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Belgium as a clinical trial location in Europe

Accelerating diversity, equity, and inclusion

Report 2022

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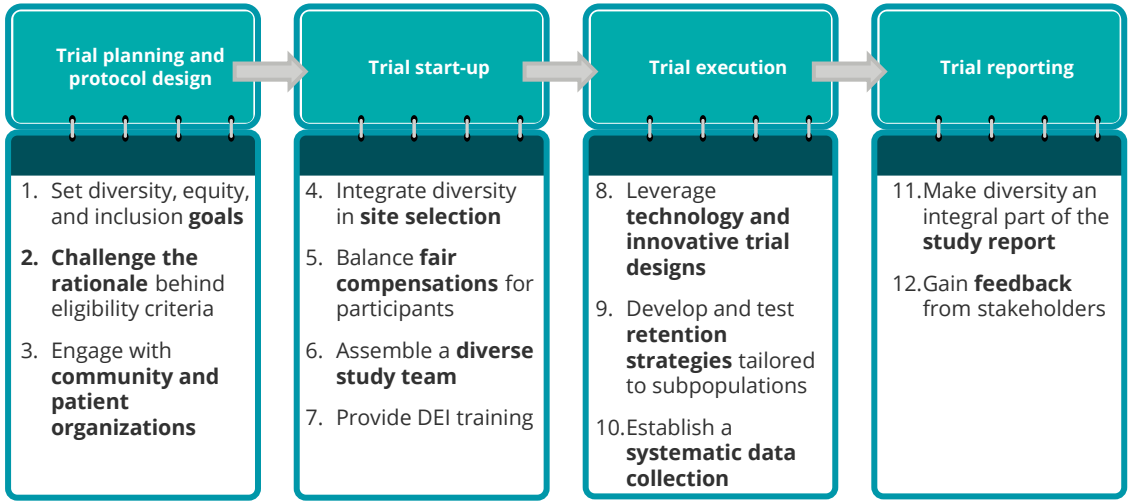
- Enhancing diversity, equity, and inclusion creates deeper insights into drug response for patients who will be taking the therapy, allowing regulators to review study results that are maximal representative
- South-East Asia is approaching the clinical trial volume of Europe, the Americas and Western Pacific, driven by a rapid increase of registrations in India
- Belgium remains consistently part of the top three countries measured by clinical trial authorisations per inhabitant. Only Spain and Poland demonstrate growth over the past decade
- While large variations between the selected countries are observed, Belgium holds its position as one of the leading European countries for phase 1 clinical trials
- A wide variety of therapeutic areas was covered in Belgium in 2022 with the largest proportion for oncology trials. 34% of all Belgian CTAs is conducted in the domain of cancer. The 5-year CAGR is showing a modest declining trend in volume of CTAs for cancer in Belgium, and a growing trend since 2016
- 24% of all CTAs in Belgium is conducted in the domain of rare diseases. The 5-year CAGR is showing a stable trend in volume of CTAs for rare diseases in Belgium, with a growing trends since 2016
- 8% of all CTAs are conducted with a paediatric investigation plan. The 5-year CAGR indicates a modest growth for this type of CTAs, significantly increasing since 2016
- Belgium holds a strong clinical trials footprint at European level with a relatively high percentage of clinical trials in Europe conducted in Belgium
- Strong regulatory, scientific expertise and quality of trials centres remain key drivers for the attractiveness of Belgium. Start-up timelines and the adoption of new technologies remain attention points
- Diversity, equity, and inclusion encourages the representation of diverse populations, such as but not limited to varying gender identities, races, ethnicities, religions, socio-economic backgrounds, cultures, and sexual orientations
- Highlighting diversity, equity, and inclusion in clinical trials presents an opportunity for diverse stakeholders to collaboratively work on various steps across the entire clinical trial lifecycle:



The importance of clinical trials and the need for diversity, equity, and inclusion

The importance of clinical trials

A vibrant clinical trial environment is essential for advancing health, driving scientific progress, and sustaining a competitive position in the global healthcare landscape

The importance of clinical trials

Clinical trials, as part of clinical development, contribute to realizing potential promising new treatments into real health benefits for people. They evaluate how innovative interventions affect health-related biomedical or behavioural outcomes in a proactive way and ensure that potential medical advancements undergo thorough evaluation before they are integrated into mainstream healthcare practices[1].

Having a thriving clinical trials ecosystem provides a variety of benefits for patients, clinicians, researchers, and society.

