112 (100)	33 (100)	611 (97.8)	126 (98)	1250 (96.7)	92 (84)
Not applicable	44 (1.9)	0 (0)	0 (0)	6 (1.0)	1 (1)	27 (2.1)	10 (9)
Estimated study population size:							
<100	260 (11.3)	13 (12)	10 (30)	88 (14.1)	14 (11)	127 (9.8)	8 (7)
100-<500	498 (21.7)	22 (20)	12 (36)	145 (23.2)	42 (33)	258 (20.0)	19 (17)
500-<1000	244 (10.6)	16 (14)	3 (9)	84 (13.4)	22 (17)	103 (8.0)	16 (15)
1000-10 000	569 (24.7)	37 (33)	4 (12)	160 (25.6)	39 (30)	301 (23.3)	28 (26)
>10 000	729 (31.7)	24 (21)	4 (12)	148 (23.7)	12 (9)	503 (38.9)	38 (35)
Age of study population:							
<18 years	148 (6.4)	9 (8)	4 (12)	41 (6.6)	10 (8)	73 (5.7)	11 (10)
≥18 years	1467 (63.8)	51 (46)	14 (42)	384 (61.4)	77 (60)	867 (67.1)	74 (68)
<18 and ≥18 years	685 (29.8)	52 (46)	15 (45)	200 (32.0)	42 (33)	352 (27.2)	24 (22)
Medical condition(s) to be studied:							
Yes	1668 (72.5)	82 (73)	24 (73)	465 (74.4)	81 (63)	924 (71.5)	92 (84)
No	632 (27.5)	30 (27)	9 (27)	160 (25.6)	48 (37)	368 (28.5)	17 (16)
Outcomes specified:							
Yes	1919 (83.4)	93 (83)	30 (91)	528 (84.5)	111 (86)	1065 (82.4)	92 (84)
No	381 (16.6)	19 (17)	3 (9)	97 (15.5)	18 (14)	227 (17.6)	17 (16)
Collaboration of a research network:							
Yes	261 (11.3)	13 (12)	6 (18)	48 (7.7)	3 (2)	169 (13.1)	22 (20)
No	2039 (88.7)	99 (88)	27 (82)	577 (92.3)	126 (98)	1123 (86.9)	87 (80)
Study uses established data source:							
Yes	742 (32.3)	36 (32)	4 (12)	179 (28.6)	13 (10)	469 (36.3)	41 (38)
No	1558 (67.7)	76 (68)	29 (88)	446 (71.4)	116 (90)	823 (63.7)	68 (62)
Status of study:							
Ongoing	816 (35.5)	44 (39)	14 (42)	223 (35.7)	48 (37)	438 (33.9)	49 (45)
Finalised	1484 (64.5)	68 (61)	19 (58)	402 (64.3)	81 (63)	854 (66.1)	60 (55)
Planned duration of study, quarters*:							
1 (0.02-0.84 years)	460 (20.0)	10 (9)	3 (9)	61 (9.8)	17 (13)	350 (27.1)	19 (17)
2 (0.84-2.17 years)	462 (20.1)	15 (13)	3 (9)	92 (14.7)	15 (12)	308 (23.8)	29 (27)
3 (2.17-4.66 years)	457 (19.9)	19 (17)	3 (9)	120 (19.2)	35 (27)	250 (19.3)	30 (28)
4 (4.66-23.03 years)	460 (20.0)	47 (42)	21 (64)	201 (32.2)	39 (30)	145 (11.2)	7 (6)
Unspecified	461 (20.0)	21 (19)	3 (9)	151 (24.2)	23 (18)	239 (18.5)	24 (22)

RMP=risk management plan.
* Quarter bounds were rounded; exact bounds in days: 1 (6-305), 2 (306-791), 3 (792-1701), 4 (1702-8412).

studies funded by the sponsor based on the divide-and-assign approach instead of integer numbers in post-authorisation studies with multiple sponsors. We used Python version 3.11.6 with code shared on GitHub for all statistical analyses.[14 17]

Web application

We created a web application to allow greater exploration of study outcomes, including by sponsor views at the aggregate and individual study level, using JavaScript 1.5 with code shared on GitHub.[18] The web

application will be made available on pas-adherence.eu once this paper is published.

Patient and public involvement

No funding was available for patient and public involvement in the study, and the team was not trained to work with the public.

Results

Composition of study samples

Figure 1 shows the composition of the study samples. Of 2760 post-authorisation studies extracted from the Catalogue of real-world data studies, we excluded 400 (14.5%) planned studies and 60 (2.2%) cancelled studies, leaving 2300 post-authorisation studies

Table 2 | Characteristics of finalised post-authorisation studies (PAS) examined for results availability. Values are numbers (percentages)

