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ORIGINAL ARTICLE

Analysis of 4616 clinical trial initial submissions received by the Medicines and Healthcare products Regulatory Agency between February 2019 and October 2023

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Aims: This study aimed to analyse clinical trial initial submissions received by the MHRA between February 2019 and October 2023.

Methods: Data on submissions were extracted from the clinical trials unit data bank. The primary end-point was the type of clinical trial initial submissions. Secondary end-points were sponsor types, participant demographics, healthy volunteers, health categories and studies involving first in human and advanced therapy medicinal products. The analysis used descriptive statistics for all categorical variables.

Results: MHRA received 4616 submissions. The highest percentage was in 2020 (22.8%) and the lowest in 2023 (17.2%). Phase 3 submissions were the highest (32.6%) and and phase 4 the lowest (5.2%). Commercial sponsors represented 85.1% of the total submissions. Both sexes were included in most trials (90%), while the number of submissions involving females only (3.7%) was lower than male only trials (6.1%). The elderly population was represented in 67.7% of trials with pregnant and breastfeeding women represented in 1.1% and 0.6% of trials, respectively. Breastfeeding women were not included in phase 1. Paediatric trials mostly involved adolescents. Healthy volunteers were included in 16.5% of the total submissions. The most common health category was cancer (29.4%), with the lowest being pain. First in human submissions represented 12.7% and advanced therapy medicinal products 3.4% of submissions.

Conclusions: These results highlight the clinical trial landscape in the United Kingdom and represent an important baseline for policymakers, healthcare providers, sponsors and patients and will enable an assessment of how policy changes can improve the variety and number of clinical trials.

KEYWORDS
clinical trials, health services research, therapeutics

The authors confirm that Andrea Manfrin is the principal investigator for this paper and that he had direct clinical responsibility for patients.

1 | INTRODUCTION

Clinical trials assess new tests for both treatment and prevention, evaluating their effects on human health outcomes.[1] Clinical trials are at the heart of all medical advances, examining new ways to prevent, detect or treat disease.[2] Clinical trials are also considered the gold standard method for evaluating healthcare interventions.[3] By their very nature, these trials are catalysts for the future of healthcare. They inspire patients' hopes for effective treatment, pave the way for new treatments and cures, and shape healthcare policy.[4] In addition to significantly improving patient outcomes, clinical research in the UK has been shown to benefit economic growth.[5] A report commissioned by the National Institute for Health and Care Research Clinical Research Network covering the financial period from 2016/17 to 2018/19 showed that clinical research had generated an estimated GB£8 billion of gross value added and 47 467 full time equivalent jobs for the UK.[6–8]

According to Gresham *et al.*,[9] understanding the clinical trial landscape is essential for various reasons. First, it offers a holistic overview of the current state and trends in clinical trial activity worldwide, helping to identify the types of trials being conducted, the population demographics, the health conditions and the potential innovative medications, providing a deeper understanding of the current state and trends in research activity.[10] This can contribute to a better decision-making process for healthcare professionals, policymakers and funders, who can gain valuable insights into the progress of various disease areas and treatment approaches. Second, it enables stakeholders to make informed decisions about resource allocation, identify research gaps, such as some specific demographics, e.g. pregnant and breastfeeding women, and prioritize areas for further investigation. For example, a study on long-term care research worldwide highlighted the shift in research trends from basic studies to practical applications, focusing on frailty in elderly people and dementia care.[11] Third, it indicates whether the clinical trial landscape in countries such as the UK is changing, whether the trials being undertaken reflect the population's needs, and whether there is a shift from small molecules to innovative therapies and interventions, such as advanced therapy medicinal product (ATMP) trials.

Clinical Trials regulation under the Medicines for Human Use (Clinical Trials) Regulations 2004 is 1 of the functions of the Medicines and Healthcare products Regulatory Agency (MHRA) as set out in the Framework Agreement between the MHRA and the Department of Health and Social Care.[12] The MHRA plays a crucial role in regulating clinical trial applications in the UK, assessing and authorizing all submissions of clinical trials of investigational medicinal products (CTIMPs).[13] It ensures clinical trials are conducted safely. This protects participants from harm and ensures reliable data for future patients. The MHRA provides oversight and guidance for the conduct of clinical trials, ensuring that they comply with legal standards, including Good Clinical Practice guidelines. The clinical trials unit at the MHRA reviews and authorizes all CTIMPs, which is a critical step before researchers can begin their studies. By providing a clear regulatory framework, the MHRA supports innovation in medicine and helps expedite the development of new therapies and treatments, such as first-in-human (FIH) and ATMPs, which can benefit patients. Therefore, the MHRA ensures that clinical trials are conducted safely and effectively, ultimately contributing to advancing medical science and protecting public health.

This study aimed to analyse clinical trial initial submissions received by the MHRA between February 2019 and October 2023.

What is already known about this subject

- Clinical trials are essential for the advancement of health research and the development of new medicines.
- Clinical trials contribute substantially to the economy of the UK and to job creation.
- Having a good understanding of the clinical trials landscape is essential for the development of health, economic and research policies.

