
# Clinical research landscape of monoclonal antibodies

## Report on 2014–2023 period

Monoclonal antibodies (mAbs) are artificial proteins that mimic the body's natural defences. They are under research or have already been shown to be effective treatments for many diseases *(1, 2)*. To understand current clinical research, identify gaps for targeted R&D, and to promote access to mAbs, we conducted a landscape analysis using WHO's International Clinical Trials Registry Platform (ICTRP) and the Global Observatory on Health Research and Development *(3, 4)*.

**KEY MESSAGES**

**Monoclonal antibodies are increasingly being investigated in clinical trials.** The number of registered interventional trials using mAbs for the treatment of malignant and infectious diseases increased from a total of 1207 in the 2004–2013 decade to 2066 in the 2014–2023 decade.

**Geographical disparities in clinical research.** While mAb clinical trials have expanded in low- and lower middle-income countries (LMICs), especially for the treatment of infectious diseases, 66% of all mAb trials registered in the 2014–2023 decade were conducted in high-income countries and, only 1% in low-income countries), contributing to missed opportunities to conduct clinically relevant research.

**Gaps in paediatric trials.** Only a small percentage of trials have explicitly recruited children and adolescents, with just 4% involving children aged 0–9 years. This underrepresentation highlights a crucial area for development to assess the efficacy and safety of mAbs in younger age groups. Addressing this gap is essential to ensure that mAbs are safe and accessible across all age groups, allowing everyone to benefit from their therapeutic effects.

**Emerging applications and research needs.** The clinical research landscape of mAbs is predominantly focused on noncommunicable diseases (NCDs): 84% of trials addressed mainly cancers and immune diseases in contrast to overall global unmet needs.

**Urgent action to improve and expand R&D is needed to address inequities in access to mAbs.** Geographical disparity in clinical research, coupled with the focus on NCDs, limits the potential of mAbs to enhance global health care. Expanding R&D across more regions, investigating a greater variety of disease areas in line with community needs and integrating funding with access plans are the crucial early steps required to remedy this situation.

# Introduction

Monoclonal antibodies (mAbs) represent an important medical innovation in modern medicine *(1, 2)*. They are of proven efficacy in various therapeutic areas such as cancer, immune diseases and infectious diseases, and have become the standard of care for several medical conditions in high-income countries, demonstrating improved outcomes over legacy treatments (e.g. for treatment of B-cell non-Hodgkin lymphoma *(5)* or multiple sclerosis *(6)*).

Increasing investments in antibodies in recent years have been partly due to their success rate in clinical development. From 17% to 25% of mAbs being tested in humans progress to full approval in contrast with small molecules, where approval is granted to only 5 to 10% of candidates *(7)*. Moreover, in 2023, on average more than 10% of novel drugs approved by the US Food and Drug Administration, European Medicines Agency and UK Medicines and Healthcare products Regulatory Agency were mAbs *(8)*.To some extent this success rate is attributable to their target selectivity, showing considerable promise (whether alone or combined with therapeutic drugs or small molecules) in the management and treatment of cancers including lymphomas, breast, cervical and gastric cancers. In view of the increasing interest in new treatments for infectious diseases – driven by concerns about antimicrobial resistance, endemic pathogens in situations where vaccine development has been unsuccessful and the emergence of pathogens with pandemic potential – there is an opportunity to further expand the development of mAbs to target infectious diseases in different populations *(9)*.

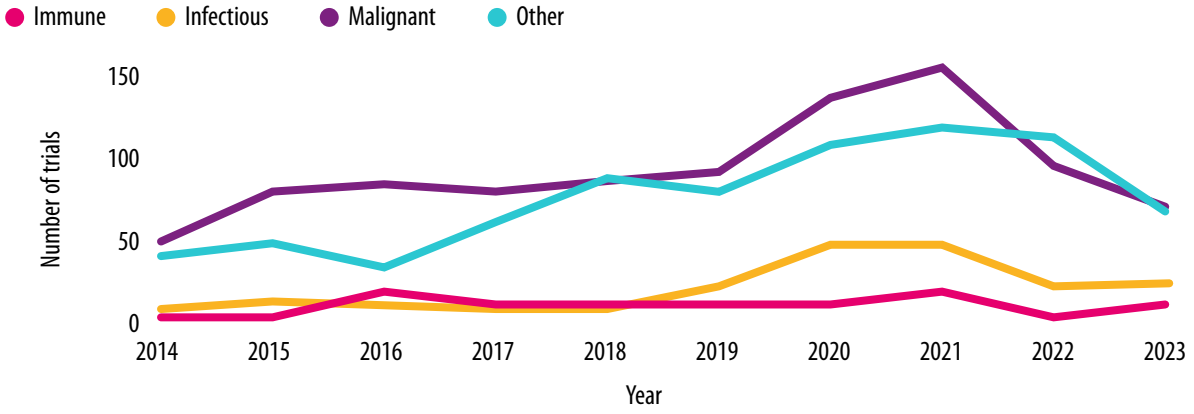
However, there is enormous global inequity in access to monoclonal antibodies: only a fraction of the monoclonal antibodies available in the USA and European Union are authorized for use in LMICs *(10)*. There is an urgent need for investment in strategies to address these inequities *(11)*. Coordinated efforts are also required to target R&D efforts more effectively and expand access to innovative mAbs for all those who would benefit from them.