Characteristic	All PAS (n=1482)	PAS according to study required by RMP					
		EU RMP category 1 (n=68)	EU RMP category 2 (n=19)	EU RMP category 3 (n=401)	Non-EU RMP-only (n=81)	Not included in RMP (n=853)	Unspecified (n=60)
Study required by a regulatory body:							
Yes	675 (45.5)	68 (100)	17 (89)	326 (81.3)	57 (70)	202 (23.7)	5 (8)
No	789 (53.2)	0 (0)	2 (11)	73 (18.2)	24 (30)	636 (74.6)	54 (90)
Unspecified	18 (1.2)	0 (0)	0 (0)	2 (0.5)	0 (0)	15 (1.8)	1 (2)
Type of funding source:							
Commercial	1160 (78.3)	67 (99)	19 (100)	400 (99.8)	79 (98)	560 (65.7)	35 (58)
Non-commercial	246 (16.6)	0 (0)	0 (0)	0 (0.0)	2 (2)	233 (27.3)	11 (18)
Mixed	40 (2.7)	1 (1)	0 (0)	1 (0.2)	0 (0)	32 (3.8)	6 (10)
Unclear	22 (1.5)	0 (0)	0 (0)	0 (0.0)	0 (0)	15 (1.8)	7 (12)
No funding	14 (0.9)	0 (0)	0 (0)	0 (0.0)	0 (0)	13 (1.5)	1 (2)
Multiple funding sources:							
Yes	135 (9.1)	8 (12)	0 (0)	24 (6.0)	7 (9)	80 (9.4)	16 (27)
No	1347 (90.9)	60 (88)	19 (100)	377 (94.0)	74 (91)	773 (90.6)	44 (73)
No of PAS funded by sponsor, quarters:							
1 (1-11 studies)	373 (25.2)	42 (62)	9 (47)	92 (22.9)	9 (11)	208 (24.4)	13 (22)
2 (12-72 studies)	390 (26.3)	9 (13)	4 (21)	138 (34.4)	25 (31)	198 (23.2)	16 (27)
3 (73-122 studies)	393 (26.5)	16 (24)	2 (11)	128 (31.9)	29 (36)	193 (22.6)	25 (42)
4 (123-176 studies)	326 (22.0)	1 (1)	4 (21)	43 (10.7)	18 (22)	254 (29.8)	6 (10)
Countries in which study is conducted:							
Multiple countries	577 (38.9)	46 (68)	12 (63)	234 (58.4)	11 (14)	260 (30.5)	14 (23)
Single country	905 (61.1)	22 (32)	7 (37)	167 (41.6)	70 (86)	593 (69.5)	46 (77)
Study type:							
Clinical trial	21 (1.4)	0 (0)	0 (0)	6 (1.5)	0 (0)	11 (1.3)	4 (7)
Non-interventional	1438 (97.0)	68 (100)	19 (100)	393 (98.0)	80 (99)	828 (97.1)	50 (83)
Not applicable	23 (1.6)	0 (0)	0 (0)	2 (0.5)	1 (1)	14 (1.6)	6 (10)
Estimated study population size:							
<100	168 (11.3)	5 (7)	5 (26)	60 (15.0)	7 (9)	84 (9.8)	7 (12)
100-<500	320 (21.6)	11 (16)	6 (32)	92 (22.9)	27 (33)	176 (20.6)	8 (13)
500-<1000	146 (9.9)	7 (10)	1 (5)	51 (12.7)	13 (16)	64 (7.5)	10 (17)
1000-10 000	347 (23.4)	25 (37)	3 (16)	92 (22.9)	24 (30)	188 (22.0)	15 (25)
>10 000	501 (33.8)	20 (29)	4 (21)	106 (26.4)	10 (12)	341 (40.0)	20 (33)
Age of study population:							
<18 years	99 (6.7)	5 (7)	1 (5)	25 (6.2)	8 (10)	55 (6.4)	5 (8)
≥18 years	955 (64.4)	31 (46)	12 (63)	254 (63.3)	48 (59)	567 (66.5)	43 (72)
<18 and ≥18 years	428 (28.9)	32 (47)	6 (32)	122 (30.4)	25 (31)	231 (27.1)	12 (20)
Medical condition(s) to be studied:							
Yes	1080 (72.9)	48 (71)	13 (68)	292 (72.8)	49 (60)	626 (73.4)	52 (87)
No	402 (27.1)	20 (29)	6 (32)	109 (27.2)	32 (40)	227 (26.6)	8 (13)
Outcomes specified:							
Yes	1208 (81.5)	55 (81)	19 (100)	330 (82.3)	67 (83)	687 (80.5)	50 (83)
No	274 (18.5)	13 (19)	0 (0)	71 (17.7)	14 (17)	166 (19.5)	10 (17)
Collaboration of a research network:							
Yes	144 (9.7)	9 (13)	2 (11)	27 (6.7)	1 (1)	97 (11.4)	8 (13)
No	1338 (90.3)	59 (87)	17 (89)	374 (93.3)	80 (99)	756 (88.6)	52 (87)
Study uses established data source:							
Yes	501 (33.8)	25 (37)	3 (16)	116 (28.9)	8 (10)	324 (38.0)	25 (42)
No	981 (66.2)	43 (63)	16 (84)	285 (71.1)	73 (90)	529 (62.0)	35 (58)
Planned duration of study, quarters*:							
1 (0.0-0.67 years)	297 (20.0)	8 (12)	3 (16)	44 (11.0)	11 (14)	220 (25.8)	11 (18)
2 (0.67-1.64 years)	293 (19.8)	12 (18)	2 (11)	55 (13.7)	9 (11)	199 (23.3)	16 (27)
3 (1.64-3.35 years)	294 (19.8)	10 (15)	3 (16)	73 (18.2)	21 (26)	173 (20.3)	14 (23)
4 (3.35-19.74 years)	295 (19.9)	21 (31)	9 (47)	124 (30.9)	26 (32)	109 (12.8)	6 (10)
Unspecified	303 (20.4)	17 (25)	2 (11)	105 (26.2)	14 (17)	152 (17.8)	13 (22)