What this study adds

- This is the first comprehensive analysis of clinical trial initial submissions received by the Medicines and Healthcare products Regulatory Agency clinical trials unit based on variables used by the Integrated Research Approval System template.
- The analysis focused on years, study types, sponsors, population demographics, healthy volunteers, health categories, first-in-human and advanced therapy medicinal products.
- The results highlight the clinical trials landscape for medicines in the UK and provide an important baseline for stakeholders to assess future improvements in the variety and number of clinical trials.

2 | METHODS

2.1 | Settings

The clinical trial initial submissions included in our study were received for assessment and authorisation between February 2019 and October 2023 by the MHRA Clinical Trials Unit (CTU). The years 2020, 2021 and 2022 include 12 months, 2019, 10.2 months (from 23 February 2019) and 2023, 10 months (until 31 October 2023). The end of February was selected because the data were imported into the new data bank called Appian just before that period, and the end of October 2023 was chosen because it was the first time we could extract all the data.

2.2 | Variables of interest

Once sponsors submit their trials via the online Integrated Research Approval System, the MHRA receives the submissions, which are ingested in our data bank. Therefore, the MHRA CTU's data bank is based on the Integrated Research Approval System template. In our data bank, the variables for each trial submission are grouped into the following domains: (i) year of submission; (ii) sponsor information; (iii) product information; (iv) conditions (health conditions); (v) study objective; (vi) study type; (vii) study design; (viii) study location; (ix) participants' age group; (x) sex; (xi) population type; (xii) decision (approval or rejection); and (xiii) trial end. As this was the first analysis conducted by the CTU, we adopted a pragmatic approach. The study's primary end-point was to analyse the type of clinical trial initial submissions. The secondary end-points included identifying the type of sponsors, participant demographics, healthy volunteers (HV), health categories, FIH studies and ATMPs, included in these submissions.

2.3 | Analysis

The analysis focused on descriptive statistics for categorical variables, including percentages and frequencies, fractions, and/or relative frequencies (frequencies divided by the sample size) obtained from the frequency distribution table. This approach allowed the creation of frequency tables, histograms, bar charts and stacked bar charts to summarize and present the results concisely. The percentages of clinical trial initial submissions received between 2019 and 2023 were presented using a bar chart. A similar approach was adopted to stratify trials according to phases and years. The differences between various parameters *vs*. trial phases were assessed and presented using a stacked bar chart or bar chart. The population demographics were analysed and presented in a tabular format. A recent publication from Australia and New Zealand[12] informed the grouping and classification of health conditions, which the authors of this manuscript further reviewed.[14] The data analysis was performed using IBM SPSS (version 29.02) and Excel for Microsoft Office 365 (version 2404).

2.4 | Governance aspects

The data did not include any information regarding patients, and all data were anonymised. The researchers did not need approval from the Independent Ethics Committee (IEC).

3 | RESULTS

3.1 | Clinical trial initial submissions received by the MHRA

The total number of clinical trial initial submissions was 4161: the highest percentage was found in 2020 at 22.8% (1052/4616) and the lowest percentage in 2023 (17.2%, 793/4616; Figure 1).

3.2 | Clinical trial initial submissions according to phases and years

Phase 3 trials were the most common, followed by phases 2, 1, multiphase and phase 4 (Figure 2). The multiphase trials included, for example, phases 1 and 2, 2 and 3, 3 and 4, and 1 with 2 and 3.

As can be seen in Figure 3, the percentages of trials in different phases varied in different years, but there was no major or consistent shift between the years.

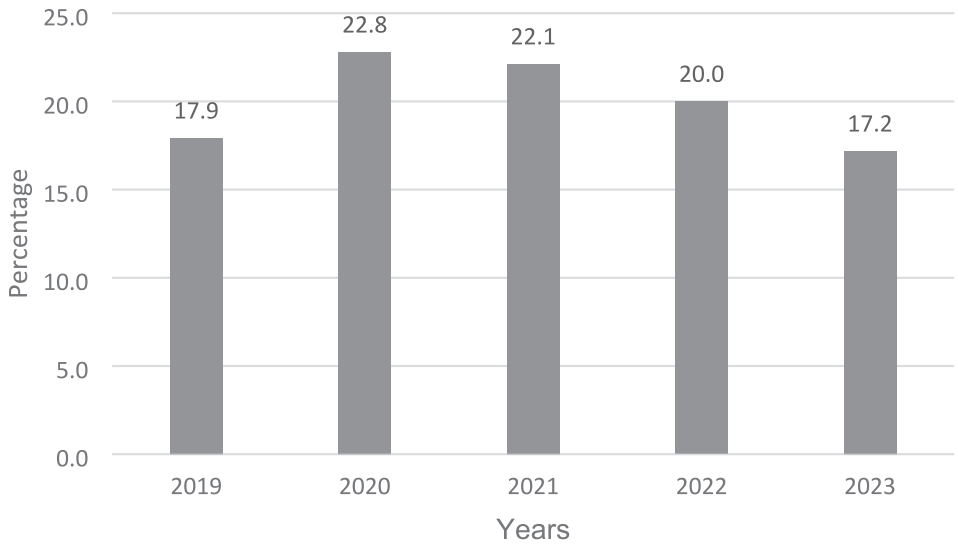


FIGURE 1 Bar chart showing the percentages of clinical trial initial submissions across the years.