To gain a greater understanding of current clinical research on mAbs and identify areas for targeted R&D, as well as to improve and expand access to mAbs, we conducted a landscape analysis using WHO's International Clinical Trials Registry Platform (ICTRP) and the Global Observatory on Health Research and Development. This report therefore focuses on mAb trials registered in ICTRP in the 2014–2023 decade, representing a total of 2066 interventional trials. It aims to provide an overview of the current mAb clinical trial landscape, with particular emphasis on their geographical distribution, enrolment criteria and therapeutic applications.

# 1. Monoclonal antibodies are an expanding area of clinical research

The number of mAb trials has been steadily growing over the years with registrations peaking in 2021 (Fig. 1), followed by a drop in 2022 and 2023. This pattern aligns with the general trend observed in ICTRP registrations for all trials, which points to the impact of the COVID-19 pandemic. However, in the context of mAb trials, this decrease in the number of trials may also be partly due to the reduction in COVID-19 trials in 2023, the de-prioritisation of non-COVID-19 trials during the pandemic, and a reflection of delays in registering some clinical trials.

**Fig. 1. Number of mAb investigational trials by year of registration and therapeutic areas**




New therapeutic antibodies have entered clinical trials, with the commencement of phase 0 trials in 2020 and an increased number of phase 1 trials. This upsurge may be partly due to an increase in new targets *(12)*. Traditionally, the industry has produced mAbs against a common set of target proteins identified as crucial in disease development or progression whereas, in 2021, 25% of new therapeutic antibodies entering trial aimed at antigens that had never before been targeted by a therapeutic agent *(13)*.

During the 2014–2023 decade, 84% of trials related to noncommunicable diseases, 11% to communicable and maternal diseases, and 5% to other conditions (including endocrine, blood and immune disorders). In 2021, at peak registration, these percentages were 80% and 15%, respectively, with a notable increase in COVID-19 trials. Almost 60% of mAb trials for noncommunicable diseases dealt with malignant neoplasms. Antibody therapies are a large and growing field of biomedical research but until COVID-19, their application had been mostly limited to cancers, autoimmune conditions and inflammation, as immunotherapy. The development of mAbs to treat or prevent infectious diseases still lags far behind that of mAbs to treat cancer.

Regarding communicable diseases, registration peaks were observed in 2020 and 2021, due to the increased number of COVID-19 trials, and accounted for the highest proportion (32%) of trials related to infectious diseases in the 2014–2023 decade, followed by sepsis (targeted at either pathogens causing sepsis or the host-inflammatory response, 27%), human immunodeficiency virus (HIV, 12%), respiratory syncytial virus (RSV, 8%), malaria (5%) and hepatitis B (4%).

# 2. Geographical disparities indicate that high-income countries dominate clinical research on mAbs

**Fig. 2. Evolution of the geographical distribution of all mAb clinical trial sites registered from 2004 to 2023 including pre- and post-COVID-19 in the 2014–2023 decade**