RMP=risk management plan.
* Quarter bounds were rounded; exact bounds in days: 1 (6-243), 2 (244-598), 3 (599-1224), 4 (1225-7211).

doi: 10.1136/bmj-2025-086693 | *BMJ* 2026;392:e086693 | the bmj

(1484 finalised; 816 ongoing) for analysis of protocol availability. As the allowed delay of 15 days for the reporting of two finalised studies was still ongoing, 1482 finalised post-authorisation studies remained for analysis of results availability. At the time of the data extraction, the median time since the study start date and date of final study report was 6.6 (interquartile range 3.6-9.2) and 7.5 (4.9-9.9) years in post-authorisation studies examined for protocol and results availability, respectively.

Description of study samples

Table 1 and table 2 show characteristics of the samples of post-authorisation studies analysed for protocol and results availability, overall and by RMP requirement. In the sample for protocol availability, 112 (4.9%) and 33 (1.4%) post-authorisation studies were EU RMP category 1 and 2 studies, and 625 (27.2%) and 129 (5.6%) were EU RMP category 3 and non-EU RMP-only studies, respectively, whereas 1292 (56.2%) post-authorisation studies were not included in an RMP and 109 (4.7%) did not specify an RMP. Similarly, in the sample for results availability, EU RMP category 1 and 2 studies accounted for 68 (4.6%) and 19 (1.3%) post-authorisation studies and EU RMP category 3 and non-EU RMP-only studies for 401 (27.1%) and 81 (5.5%) post-authorisation studies, respectively, whereas 853 (57.6%) post-authorisation studies were not included in an RMP and 60 (4.0%) did not specify an RMP. Most post-authorisation studies were conducted in single country rather than multiple countries (58.9% *v* 41.1% and 61.1% *v* 38.9% in the samples for protocol and results availability, respectively).

Adherence to uploading protocol and results

Figure 2 shows the study outcomes in the total samples of post-authorisation studies and in subgroups according to RMP requirement. Overall, 1370 (59.6%) of 2300 ongoing and finalised post-authorisation studies had uploaded the protocol, and 1014 (68.4%) of 1482 finalised studies had uploaded results. The abstract only and the final report was uploaded for 513 (34.6%) and 501 (33.8%) post-authorisation studies, respectively, with a median number of pages of 4 (interquartile range 3-7) and 77 (44-132), respectively. Forty nine post-authorisation studies with an abstract only had uploaded a results publication. In post-authorisation studies according to RMP requirements, protocols and results were posted for 76 (68%) of 112 and 61 (90%) of 68 EU RMP category 1 studies, 21 (64%) of 33 and 17 (90%) of 19 EU RMP category 2 studies, 419 (67.0%) of 625 and 304 (75.8%) of 401 EU RMP category 3 studies, 87 (67%) of 129 and 56 (69%) of 81 non-EU RMP-only studies, and 715 (55.3%) of 1292 and 547 (64.1%) of 853 post-authorisation studies not included in an RMP, respectively.

Figure 3 shows the proportions of post-authorisation studies with uploaded protocol and results by calendar year of the study start date and date of final study report, showing no clear pattern in protocols and a plateauing in results over time. Table 3 shows the proportions of post-authorisation studies with protocol and results uploaded by the 20 most frequent sponsors, ranging from 31% to 100% and 29% to 100% for protocols and results, respectively. Proportions of post-authorisation studies with uploaded protocol and results by all sponsors are shown in supplementary table S3. The web application enables display of these proportions in the form of a sortable bar chart and also shows the upload status of individual post-authorisation studies by sponsor.

When examining protocol availability by study status, we found that 1030 (69.4%) of 1484 finalised post-authorisation studies had uploaded the protocol compared with 340 (41.7%) of 816 ongoing post-authorisation studies (table 4). After cross tabulation, we found that 824 (81.2%) of 1015 finalised post-authorisation studies that had uploaded results had also posted the protocol. When we excluded post-authorisation studies that started before mid-2012, 70 (69%) of 102 EU RMP category 1 studies and 20 (69%) of 29 EU RMP category 2 studies had posted the protocol, and 55 (93%) of 59 EU RMP category 1 studies and 15 (88%) of 17 EU RMP category 2 studies

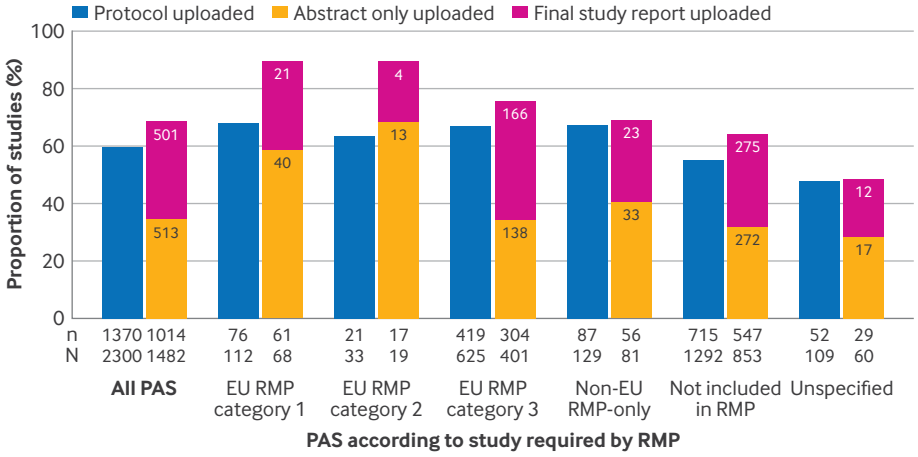

Fig 2 | Proportions of finalised and ongoing post-authorisation studies (PAS) that made protocol public and proportions of finalised PAS that made abstract only and final report public. RMP=risk management plan