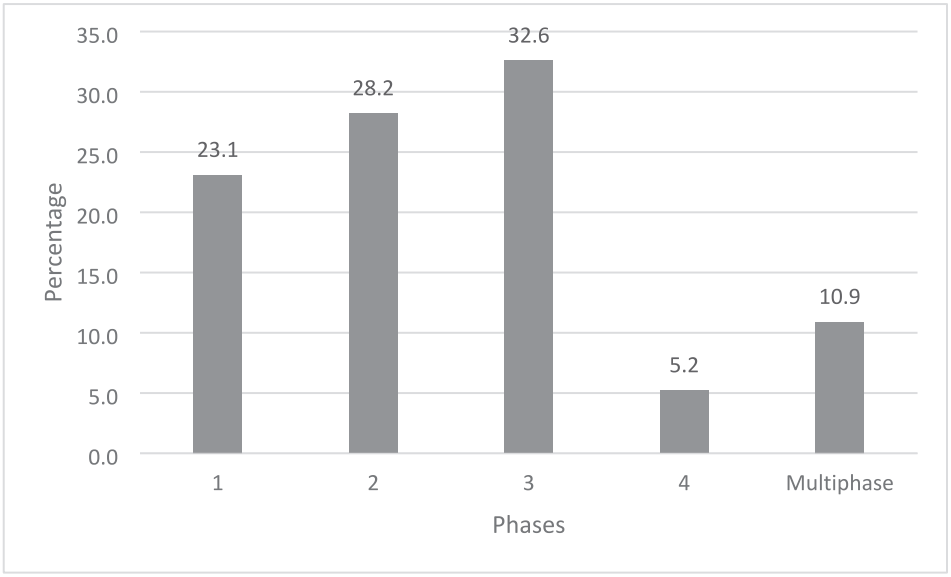


FIGURE 2 Bar chart illustrating the percentages of clinical trial initial submissions received by the Medicines and Healthcare products Regulatory Agency stratified by phases.

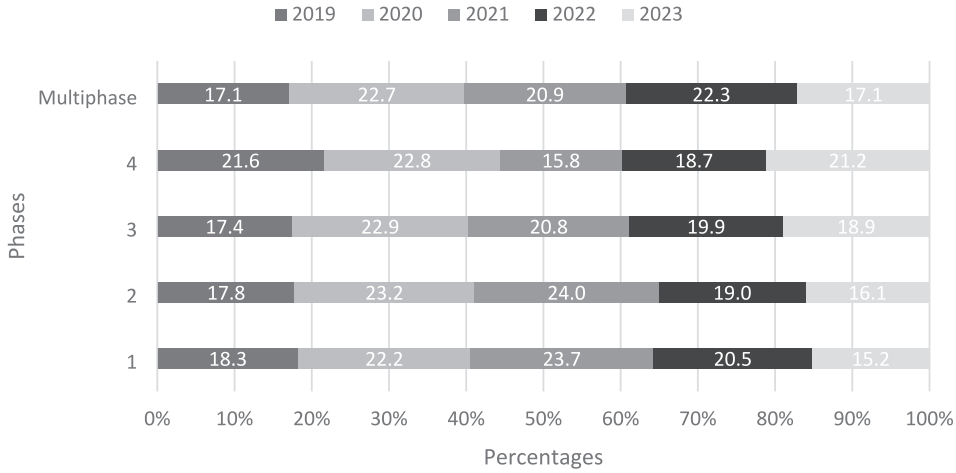


FIGURE 3 Stack bar chart of clinical trial initial submission according to phases and years, shown as percentages.

3.3 | Clinical trial initial submission according to sponsors and phases

Commercial and noncommercial trials accounted for 85.1% (3927/4616) and 14.9% (689/4616) of all trials, respectively. Most commercial trials were phase 3 (33.9%; 1330/3927; Figure 4), while phase 2 trials represented the largest percentage of noncommercial submissions (37.3%; 257/689). The percentage of phase 4 clinical trials for noncommercial sponsors was 18.7% (129/689), more than 6-fold that of commercial sponsors (2.9%; 112/3927). Multiphase trials were more commonly submitted by commercial sponsors (Figure 4).