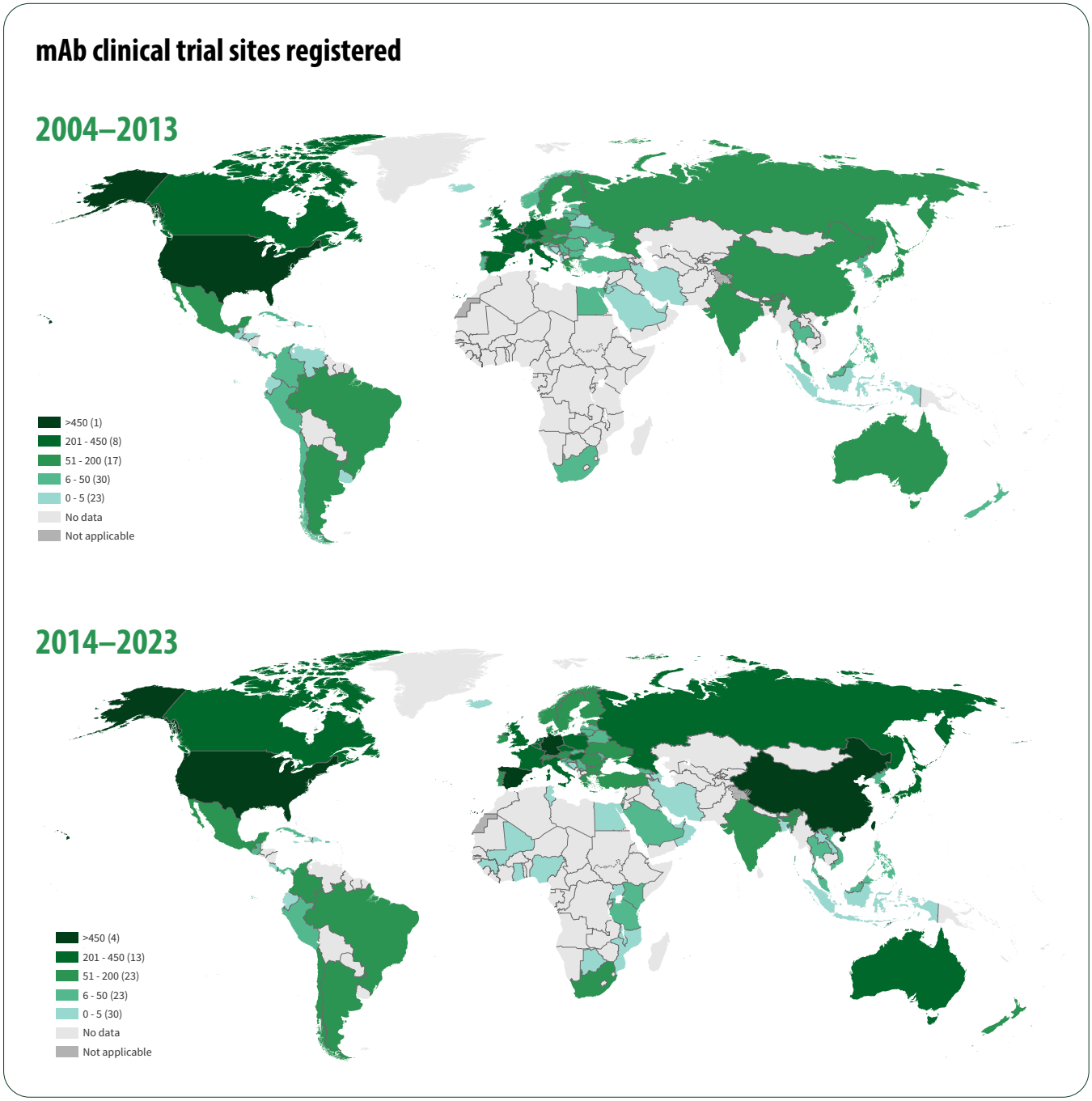
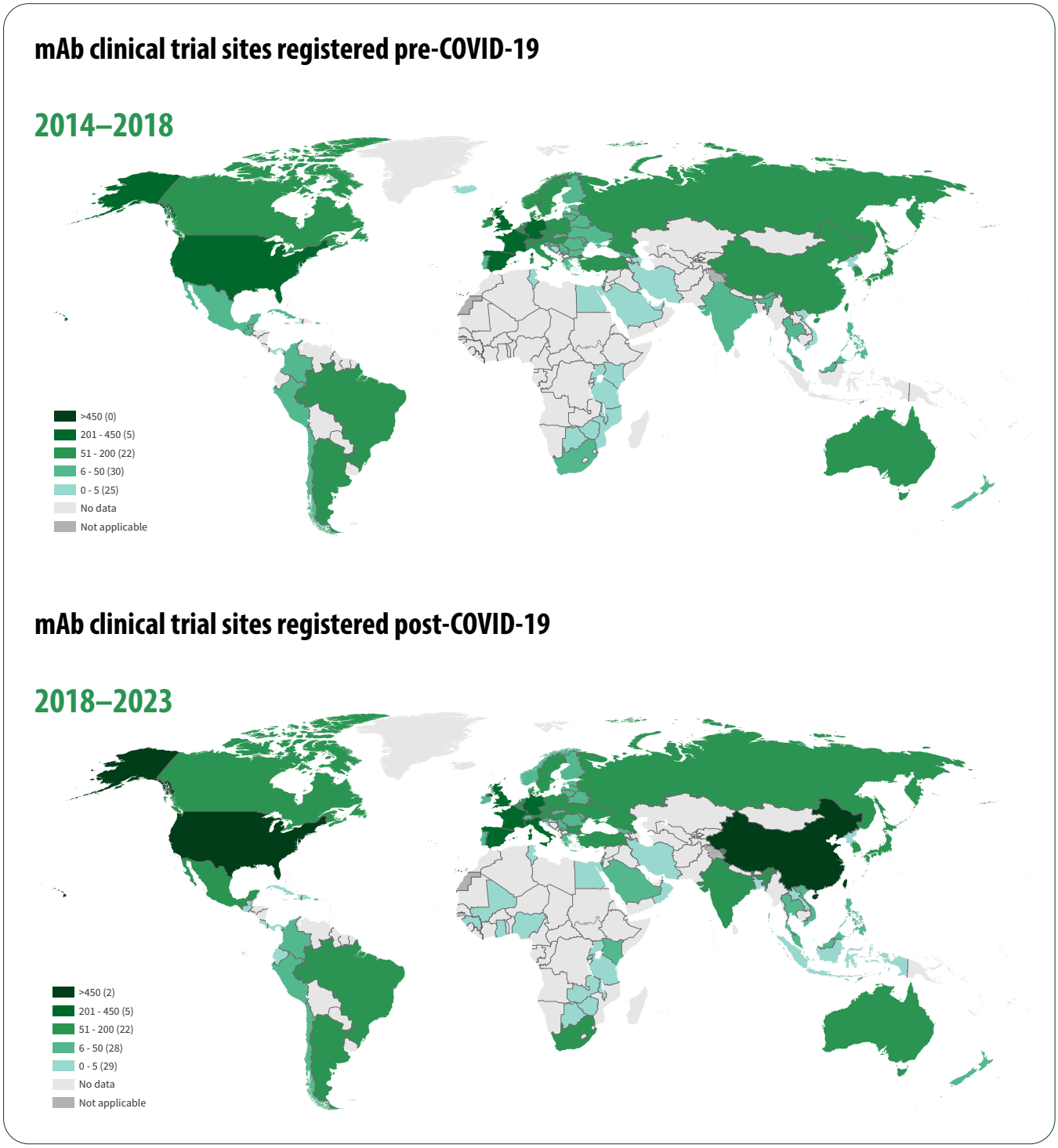
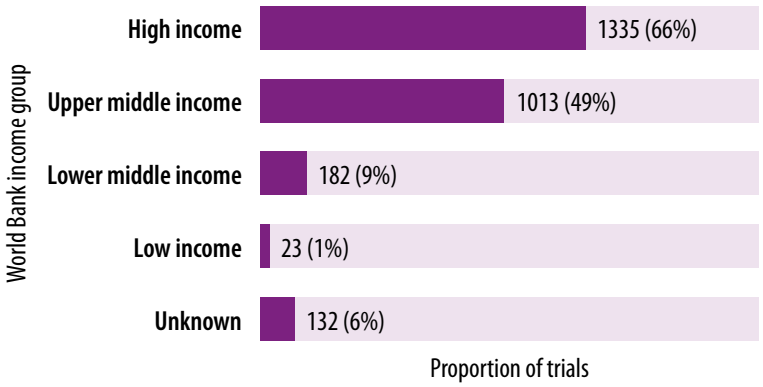