Clinical trials offer people the opportunity to access the latest treatments that may not be available through traditional means with the potential to improve their health and quality of life. It is a way for patients to actively participate in the management of their health while fostering a sense of purpose by helping clinicians and researchers to get a better understanding of their condition, thereby contributing to improved treatment options for the future.

The health industry epicentre gravitates towards the highest level of scientific and operational expertise worldwide. Countries actively engaged in creating an appealing clinical research ecosystem maximise their chances to attract and retain investments and talent, elements that are indispensable for a thriving knowledge economy. Every euro invested in industry-sponsored trials is estimated to yield a substantial two euros for the economy[2].

Clinical trials have the potential to positively impact the lives of many. To ensure that medical innovation benefits all populations, it is pivotal to address gaps in representation and promoting diversity across all facets of clinical trials, thereby contributing to the creation of a more robust and equitable clinical trial ecosystem.

Purpose of this report

The added value of clinical trials requires monitoring of Belgium's position as a clinical trial location.

The objective of this report is threefold:

- Provide insights on characteristics of clinical trials authorised in Belgium
- Perform a benchmark of Belgium as clinical trial location against nine other European countries
- Create awareness and offer recommendations to foster inclusivity and enhance the overall health equity

Detailed information around the methodology is mentioned in the appendix.

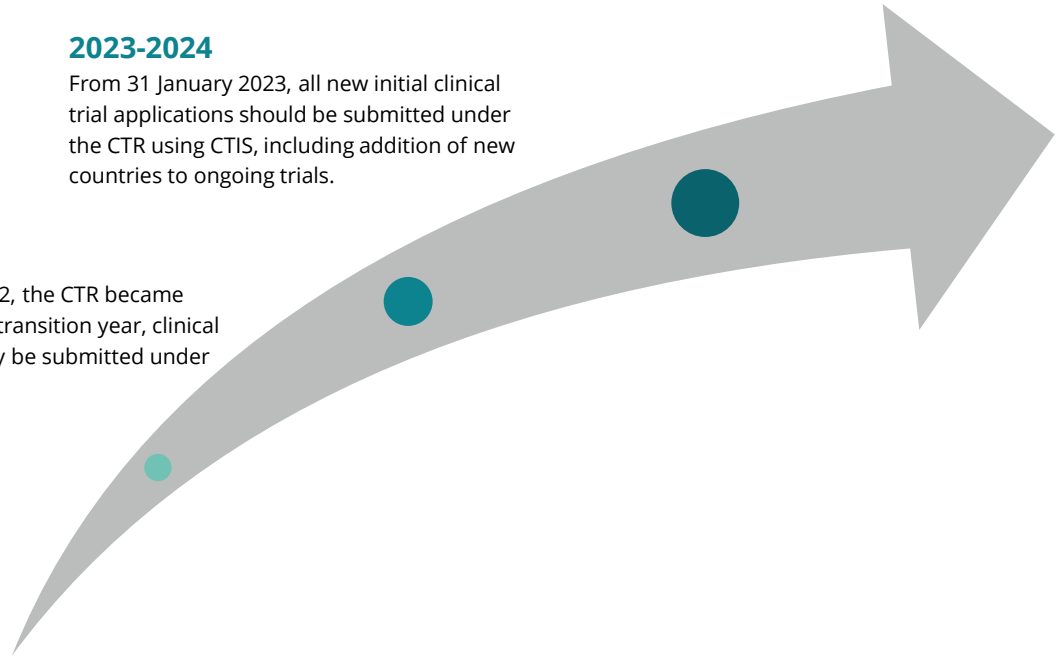
A changing regulatory environment

The implementation of the new EU regulation underscores the importance for Belgium to proactively monitor its historically robust clinical trials landscape and take actions accordingly

The recent implementation of the European Union Clinical Trial Regulation 536/2014 (EU CTR) has brought significant changes to the regulatory landscape in Europe. This transformative shift, effective from 31 January 2022, replaces the previous EU Clinical Trials Directive 2001/20/EC and aims to establish a **harmonized approach for the conduct of clinical trials across the European Union and European Economic Area**.

The EU CTR will bring many changes in clinical trials all over Europe, including a harmonized approach process, fixed timelines and single decision approach (per country). It will be facilitated by the implementation of the Clinical Trial Information System (CTIS). CTIS is a mandatory single electronic portal for all submissions, contributing to increased transparency and consistency in the clinical trial process while ensuring the highest safety standards for participants[3,4].

Three-year transition phase from CTD to CTR[3,4]



The importance of diversity, equity, and inclusion in clinical trials

Enhancing diversity, equity, and inclusion creates deeper insights into drug response for patients who will be taking the therapy, allowing regulators to review study results that are maximal representative

Why is diversity, equity, and inclusion important in clinical trials?