3.4 | Population demographics and their split across clinical trial phases

The types of populations included in the trial submissions (Table 1) differed because some included only 1 type of population (e.g., male-only or female-only). In contrast, others included many different populations, such as adults, the elderly or adolescents. For this reason, the percentages included in Table 1 do not add up to 100% because each type of population was used as the numerator and the total number of clinical trial initial submissions (4616) as the denominator. The percentage of clinical trials with missing data regarding sex was 0.2% (10/4616). Most trials had the intention to recruit both sexes (90%; 4155/4616), while female-only trials accounted for 3.7% (169/4616) of submission. The elderly were represented in 67.1% (3125/4616) of trials. The percentage of women with childbearing potential included was 33.1% (1528/4616), while pregnant and breastfeeding women were rarely included in trials. Most paediatric trials focused on adolescents (14.4%; 667/4616) with a very small number being in utero trials.

The data presented in Figure 5 summarize the demographics of clinical trials' initial submissions according to sex and age range. Again, there were fluctuations in different years for the different groups but no major or consistent shifts.

The percentages of breastfeeding and pregnant women involved in clinical trials differed across the phases except for the multiphase trials (Figure 6). Phase 1 did not involve breastfeeding women. The

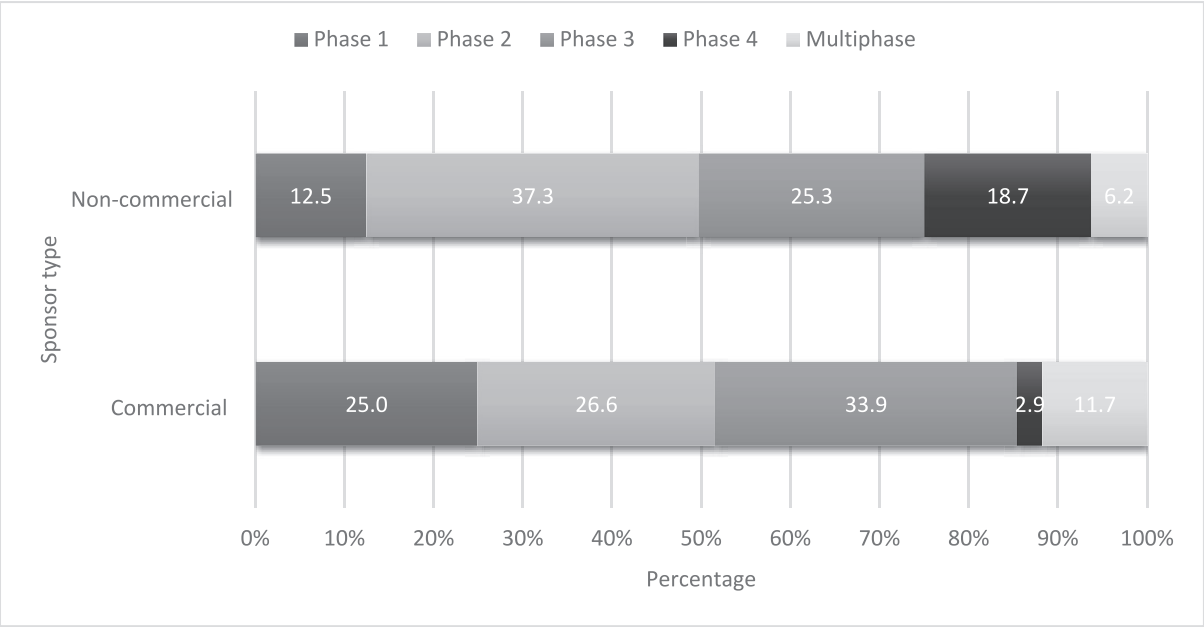


FIGURE 4 Stack bar chart showing clinical trial initial submissions grouped by sponsors and stratified by phases.

TABLE 1 Population characteristics of the clinical trial initial submissions

Demographic characteristics	%* (*n*/*N*)
Sex	
Both sexes	90.0 (4155/4616)
Male (only)	6.1 (282/4616)
Female (only)	3.7 (169/4616)
(Missing data)	0.2 (10/4616)
Age	
Elderly (≥65 years)	67.7 (3125/4616)
Adults (18–64 years)	24.1 (1113/4616)
Women	
Women with child-bearing potential	33.1 (1528/4616)
Pregnant women	1.1 (52/4616)
Breastfeeding women	0.6 (26/4616)
Paediatrics and in utero	
Adolescent (12–17 years)	14.4 (667/4616)
Children (2–11 years)	9.5 (440/4616)
Infants/toddlers (28 days–23 months)	4.7 (219/4616)
Newborn	1.4 (63/4616)
Preterm newborn infants	0.5 (23/4616)
In utero	0.1 (6/4616)

*The percentages do not add up to 100% because they are calculated by dividing each frequency (*n*) by the total number of clinical trials initially submitted (*N*).

percentage of pregnant women in phase 2 was almost twice that of breastfeeding women. The percentages of breastfeeding women engaged in phases 3 and 4 clinical trials were higher than those involving pregnant women.