**Fig. 2.** *continued*



The geographical distribution of clinical trials has evolved over time. Initially largely conducted in high-income countries (HICs), clinical research sites have expanded to LMICs in the 2014–2023 decade (Fig. 2). However, there remains a significant geographical imbalance in the conduct of clinical research: 66% of all mAb trials registered in ICTRP from 2014 to 2023 took place in at least one HIC, 49% had at least one site in an upper middle-income country (UMIC), 9% included a site in a LMIC and only 1% involved a low-income country (LIC) (Fig. 3).

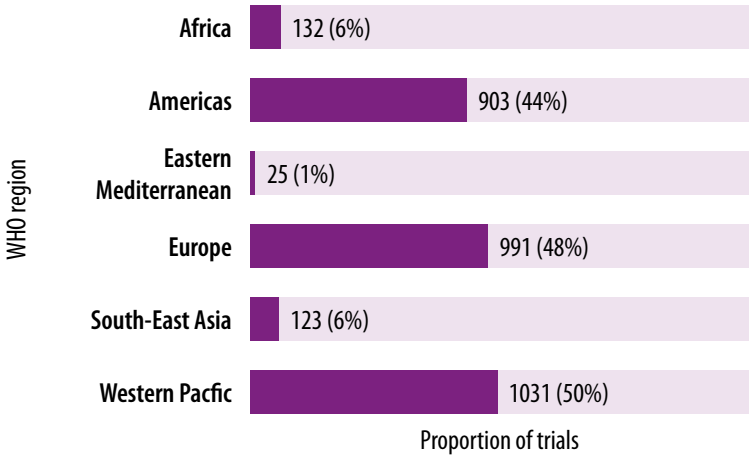
### Fig. 3. Proportion of registered mAb trials by country income group (World Bank)




*Note:* The total percentage of trials exceeds 100% because multi-site trials conducted in multiple countries have been accounted in every income group they took place.