Clinical trials aim to develop new medical interventions by evaluating safety and efficacy before widespread use, generating crucial evidence for regulatory approvals.

Due to the association of health disparities with both demographic (e.g., race, age, ethnicity, gender) and non-demographic characteristics (e.g., socio-economic status), populations can exhibit different outcomes.

Enrolling participants with a broad spectrum of baseline characteristics that accurately reflects potential drug users upon approval becomes necessary to further confirm the product's value.

Moreover, diversifying trial participants actively improves access to innovative treatment options, particularly benefitting minority groups that may have been excluded or not adequately reached for inclusion in clinical trials. This, in turn, actively reduces health disparities and actively enhances public health as a whole.

Real-world example of the need for inclusion in clinical trials for Asthma[5]

Asthma disparities are closely tied to factors such as race, ethnicity, and the environment. Epidemiological research conducted in the United States indicates a higher prevalence of asthma in women compared to men, with a particular emphasis on its prevalence among children, particularly boys.

Additionally, African Americans exhibit a higher prevalence of asthma than other ethnic groups. Environmental factors, including tobacco use, pollution, and obesity, are identified as additional risk factors.

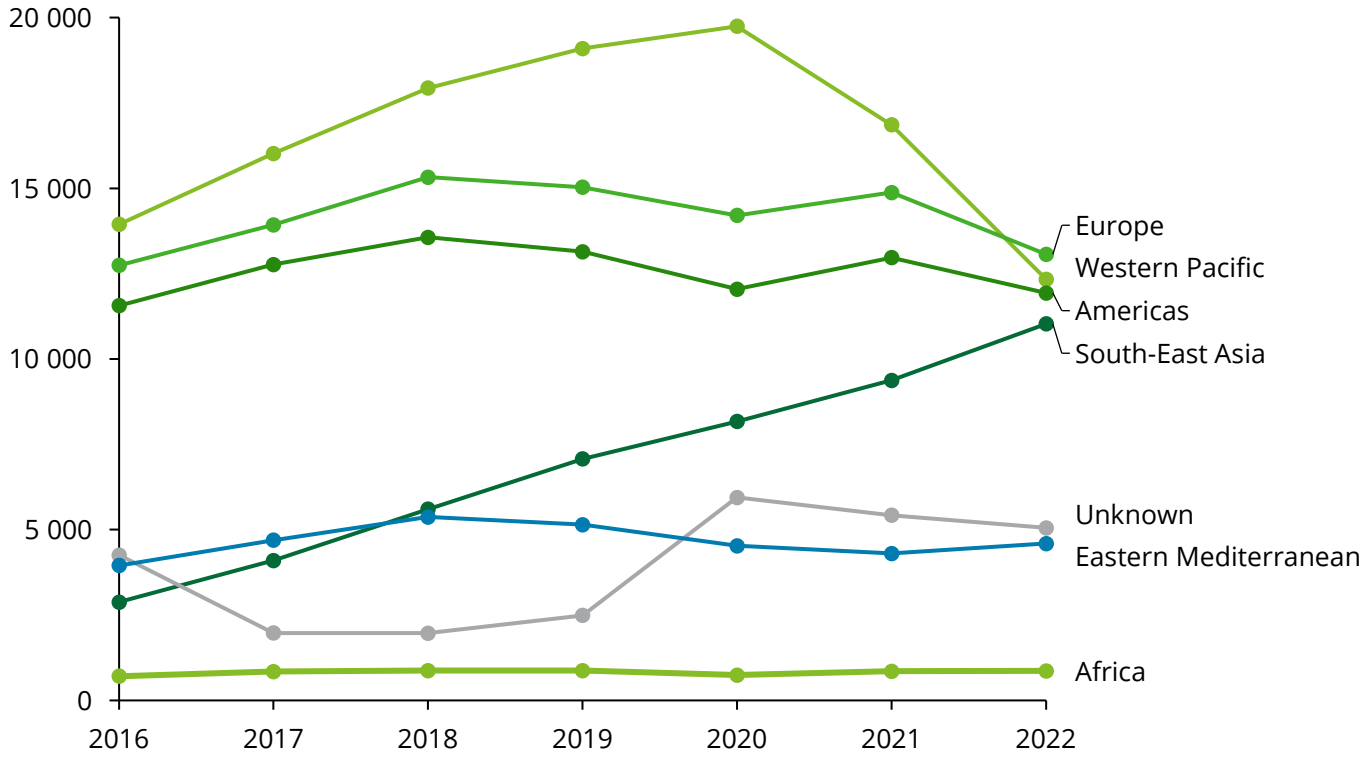
The notable differences in asthma prevalence and mortality rates among minority groups emphasize the importance of addressing various factors in clinical trials. Consequently, it becomes crucial during trials to gather data extending beyond biomedical metrics, encompassing aspects like patients' living conditions and dietary habits.