3.5 | Healthy volunteers (HV)

The percentage of HV included in the clinical trial initial submissions was 16.5% (761/4616). As would be expected, phase 1 represented the largest percentage (79.1%; 602/761), followed by phase 2 (8.5%; 65/761), phase 3 (6.2%; 47/761) and phase 4 (2.2%; 17/761). For multiphase trials, HV were represented in phases 1 and 2 (2.5%; 19/761) and phases 2 and 3 (1.4%; 11/761). Both sexes were represented in most of the trials (76.5%; 582/761), with trials involving male only and female only HV representing 19.4 and 4.1% of trials, respectively.

3.6 | Health categories

Figure 7 summarizes the health categories identified in the clinical trial initial submissions. The largest percentage of initial clinical trial submissions was in cancer (29.4%; 1356/4616), followed by metabolic and endocrine and neurological. All the other categories represented <10% of the total submissions. The other health categories included studies on pharmacokinetics and pharmacodynamics, testing modified released formulations, and bioavailability.

3.7 | First in human and advanced therapy medicinal products

FIH submissions represented 12.7% (584/4616) of the total submissions, with most from commercial sponsors (92.8%; 542/584). ATMP submissions represented 3.4% (156/4616) with most being from commercial sponsors (87.2%; 136/156). There were some yearly fluctuations in ATMP and FIH submissions in different years (Figure 8).

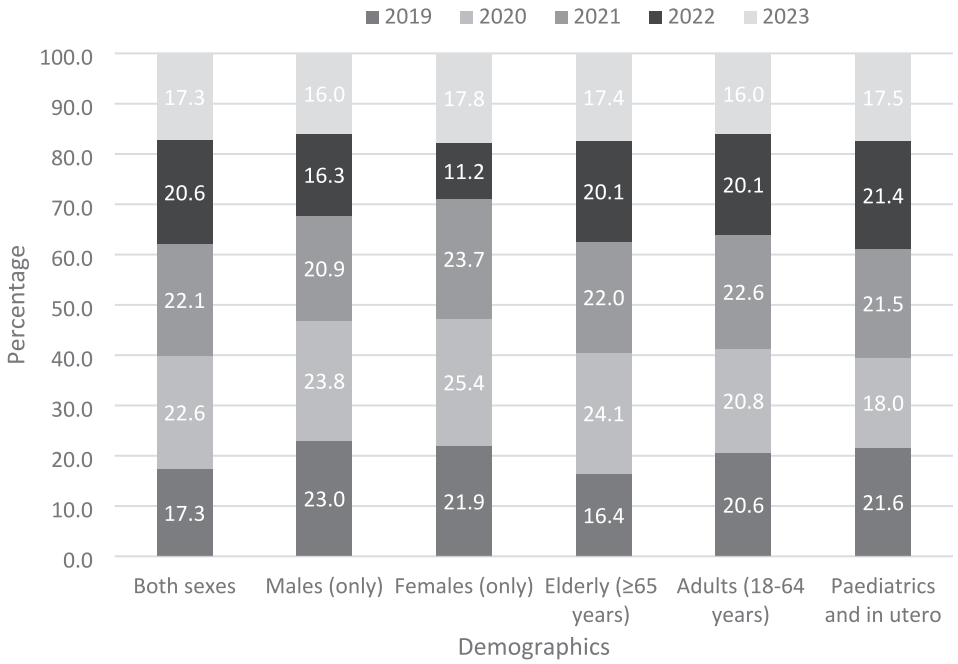


FIGURE 5 Demographics of clinical trial initial submissions across the years.

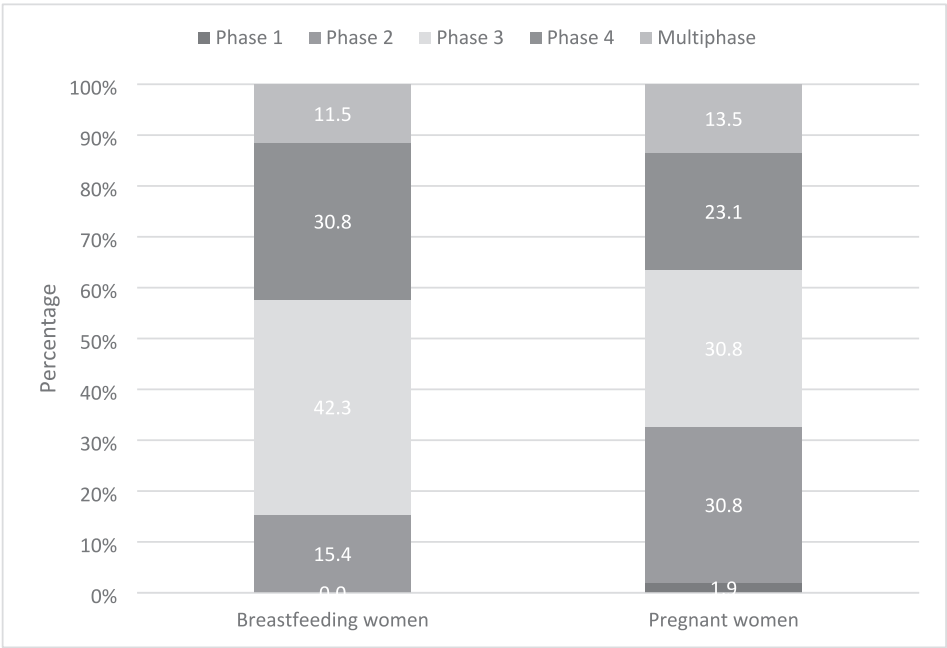


FIGURE 6 Clinical trial initial submissions involving breastfeeding and pregnant women.