In the 2014–2023 decade, most clinical research on mAbs was carried out in the Americas and Europe. However, since 2018, there has been a notable increase in clinical research in the Western Pacific region, particularly in China. This region is now one of the three main areas for ongoing clinical research on mAbs (Fig. 4). China has become an important player in the field of advanced therapies by increasing its focus on innovations, encouraging international collaboration and improving its regulatory environment for clinical research and new drug approvals.

### Fig. 4. Proportion of registered mAb trials by WHO region




*Note:* The total percentage of trials exceeds 100% because multi-site trials conducted in multiple countries have been accounted in every region they took place.

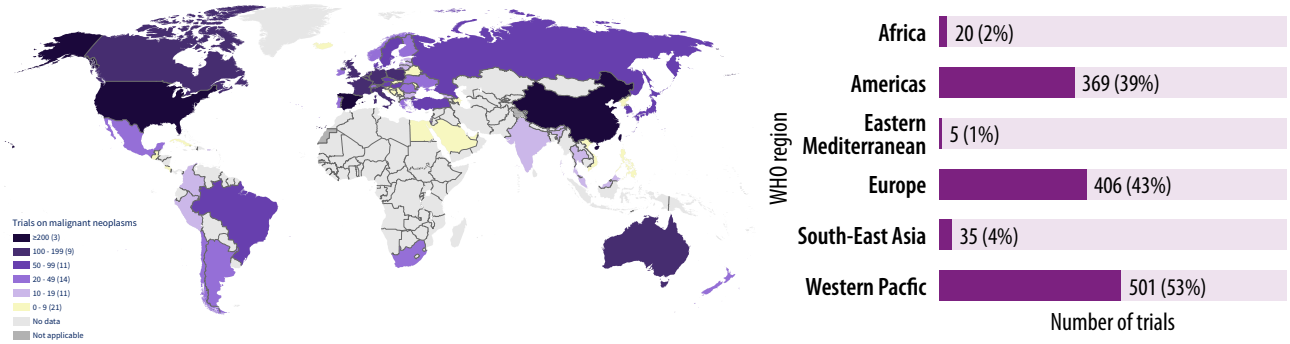
Most studies on mAbs taking place in Africa are focused on immune and infectious diseases, and very few target cancer treatment (Fig. 5). Although cancer is a rapidly growing health concern in Africa, it is significantly understudied in this region *(14)*. Researchers from African countries published five times more research results on infectious diseases between 2009 and 2020 than they did on cancer *(15)*. Several factors

contribute to this disparity. Cancer research lacks domestic and international support across sub-Saharan Africa, which translates into a lack of funding and infrastructure for locally relevant priorities, and limited expertise. Reaping the benefits of increased R&D and clinical research on mAbs will require closer engagement between funders, governments and the scientific community.

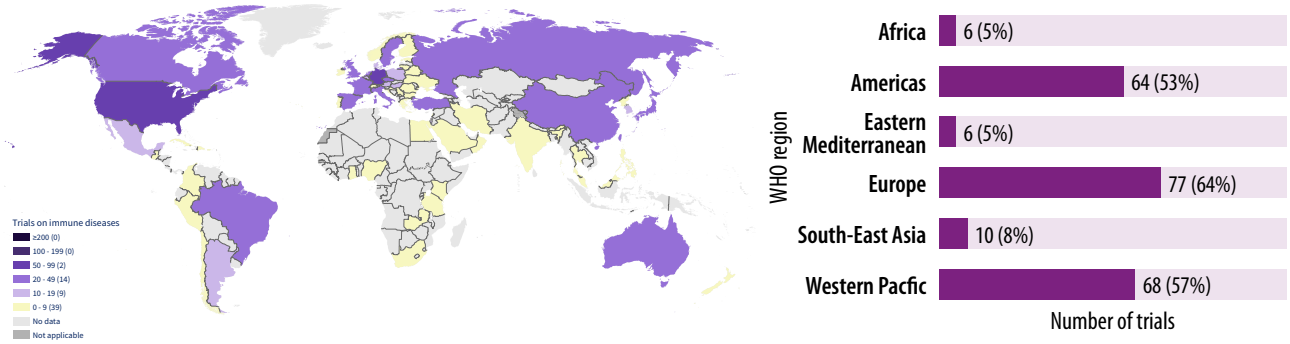
Moreover, without clear processes and guidelines to conduct clinical trials and obtain regulatory approval of mAbs in LMICs, current inequities arising from geographical disparities of clinical research on mAbs are likely to persist and increase in the years to come. In many LMICs, guidelines and approval processes for mAbs are protracted and often poorly defined *(10)*. There is a need for effective and harmonized regulatory processes to ensure product developers receive appropriate guidance in a timely manner to avoid delays in obtaining approval and launching products.