Belgium as a clinical trial location in Europe

Global evolutions in clinical trials

South-East Asia is approaching the clinical trial volume of Europe, the Americas and Western Pacific, driven by a rapid increase of registrations in India

Number of clinical trials by WHO region (2016-2022)[6]



Dynamic shifts in clinical trials globally

The Western Pacific stood out as the region with the highest number of trial registrations per year among WHO regions until 2021. Its numbers are mainly driven by China (46% of total region) and Japan (31% of total region). Both countries experienced a significant decrease of clinical trials reported between 2020 and 2022, which may be explained by a combination of strict COVID-19 countermeasures and changes to the regulatory landscape like the implementation of the Japanese Clinical Trials Act in 2018[7].

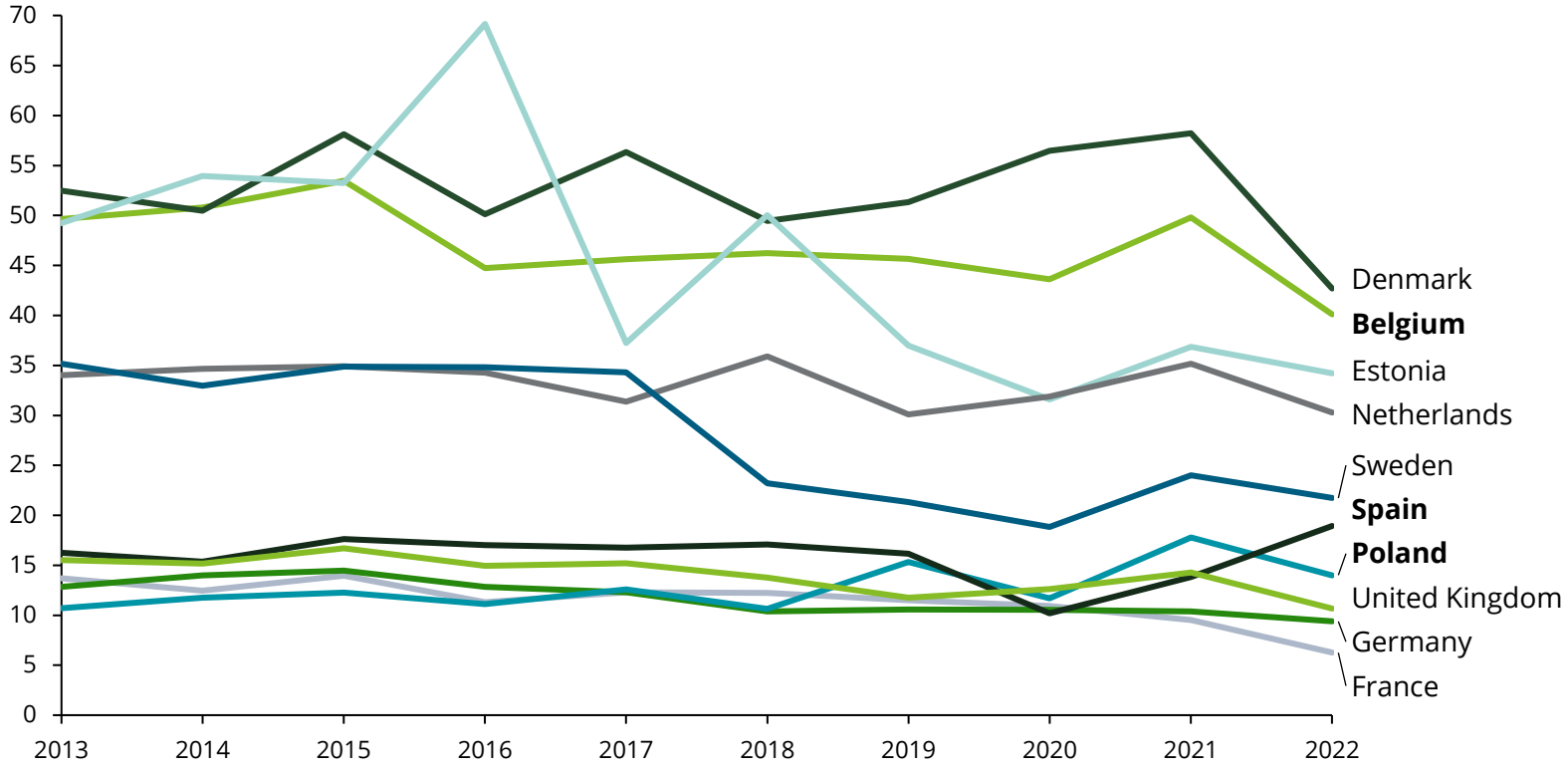
South-East Asia, by contrast, has experienced a significant growth in the past years. Having tripled its numbers, the region is approaching the levels seen in the leading regions. This increase is mainly attributed to India, contributing for approximately 80% of the region's total. Multiple factors for this rise are identified including the ease of regulatory compliance, the low cost of conducting studies and a growing patient population[8].