4 | DISCUSSION

4.1 | Summary of results

Between February 2019 and October 2023, the MHRA CTU received 4616 initial clinical trial submissions, the highest percentage in 2020 and the lowest in 2023. Phase 3 submissions were the most common. Approximately 85% of clinical trial submissions were from commercial sponsors, mostly phase 3 trials. Both sexes were represented in most trials, with male-only trials being twice as common as female-only trials. Regarding the diversity of participants, elderly were represented more commonly than adults (aged 18–64 years), with adolescents being the most commonly studied paediatric population, and breastfeeding and pregnant women being present in very low percentages. Breastfeeding and pregnant women were most likely to be recruited to phase 3 and 4 trials, with only a negligible percentage of pregnant women included in phase 1. Trials involving HV represented less than a fifth of the total submissions, and these were most commonly phase 1 trials. The most common health category was cancer and the least common being nephrology and pain. The percentage of FIH studies was >3 times higher than ATMPs.

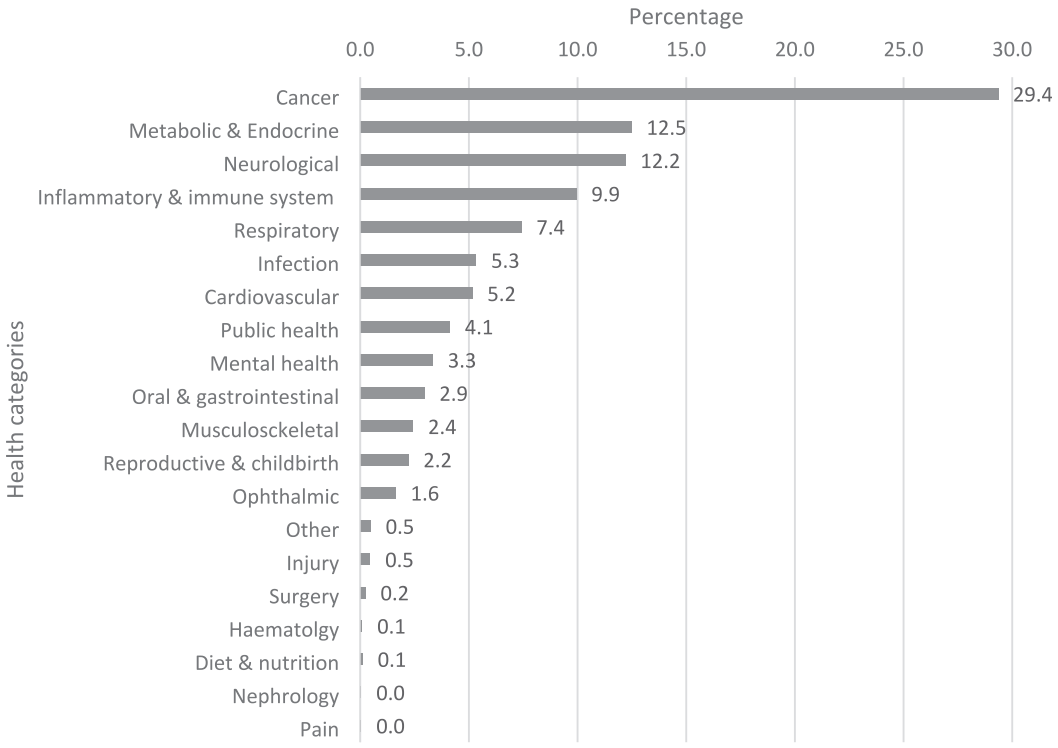
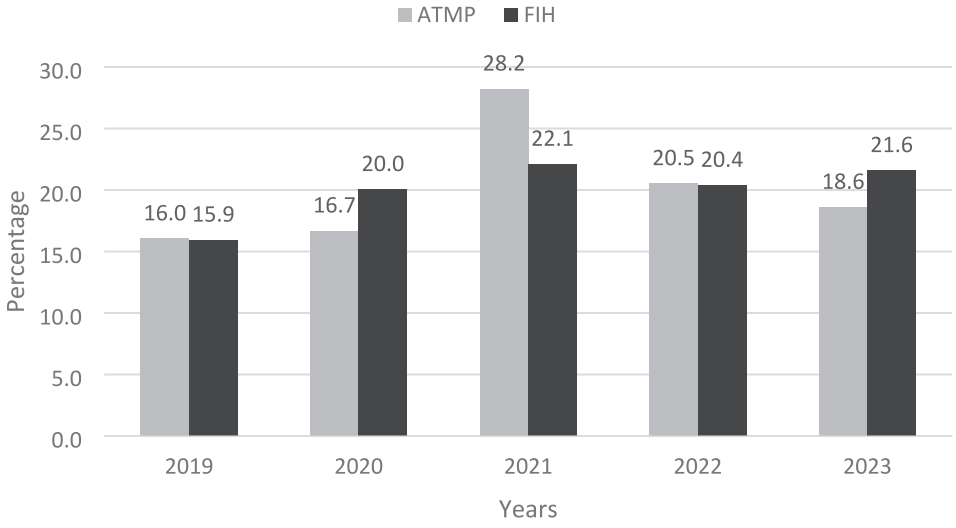