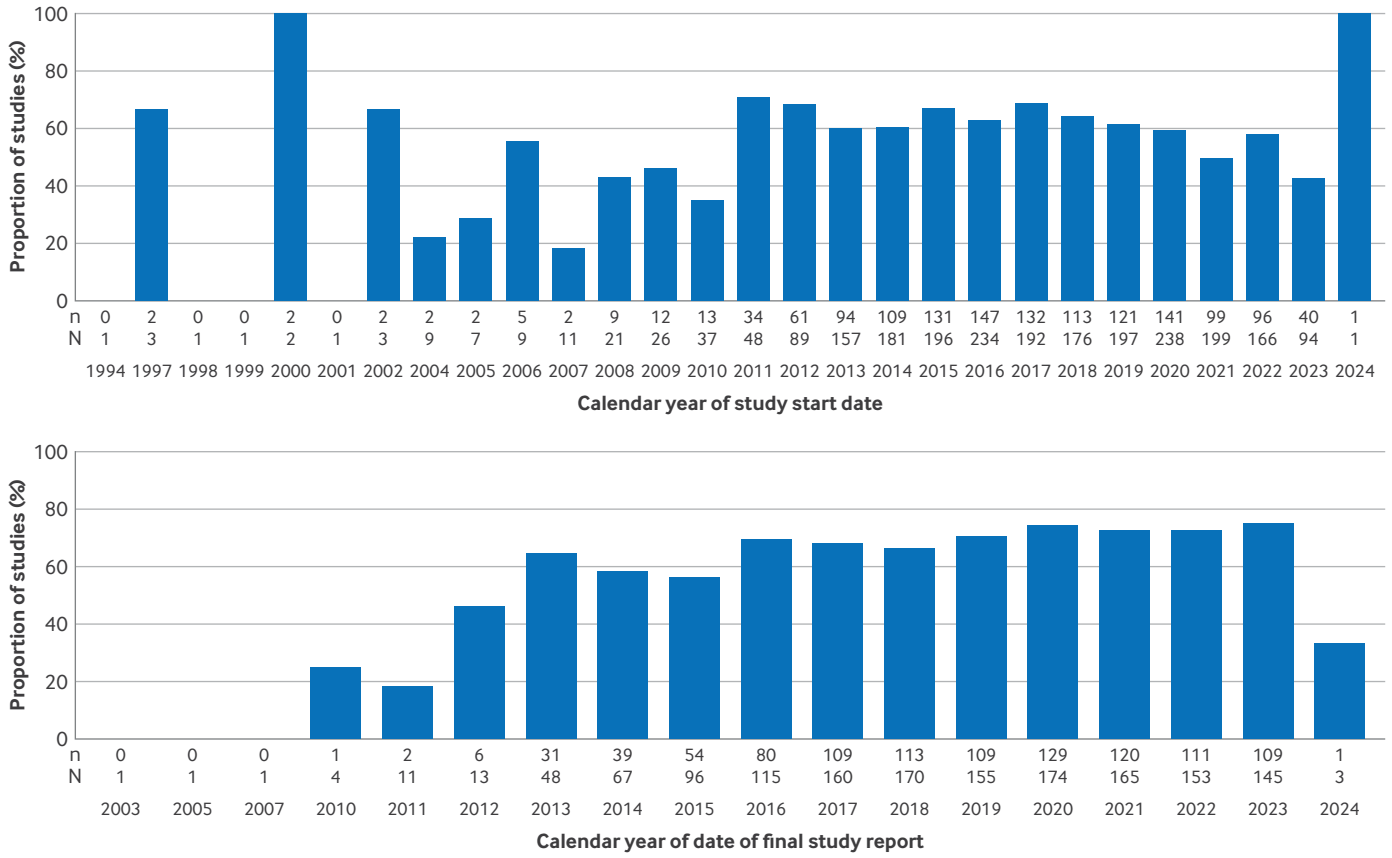

Fig 3 | Proportions of finalised and ongoing post-authorisation studies that made protocol public by calendar year of study start date (top) and proportions of finalised post-authorisation studies that made results public by calendar year of date of final study report (bottom)

had uploaded results. Furthermore, when exploring extended delays, we observed a stable adherence to uploading the protocol for delays up to three years in ongoing and finalised post-authorisation studies and a decreasing adherence to uploading the results with increasing delay in finalised post-authorisation studies (supplementary figures S1-S5).