**Fig. 5. Geographical distribution of mAb trials registered for A: malignant neoplasms; B: immune diseases; and C: infectious diseases**

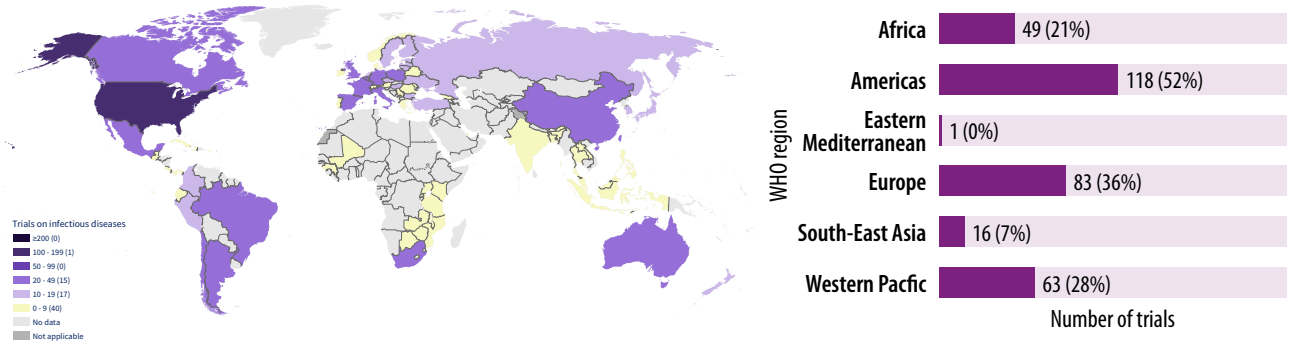
**A • mAb clinical trials registered for malignant neoplasms**




**B • mAb clinical trials registered for immune diseases**



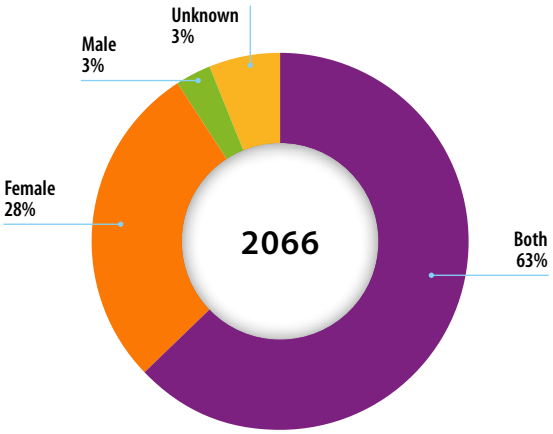

**C • mAb clinical trials registered for infectious diseases**



# 3. Gender representation and paediatric and adolescent clinical research

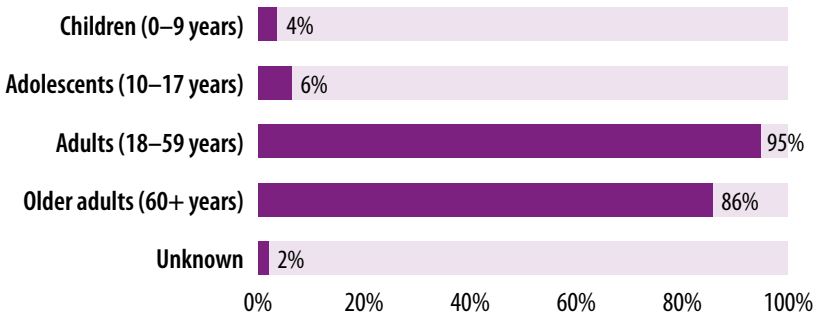
Diversity in clinical research plays a critical role in ensuring the applicability of results across different user demographics and contexts. Assessing diversity and inclusiveness can be achieved by reviewing enrolment criteria. A majority of mAb trials (approximately 63%) have recruited both male and female participants (Fig. 6) where relevant. In contrast, about 28% of trials have recruited female participants only, often targeting diseases that specifically affect women such as ovarian cancer, or predominantly affect women such as certain autoimmune diseases, e.g. lupus, rheumatoid arthritis and hormonal disorders *(16)*.

**Fig. 6. Gender distribution in enrolment criteria for mAb clinical trials (2014–2023)**




Regarding age-based enrolment criteria, most trials (approximately 96%) have recruited solely adults. Only a small fraction specifically included children aged 0–9 years (4%) and adolescents aged 10–17 years (6%) (Fig. 7). This skewed distribution shows that clinical research has the potential to expand into relevant areas of paediatric and adolescent medicine in order to gain a fuller understanding of the efficacy and safety of mAbs across all age groups.