FIGURE 7 Clinical trial initial submissions according to health categories.

FIGURE 8 Clinical trial initial submissions involving first-in-human studies and advanced therapy medicinal products.



4.2 | Comparison with existing literature

The submissions received by the MHRA appear to align with the IQVIA Institute for Human Data Science report.[8] Phase 3 trials were the most popular, followed by phase 2, while phase 4 was the least popular. However, the WHO Global Observatory on Health Research and Development, which includes clinical trials from 1999 to 2022, showed that phase 2 studies were the most popular, followed by phase 3.[15]

The percentage of commercial clinical trial initial submissions was 85% (mostly common phase 3) and is consistent with the review of 809 trials conducted by Fuentes Camp *et al.*[16] The authors found a higher percentage of noncommercial *vs.* commercial trials in phase 4, which also aligns with our findings. The analysis conducted by Seidler *et al.*[14] included all trials (>18 000) registered in the Australian New Zealand Clinical Trials Registry (ANZCTR) from 2006 to 2020. Their findings showed that 45% of their trials had some industry involvement and that the primary sponsor was 36% commercial and 61% noncommercial. These findings are different from our results, but the main reason could be that our analysis included only CTIMP, while they included all trials.

Most trials involved both sexes, with a lack of presence of nonbinary or transgender populations in the clinical trial submissions.

This could be due to the trial inclusion criteria or our database's extraction criteria. Presumably, the most probable cause is the former. Most trials involving HV were in phase 1, while the remaining were scattered across the other phases, including multiphase trials. The involvement of HV in late and multiphase trials is no surprise because of the need to develop medicines for infectious diseases and prevention.[17]

Our analysis showed that the number of trial submissions involving males only was almost twice the number involving females only. Thornton and Dixon-Woods have previously highlighted this well-known, long-standing problem.[18] The elderly population was well represented in the clinical trial submissions we received, but Schwartz *et al*.[19] suggested potential solutions to further support the recruitment by removing barriers such as transportation and complex trial design, improving the perception of and access to drug evaluation research. In our analysis, we could not identify trials conducted for underserved populations, such as the very elderly and frail, due to the lack of this information in our database. Our results indicated that the presence of pregnant and breastfeeding women was limited. A recent mixed-methods systematic review identified 5 overarching themes in these areas: (i) interplay between perceived risks and benefits of participation in women's decision-making; (ii) engagement between women and the medical and research ecosystems; (iii) gender norms and decision-making autonomy; (iv) factors affecting clinical trial recruitment; and (v) upstream factors in the research ecosystem.[20,21] It is known that women's physiological changes in pregnancy and breastfeeding could alter the pharmacokinetics and pharmacodynamics of drugs, resulting in potential risk for the mother, child and/or foetus.[22] There is an emerging opinion that the participation of pregnant women in clinical trials should be redefined as *scientifically complex* rather than *vulnerable*, and that more scientific effort is required.[23] Now, many drug manufacturers use innovative nonclinical methods, such as developmental and reproductive toxicology (DART) studies, which are indicative of potential risks in pregnant and breastfeeding women. Regulatory agencies should use the information provided by DART.[24]

Trials involving diverse participants in diverse settings are more likely to produce generalizable results.[25–28] In this area, there is an opportunity to support the uptake and expansion of in silico trials in research involving pregnant and breastfeeding women and personalized medicine.[29–32] The health categories identified in our analysis showed that cancer was the most common, representing almost 30% of the submissions. This finding is aligned with the analysis conducted by Seidler *et al*. in Australia and New Zealand.[14,33]

4.3 | Strengths and limitations

This analysis was supported by the data included in the clinical trial initial submissions. We have used descriptive statistics, which aids clarity of presentation, but is limited by the fact that it does not provide insight into the causes of data trends and relationships. Thus, the results cannot be generalized to make predictions or infer conclusions beyond the data included in the sample. Nevertheless, this first study aims to lay the baseline for the future evaluation of a more in-depth analysis using inferential statistics to identify causes, trends and relationships.