Associations of study characteristics with adherence

Table 4 shows multivariable associations of study characteristics with the main study outcomes (univariable associations are shown in supplementary table S4). Study documents were more likely to be uploaded for EU RMP category 1 studies (protocol: odds ratio 1.99, 95% confidence interval 1.25 to 3.19; results: 8.05, 3.45 to 18.75), EU RMP category 3 studies (protocol: 1.83, 1.43 to 2.35; results: 1.67, 1.20 to 2.34), and non-EU RMP-only studies (protocol: 2.15, 1.40 to 3.30) compared with post-authorisation studies not included in an RMP. Furthermore, study documents were more likely to be uploaded for post-authorisation studies carried out in multiple countries than for those conducted in single countries (protocol: odds ratio 1.31, 1.06 to 1.62; results: 1.35, 1.01 to 1.80) and less likely if the sponsor funded a smaller number of studies (quarter 1 *v* 4—protocol: 0.56, 0.43 to 0.74; results: 0.08, 0.05 to 0.13). Results were less likely to be uploaded for post-authorisation studies funded by multiple sponsors than for those with single sponsors (odds ratio 0.39, 0.25 to 0.63) and by non-commercial compared with commercial sources (0.62, 0.40 to 0.95), if the study was from a research network than if not (0.63, 0.40 to 0.97), and if planned duration was unspecified compared with planned duration in quarter 1 (0.67, 0.45 to 0.99). Post-authorisation studies were more likely to have results uploaded if an outcome was specified than if it was unspecified (odds ratio 1.76, 1.26 to 2.46). We observed consistent results in models excluding potentially influential outliers, truncating study start dates and dates of final study report before 6 November 2010, and excluding EU RMP category 1 and 2 studies that started before mid-2012 (supplementary tables S5-S7). Findings were also consistent in models additionally including the covariate study required by a regulatory body (supplementary table S8). When we used the covariate number of post-authorisation studies funded by sponsor based on the divide-and-assign approach, protocols and reports were still less likely to be uploaded if the sponsor funded a smaller number of post-authorisation studies, but results were no longer less likely to be uploaded for post-authorisation studies with non-commercial funding (supplementary table S9).

doi: 10.1136/bmj-2025-086693 | *BMJ* 2026;392:e086693 | the bmj

Table 3 | Proportions of post-authorisation studies (PAS) examined for protocol and results availability that made protocol and results public, by 20 most frequent sponsors. Values are numbers or numbers (percentages)

		Protocol availability		Results availability	
Sponsor	PAS funded*	PAS examined	PAS with protocol made public	PAS examined	PAS with results made public
Pfizer	176	142	119 (84)	91	83 (91)
EMA	157	155	100 (65)	135	106 (79)
Amgen	143	137	101 (74)	103	98 (95)
Boehringer Ingelheim	122	93	34 (37)	51	29 (57)
GlaxoSmithKline	101	95	81 (85)	63	44 (70)
Merck Sharp and Dohme	97	84	52 (62)	56	39 (70)
AstraZeneca	95	80	52 (65)	45	24 (53)
Eli Lilly	92	70	50 (71)	45	38 (84)
Novartis	77	66	58 (88)	46	38 (83)
Bayer	75	73	68 (93)	61	59 (97)
Takeda	72	68	26 (38)	47	40 (85)
F Hoffmann-La Roche	58	57	38 (67)	34	19 (56)
Sanofi	58	55	29 (53)	33	27 (82)
Teva	40	36	11 (31)	24	7 (29)
Bristol-Myers Squibb	39	32	12 (38)	19	9 (47)
Gilead Sciences	35	35	33 (94)	30	26 (87)
AbbVie	31	25	23 (92)	9	9 (100)
ViiV Healthcare	26	26	22 (85)	19	17 (89)
Biogen	24	21	14 (67)	14	13 (93)
Innovative Medicines Initiative	22	17	17 (100)	11	9 (82)

EMA=European Medicines Agency.
*Comprises all studies registered in EMA Catalogue of real-world data studies, including planned studies.

Discussion

Assessing the adherence to legislation and recommendations to make public the protocols and results of post-authorisation studies registered with the EMA, our study shows that only six out of every 10 finalised and ongoing post-authorisation studies uploaded the protocol and less than seven out of every 10 finalised studies uploaded the results in the Catalogue of real-world data studies. Only about half of post-authorisation studies that uploaded results provided a final report, with the other half uploading only an abstract. Among post-authorisation studies with legal requirements (EU RMP category 1 and 2 studies), seven out of every 10 finalised and ongoing studies uploaded the protocol and nine out of every 10 finalised studies uploaded results. Adherence varied considerably between sponsors, as shown by the ranking of the top 20 funding sources and of all sponsors in the web application. Notably, EMA sponsored post-authorisation studies showed similar proportions of protocol and results availability as observed in the total sample of post-authorisation studies examined. Investigating associations, we observed that post-authorisation studies not included in an RMP were less likely to have uploaded the protocol and results than those included in an EU or non-EU RMP, but precision was low for estimates of associations for EU RMP category 2 studies owing to small numbers.

Research in context

One previous survey by a research network coordinated by the EMA reported on post-authorisation studies registered with the EMA from 2010 to 2018, showing that 360 (63.0%) of 571 studies requested by regulatory authorities had made the protocol available in the EU PAS Register.[11] Our study extends this previous study in two important ways. Firstly, we report here on the availability of protocols for all EMA registered post-authorisation studies, including also studies not requested by regulators. Secondly, and even more importantly, we distinguish post-authorisation studies according to RMP requirements, showing that post-authorisation studies not included in an RMP are less likely to publicly post the protocol (and results).