**Fig. 7. Age distribution in enrolment criteria for mAb clinical trials (2014–2023)**



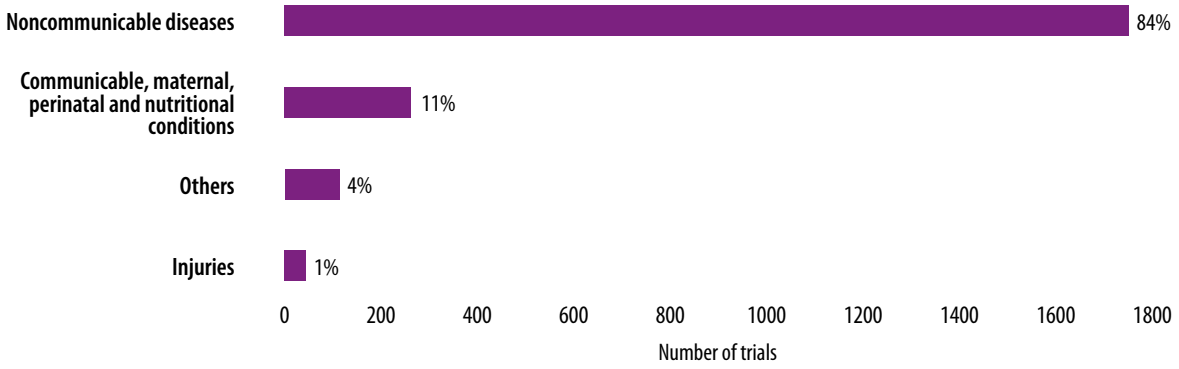

*Note:* The total percentage of trials exceeds 100% because trials enrolling across age groups have been accounted in every age group they took place.

As treatments, mAbs have proved to be highly successful for autoimmune diseases and against infectious pathogens, either as primary/preventive therapy or salvage therapy among paediatric patients. Although target discovery for paediatric cancers continues to expand, most mAb trials do not advance to phase 1 or are abandoned when the first difficulties are encountered with regulatory approval *(17)*. Recent investigation on the use of monoclonals for infectious diseases *(9)* such as RSV *(18)*, malaria *(19)* and HIV *(20)* have illustrated the potential of monoclonals to prevent diseases that are important contributory factors to global child mortality and morbidity and underline the need to expand investigation into similar solutions for other diseases in the future.

# 4. Noncommunicable diseases as the main area of clinical research on mAbs

A closer look at the therapeutic indications under investigation reveals a predominant focus on noncommunicable diseases, which accounted for 84% of all trials (Fig. 8). Of these, 54% targeted malignant neoplasms, particularly lymphomas and multiple myeloma (166 trials). Apart from cancers, mAbs are increasingly used for the treatment of disorders affecting the endocrine, blood and immune systems (60 trials). For example, mAbs that target specific immune checkpoint inhibitors have shown promise in treating autoimmune diseases by recalibrating the immune system response *(21)*.

**Fig. 8. Proportion of clinical trials registered between 2014 and 2023 assessing mAbs for noncommunicable vs communicable diseases**




Regarding communicable diseases, the response to the COVID-19 pandemic highlighted the potential of mAbs to manage viral outbreaks. Eleven percent of trials targeted "communicable, maternal, perinatal and nutritional conditions", a category that includes infectious diseases. Of these conditions, respiratory infections accounted for 44% of trials, with a significant number of COVID-19 trials (59%, 61 trials).

This area of research is crucial for the development of therapies that can be rapidly deployed against new or re-emerging infectious threats. Other trials are currently assessing mAbs in a widespread number of other infectious diseases such as HIV (24 trials), respiratory syncytial virus (RSV) (16 trials), malaria (10 trials), etc., all of which continue to represent a substantial global disease burden (Fig. 9).