4.4 | Implications for future practice, policy and research

Clinical trials are central to advancing scientific knowledge and can have an impact on many areas, including (but not limited to) new drug development, understanding of disease mechanisms and identification of biomarkers. Apart from their impact on healthcare, clinical trials contribute significantly to global and local economies, and thus have broader societal benefits. The clinical trials industry creates millions of jobs across multiple sectors. Lord O'Shaughnessy's review of clinical trials emphasized the need to make the UK attractive for international clinical trials with a specific focus on commercial trials.[34] Our data analysis confirmed that 85% were from commercial sponsors, which shows that pharmaceutical and biotech companies invest heavily in clinical trials in the UK to develop new drugs and therapies. It is important to note that the global clinical trials market size was valued at US$57.76 billion in 2023, projected to grow to US$106.78 billion by 2032.[35] Our data provide information about the strengths and variety of clinical trials in the UK, which may be relevant for future growth in particular areas, where there are gaps, and investment opportunities. To this end, it is interesting to note that trials focusing on pain were uncommon, despite the unmet need in this area. Interestingly, despite the fact that cardiovascular disease is the commonest of deaths, the percentage of clinical trial submissions was only 5.2%. This is surprising and worrying and it will be important to monitor this and any downward trend identified and reversed. Furthermore, according to the UK Life Sciences Vision, our data suggest the need to conduct more trials involving respiratory and mental health conditions, which were only 7.4 and 3.3%, respectively.[36]

In December 2024, the new clinical trials regulations were laid before Parliament and debated in the House of Commons and the House of Lords in February 2025. The discussions reinforced the importance of creating an agile, innovative and, above all, patient-centred regulatory framework for clinical trials. Once the debates have concluded in the Northern Ireland Assembly, there will be a 12-month implementation period for the MHRA to update processes and procedures and to publish new guidance to comprehensively prepare the sponsors for the new regulations before they come into force. The results of our analysis, such as population demographics, study types, FIHs and ATMPs, were instrumental in supporting the development of the criteria for introducing notifiable trials in the new clinical trials regulations. Thus, introducing automatic authorisation for notifiable trials and some specific modifications (in the current legislation called amendments) will make trial approvals and modifications more efficient, enabling low-risk trials to receive MHRA authorisation more quickly. This is aligned with Lord O'Shaughnessy's recommendations suggesting that the MHRA should continue adapting its

regulatory processes to ensure that the UK remains at the forefront of clinical trial innovation.

The new regulations will benefit patients by allowing faster access to innovative treatments, better access to trial information, and greater transparency in research efforts. They will solidify the MHRA's position as a global leader in clinical trial regulation while maintaining our commitment to safety and innovation. They will support industry and academia, allowing them to rely on some documents originally prepared for the European Union, European Economic Area and USA. They will allow for a quicker submission process and, when coupled with a risk proportionate review, will result in faster MHRA approvals for lower-risk trials.

Understanding the distribution of clinical trials across various therapeutic areas can help companies and investors assess the risk associated with a particular clinical trial. For example, some therapeutic areas might have a higher clinical success rate, while others might have regulatory or scientific challenges. Understanding the types of clinical trials can help patient advocacy groups and clinical researchers with recruitment efforts. By knowing which trials are being conducted, they can reach out to specific patient populations and inform them about potential opportunities for participation. Patients with under-researched diseases or conditions can benefit from knowing about ongoing clinical trials. Furthermore, the trials submitted to the MHRA allow access to new treatments or therapies unavailable through conventional means because they include CTIMPs.

Overall, our data provide a useful baseline that can be used to determine the current gaps and how policy changes, investments and pharmaceutical company priorities will change the landscape in terms of the number and variety of clinical trials over the years.

5 | CONCLUSIONS

To the best of our knowledge, this is the first analysis conducted by the UK regulator of the many clinical trial initial submissions received across the years. The study highlights phases, sponsors, participant demographics across phases, healthy volunteers, health categories and trials involving FIH and ATMP. Although the MHRA has received a variety of submissions, it also highlights a crucial need for more diverse demographics. Trials should represent the populations using the medications. These data are an important first step towards creating a system to inform policymakers, researchers, healthcare providers, sponsors, investors and patients about submissions received by the MHRA. This will help support the decision-making process and funding allocations to enhance the UK Life Sciences Vision, and the need for national and international collaboration in an area that is highly relevant to health, the economy and job creation.

AUTHOR CONTRIBUTIONS

Andrea Manfrin conceptualized the paper, designed and performed the data analysis, drafted the first version of the manuscript, and finalized the last version before submission. Kingyin Lee contributed to the analysis, reviewed and edited the first draft, and reviewed the final draft. James Pound reviewed the first draft, provided comments and reviewed the final draft. Munir Pirmohamed reviewed the data analysis results, provided input into the first draft, and reviewed and approved the final draft. June Raine conceptualized the paper, reviewed the first draft, provided comments and suggestions and reviewed the final draft.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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13. IS IT A CLINICAL TRIAL OF A MEDICINAL PRODUCT? A B C D E A CLINICAL TRIAL OF A MEDICINAL PRODUCT? A NON-INTERVENTIONAL CLINICAL TRIAL? Is it a medicinal product (IMP)? i Is it not a medicinal product?
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