As far as we know, our study is the first to report on the public availability of results from post-authorisation studies registered with EMA. Previous studies showed that post-authorisation studies are often postponed, delayed, and not finalised,[19] so that uncertainties about potential benefits and harms of drugs for patients persist over longer periods than planned.[20] This is particularly relevant to patient groups for which safety information is limited or missing—for example, pregnant women and patients with relevant comorbidities.[4] Our study shows that by not making results public, post-authorisation studies registered with EMA often keep failing to close such information gaps, even if finalised. This finding extends the results of a previous study from our group in which the literature was searched for publications from post-authorisation studies notified to German regulators in 2008-10, showing that reports of post-authorisation studies are rarely found in scientific journals,[21] further emphasising the importance of publicly posting the results of these studies in study registers.

One previous study investigated adherence to European Commission requirements to report results

Table 4 | Multivariable associations of study characteristics with protocol and results made public in post-authorisation studies (PAS) examined for protocol and results availability

	Protocol availability			Results availability		
		PAS with protocol made public			PAS with results made public	
Characteristic	No of PAS examined	No (%)	Odds ratio (95% CI)	No of PAS examined	No (%)	Odds ratio (95% CI)
Study required by an RMP:						
Not included in an RMP	1292	715 (55.3)	Reference	853	547 (64.1)	Reference
EU RMP category 1	112	76 (68)	1.99 (1.25 to 3.19)	68	61 (90)	8.05 (3.45 to 18.75)
EU RMP category 2	33	21 (64)	1.59 (0.72 to 3.53)	19	17 (90)	3.99 (0.85 to 18.66)
EU RMP category 3	625	419 (67.0)	1.83 (1.43 to 2.35)	401	304 (75.8)	1.67 (1.20 to 2.34)
Non-EU RMP-only	129	87 (67)	2.15 (1.40 to 3.30)	81	56 (69)	0.87 (0.49 to 1.52)
Unspecified	109	52 (48)	1.40 (0.88 to 2.23)	60	29 (48)	1.21 (0.64 to 2.30)
Type of funding source:						
Commercial	1785	1085 (60.8)	Reference	1160	840 (72.4)	Reference
Non-commercial	391	219 (56)	0.99 (0.73 to 1.35)	246	149 (61)	0.62 (0.40 to 0.95)
Mixed	60	33 (55)	0.83 (0.43 to 1.60)	40	13 (33)	0.46 (0.20 to 1.08)
Unclear	36	15 (42)	0.49 (0.23 to 1.02)	22	7 (32)	0.18 (0.07 to 0.47)
No funding	28	18 (64)	2.15 (0.91 to 5.06)	14	5 (36)	0.27 (0.08 to 0.85)
Multiple funding sources:						
No	2065	1244 (60.2)	Reference	1347	953 (70.7)	Reference
Yes	235	126 (54)	0.77 (0.55 to 1.10)	135	61 (45)	0.39 (0.25 to 0.63)
No of PAS funded by sponsor, quarters*:						
4	519	348 (67.1)	Reference	326	286 (88)	Reference
1	611	293 (48.0)	0.56 (0.43 to 0.74)	373	191 (51)	0.08 (0.05 to 0.13)
2	604	349 (57.8)	0.75 (0.56 to 0.99)	390	259 (66)	0.20 (0.12 to 0.32)
3	566	380 (67.1)	1.20 (0.89 to 1.60)	393	278 (71)	0.30 (0.18 to 0.49)
Countries in which study is conducted:						
Single country	1355	759 (56.0)	Reference	905	574 (63.4)	Reference
Multiple countries	945	611 (64.7)	1.31 (1.06 to 1.62)	577	440 (76.3)	1.35 (1.01 to 1.80)
Study type:						
Non-interventional	2224	1344 (60.4)	Reference	1438	990 (68.8)	Reference
Clinical trial	32	10 (31)	0.33 (0.14 to 0.77)	21	12 (57)	0.86 (0.30 to 2.48)
Not applicable	44	16 (36)	0.43 (0.22 to 0.87)	23	12 (52)	0.53 (0.20 to 1.45)
Estimated study population size:						
100-<500	498	279 (56.0)	Reference	320	230 (72)	Reference
<100	260	155 (60)	1.34 (0.95 to 1.88)	168	123 (73)	0.99 (0.61 to 1.61)
500-<1000	244	140 (57)	1.01 (0.72 to 1.41)	146	92 (63)	0.68 (0.42 to 1.09)
1000-10 000	569	329 (57.8)	1.14 (0.87 to 1.49)	347	232 (67)	0.74 (0.50 to 1.08)
>10 000	729	467 (64.1)	1.38 (1.03 to 1.85)	501	337 (67.3)	0.84 (0.57 to 1.24)
Age of study population:						
≥18 years	1467	850 (57.9)	Reference	955	652 (68.3)	Reference
<18 years	148	89 (60)	1.02 (0.69 to 1.49)	99	64 (65)	1.37 (0.81 to 2.30)
<18 and ≥18 years	685	431 (62.9)	1.15 (0.92 to 1.42)	428	298 (70)	1.34 (0.99 to 1.82)
Medical condition(s) to be studied:						
Yes	1668	995 (59.7)	Reference	1080	747 (69.2)	Reference
No	632	375 (59.3)	0.97 (0.78 to 1.21)	402	267 (66)	0.86 (0.64 to 1.16)
Outcomes specified:						
No	381	231 (61)	Reference	274	166 (61)	Reference
Yes	1919	1139 (59.4)	1.08 (0.83 to 1.40)	1208	848 (70.2)	1.76 (1.26 to 2.46)
Collaboration of a research network:						
No	2039	1185 (58.1)	Reference	1338	928 (69.4)	Reference
Yes	261	185 (71)	2.19 (1.57 to 3.05)	144	86 (60)	0.63 (0.40 to 0.97)
Study uses established data source:						
No	1558	885 (56.8)	Reference	981	684 (69.7)	Reference
Yes	742	485 (65.4)	1.20 (0.96 to 1.51)	501	330 (65.9)	0.83 (0.61 to 1.12)
Status of study:						
Finalised	1484	1030 (69.4)	Reference	-	-	-
Ongoing	816	340 (41.7)	0.23 (0.18 to 0.29)	-	-	-
Planned duration of study, quarters†:						
1	460	296 (64.3)	Reference	297	198 (67)	Reference
2	462	298 (64.5)	1.20 (0.89 to 1.62)	293	204 (70)	1.09 (0.73 to 1.62)
3	457	257 (56.2)	0.98 (0.72 to 1.33)	294	204 (69)	1.12 (0.75 to 1.69)
4	460	280 (60.9)	1.43 (1.01 to 2.02)	295	227 (77)	1.23 (0.80 to 1.90)
Unspecified	461	239 (51.8)	0.82 (0.60 to 1.12)	303	181 (60)	0.67 (0.45 to 0.99)