**Fig. 9. The top 10 therapeutic areas associated with mAb clinical trials registered between 2014 and 2023 in noncommunicable and communicable diseases, including number of trials for each condition**

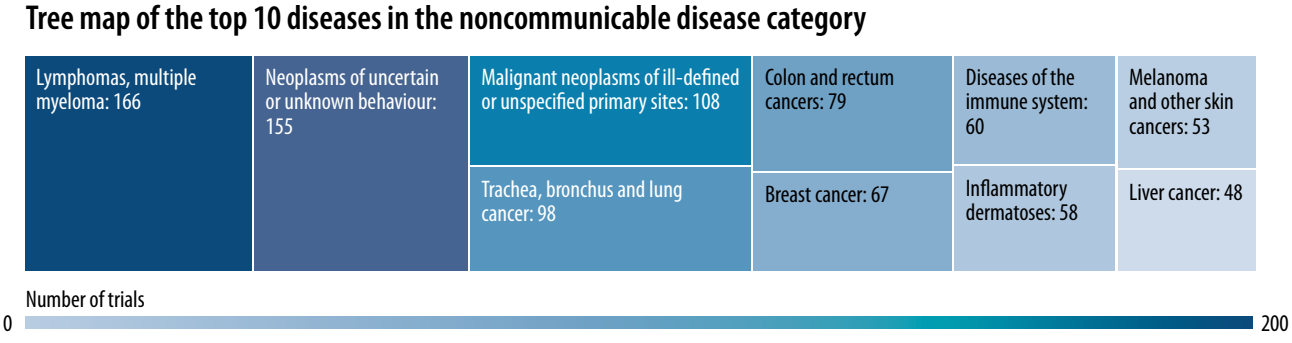
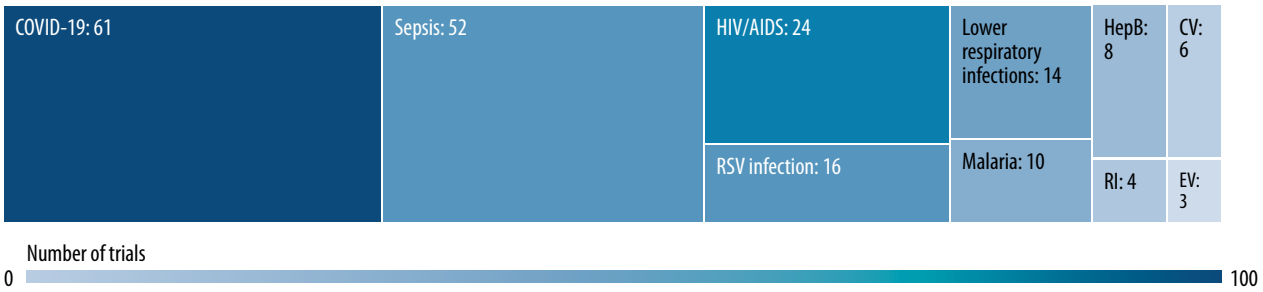


**Fig. 9.** *continued*

**Tree map of the top 10 diseases in communicable, maternal, perinatal and nutritional conditions categories**




HepB: Hepatitis B
CV: Coronavirus infection, unspecified
RI: Respiratory infections, not elsewhere classified
EV: Ebola virus disease

# Conclusion

The 2014–2023 decade marked continued and growing clinical investigation of mAbs, both for existing and new targets. While the geographical spread of clinical trials has improved in more recent years, HICs still continue to host the majority of trials, limiting potential downstream access to the resulting health products on a global scale.

Moreover, the current clinical trials landscape for mAbs shows a promising but uneven picture. The continuing underrepresentation of paediatric populations and communicable diseases in mAb research suggests crucial areas for future exploration and investment. Advocacy for increased access of new therapies in LMICs may encourage clinical studies to be carried out in settings where they can have real impact, generating evidence to support policy and implementation.

Global coordination and prioritization are needed to ensure that new clinical trials address the most pressing unmet needs, particularly those affecting LMICs, which are not proportionally represented in the current R&D landscape. This imbalance is moulded by the multifactorial context, including how research priorities are set and the resulting lack of funding for priorities relevant to LMICs as well as limitations in the global clinical trial infrastructure and research ecosystem.

A global prioritization exercise, considering unmet needs both in terms of diseases and underserved populations, would enable a more targeted and coordinated R&D approach from the early stages, and stimulate the development of health products which are currently not available where they are needed.

More broadly, strategic global health initiatives should aim to prioritize not only the clinical development of mAbs but their manufacture, approval, distribution and accessibility, thus guaranteeing that access considerations are embedded in R&D plans from the earliest stages.

Effectively addressing these issues requires bringing together stakeholders: funding bodies, research institutions, regulatory agencies, private sector, civil society and normative agencies. Adopting a collaborative, multisectoral approach would ensure adequate financing for prioritized R&D topics, draw in key stakeholders including end-users, generate clear regulatory guidance and give rise to supportive policies for the development, approval and global use of mAbs *(22)*. Efforts must be geared not just towards creating new applications but also towards making sure that they are accessible to all populations, thereby addressing current and future health inequities.

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Unless otherwise specified, data for all visualizations and key messages in the report are taken from the Global Observatory on Health Research and Development (GOHRD). Data in this brief are derived from the interactive dashboard which can be accessed via the link below:

https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/clinical-trials-on-mAbs