Odds ratios and 95% CIs from multivariable logistics regression analyses with all variables included in models plus time since study start date (odds ratio per year 0.93, 95% CI 0.91 to 0.96) in model for protocol availability and time since date of final study report (0.94, 0.90 to 0.98) in model for results availability.
CI=confidence interval; RMP=risk management plan.
*Quarter bounds in PAS examined for protocol availability: 1 (1-9), 2 (10-58), 3 (59-110), 4 (111-176) studies; quarter bounds in PAS examined for results availability: 1 (1-11), 2 (12-72), 3 (73-122), 4 (123-176) studies.
†Quarter bounds in PAS examined for protocol availability: 1 (6-305), 2 (306-791), 3 (792-1701), 4 (1702-8412) days; quarter bounds in PAS examined for results availability: 1 (6-243), 2 (244-598), 3 (599-1224), 4 (1225-7211) days.

doi: 10.1136/bmj-2025-086693 | *BMJ* 2026;392:e086693 | the bmj

of clinical trials within 12 months of study completion. Using data on 7274 trials registered in the EU Clinical Trials Register (EUCTR) up to January 2018, this study showed that only 49.5% of trials reported results as required.[15] An online tool developed by this study to monitor the reporting of trial results in the EUCTR, overall and by sponsor, showed that adherence to requirements had improved to about 80% in June 2025.[22] Of note, all post-authorisation studies included in the EUCTR are clinical trials, which represent a small fraction of post-authorisation studies conducted. The EMA has declared that it is aiming to achieve a similar transparency in post-authorisation studies as in clinical trials,[2] but so far data on the reporting of results from EMA registered post-authorisation studies have been lacking.

This study covers all post-authorisation studies registered in the EMA Catalogue of real-world data studies up to February 2024, including studies previously registered in the EU PAS Register. As registration of EU RMP category 1 and 2 studies is required by legislation, our sample should include all such post-authorisation studies imposed by the EMA that started since mid-2012, but studies may also be missing. Data on adherence to legislation to register post-authorisation studies are currently lacking.

Implications of results

The adherence observed and associations described by our study may inform regulatory and legislative action. Firstly, the limited adherence observed in post-authorisation studies subject to EU legislation—that is, EU RMP category 1 and 2 studies—implies that stricter oversight by the EMA and other competent authorities is needed. If legal requirements are still not met, the EMA should ultimately make use of its rarely executed power to impose fines and withdraw marketing authorisations, depending on the level of uncertainty surrounding risks or benefits.[23] Secondly, poorer adherence in post-authorisation studies not included in an RMP suggests that legal provisions may also be needed for these studies instead of regulatory recommendations. Of note, a legal requirement to make public the results of all post-authorisation studies registered with the EMA would be in line with EU legislation for clinical trials. Thirdly, study characteristics associated with adherence may inform regulators about post-authorisation studies to be specifically targeted. For instance, post-authorisation studies with sponsors funding fewer studies may be better incentivised as they were less likely to post protocols and results. However, whether such a targeting strategy will actually have a favourable impact on adherence would need to be evaluated. Fourthly, better adherence to uploading the protocol in finalised than in ongoing post-authorisation studies and in finalised studies with than without uploaded results suggests that protocols and results are often posted together after the end of the study. However, marketing authorisation holders should upload the protocol before the study begins, to ensure that no post hoc changes are made.

The Catalogue of real-world data studies allows easy filtering of post-authorisation studies according to RMP requirements and study status, among other criteria, but not with regard to the availability of protocol and results. This is in contrast to the ClinicalTrials.gov database, in which a one click filter can be applied to identify studies with protocols, statistical analysis plans, and informed consent forms. We suggest that the catalogue should integrate similar features allowing the display of finalised and ongoing post-authorisation studies according to the upload status of the protocol and results, as in our web application. This would enable public scrutiny and may raise public awareness, which could support regulatory oversight and create pressure on marketing authorisation holders and other entities responsible for registered post-authorisation studies. Furthermore, marketing authorisation holders could receive reminders to comply with requirements and recommendations on the basis of the study status and uploads.

In contrast to other registration databases such as the EUCTR and ClinicalTrials.gov, the Catalogue of real-world data studies supports only upload of study results, with no standardised data entry from study reports into structured, spreadsheet-like data. Since 2013 specific documents formats have been required for the protocol and final report of imposed post-authorisation studies by Regulation (EU) No 520/2012,[24 25] but not from other post-authorisation studies. In our study, we found heterogenous document formats, particularly in non-imposed post-authorisation studies—for example, reports lacking discussion and conclusion sections. Standardised formats for data entry and/or documents would thus be desirable in reports of all post-authorisation studies registered.

It is important to remember that transparency of protocols and results of post-authorisation studies is distinct from the question of a study's scientific rigour. Critical appraisal of study documents would be the necessary next step[26]; however, the availability of documents (as assessed in our study) is a basic necessity for any such evaluation. In this context, access to more detailed and comprehensive documents may also be needed, such as the full clinical study report, anonymised individual participant data, and regulatory documents that are not included in the catalogue and can be obtained only through freedom of information requests to the EMA, if available.[27]

The EMA promotes the use of FAIR principles (improved findability, accessibility, interoperability, and reusability of data)[28 29] and claims to comply with these in the catalogue.[30] In our view, great potential exists for improvements in this regard. For instance, upload dates of documents should be provided, which is currently not the case, impairing richness of metadata with relevant attributes. This would be particularly important for the protocol to show whether the analysis plan was specified before the start of the study. The EMA applies standard procedures for checking the completeness and

accuracy of metadata and required documents in the catalogue.[31] Furthermore, the EMA recommends that information should be provided on data quality checks for real world data used in regulatory assessments.[32] In line with this, new data quality specifications and characterisations have been included as mandatory data field in the catalogue.[13] However, at the time of our data extraction, these data fields were specified as "unknown" in all post-authorisation studies, lacking updates by responsible entities.

Strengths and limitations of study

To the best of our knowledge, this is the first study to investigate whether post-authorisation studies registered with the EMA make the protocols and results public in line with EU legislation and EMA recommendations. Our study shows that assessing the upload status of post-authorisation studies' protocols and results in the Catalogue of real-world data studies is feasible and provides a meaningful assessment of research transparency. We report on adherence of post-authorisation studies at an aggregate level by study characteristics and sponsors, and we deliver a web application that displays adherence of post-authorisation studies by sponsors also at an individual study level. This application thus enables inspection, at a glance, of the adherence not only of grouped post-authorisation studies but also of single studies by sponsors—that is, to scrutinise which post-authorisation studies actually succeed and fail to deliver.

Our study has some limitations. Firstly, as a cross sectional study, it provides a snapshot of the assessed adherence in February 2024. However, with additional resources, the approach could be extended to continuous monitoring, in particular based on the developed web application. Secondly, our study relies on the timeliness of entry of metadata for post-authorisation studies by responsible entities in the catalogue. Any delay in updating the study status to "ongoing" and "finalised" would result in post-authorisation studies incorrectly being excluded from our primary analyses. This would likely lead to an overestimation of the adherence, with the actual level being poorer than observed. Thirdly, document upload dates are unavailable in the catalogue, which hampers analysis of adherence at the time post-authorisation studies became ongoing or finalised. Assessing adherence at the time of data extraction instead results in varying lengths of time since the study start date and date of final study report. However, we have adjusted the multivariable models to account for these time periods.

Conclusions

Using data extracted from the Catalogue of real-world data studies in February 2024, this study shows that adherence to public posting of protocols and results of post-authorisation studies registered with the EMA since November 2010 is insufficient: only six out of every 10 finalised and ongoing post-authorisation studies uploaded the protocol and less than seven out of every 10 finalised studies uploaded the results. Assessing data on the upload status of the protocols and results of EMA registered post-authorisation studies is feasible and helps to scrutinise whether the studies adhere to legislation and recommendations to make these study documents public.

We thank Jakob Stimpfl for technical advice on online data scraping and web application design.

Contributors: All authors participated in critically reviewing the report and interpreting the findings. CP developed the research idea and designed the study. PR extracted and analysed the data and drafted the report. PR and CP are the guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding: None.

Competing interests: All authors have completed the ICMJE uniform disclosure form at https://www.icmje.org/disclosure-of-interest/ and declare: PD has received grants from the US Food and Drug Administration (through University of Maryland M-CERSI; 2020) and Arnold Ventures (2017-22; 2025-26) and is senior editor, investigations, at *The BMJ*; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Not required.

Data sharing: The downloaded and scraped datasets and the downloaded study documents from the Catalogue of real-world data studies are made available at GitHub and Zenodo.[17 33] An inventory list of all study documents indicating the corresponding EU PAS numbers, upload sections, and page counts is included.

Transparency: The corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained.

Dissemination to participants and related patient and public communities: Parts of the research were presented as a poster at the 20th Annual Meeting of the German Society of Epidemiology. We plan to disseminate the research through a press release, share it across social media, and present it to masters students at the Berlin School of Public Health.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Web appendix: Supplementary tables and figures
Web appendix: STROBE checklist