Note: The WHO International Clinical Trials Registry Platform comprises both interventional and observational trials. Given that clinical trials are counted in the region where they are conducted, multi-regional clinical trials are registered in multiple regions simultaneously.

European evolutions in clinical trials

Belgium remains consistently part of the top three countries measured by clinical trial authorisations per inhabitant. Only Spain and Poland demonstrate growth over the past decade

Evolution of CTAs per 1 million capita in cohort countries (2013-2022)[9]



Country	CAGR 2013-2022
Poland	+3%
Spain	+2%
Netherlands	-1%
Belgium	**-2%**
Denmark	-2%
Estonia	-3%
Germany	-3%
Sweden	-4%
United Kingdom	-4%
France	-7%

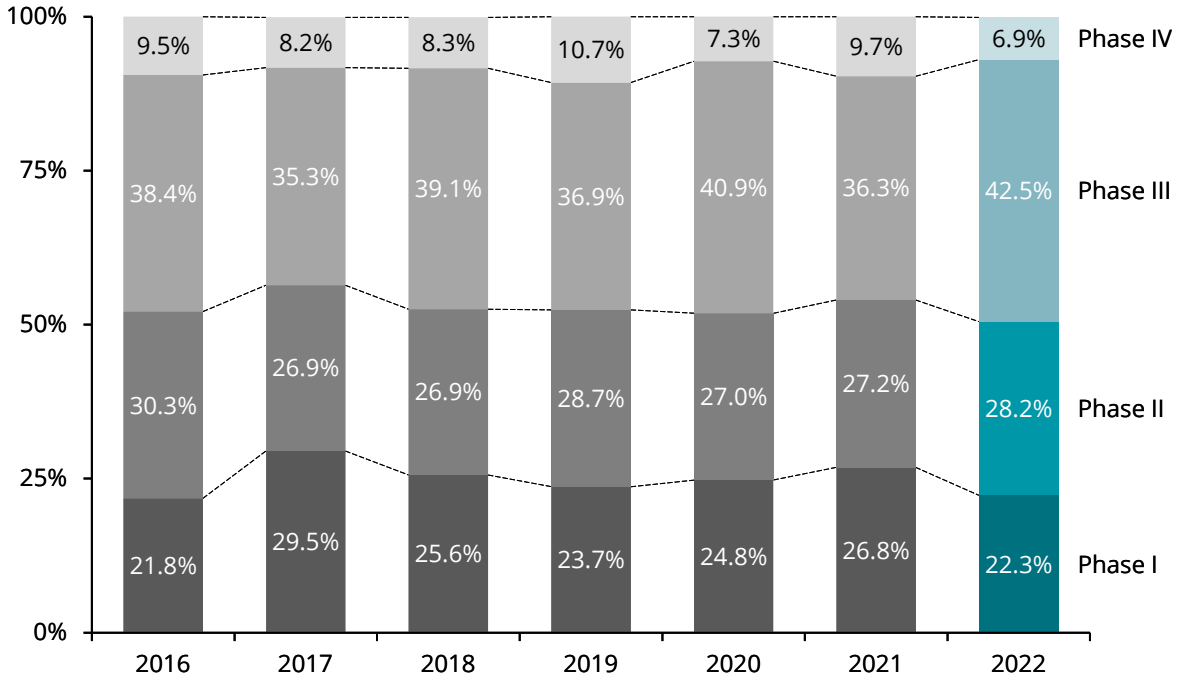
CAGR: Compound annual growth rate

European evolutions in clinical trials

While large variations between the selected countries are observed, Belgium holds its position as one of the leading European countries for phase 1 clinical trials

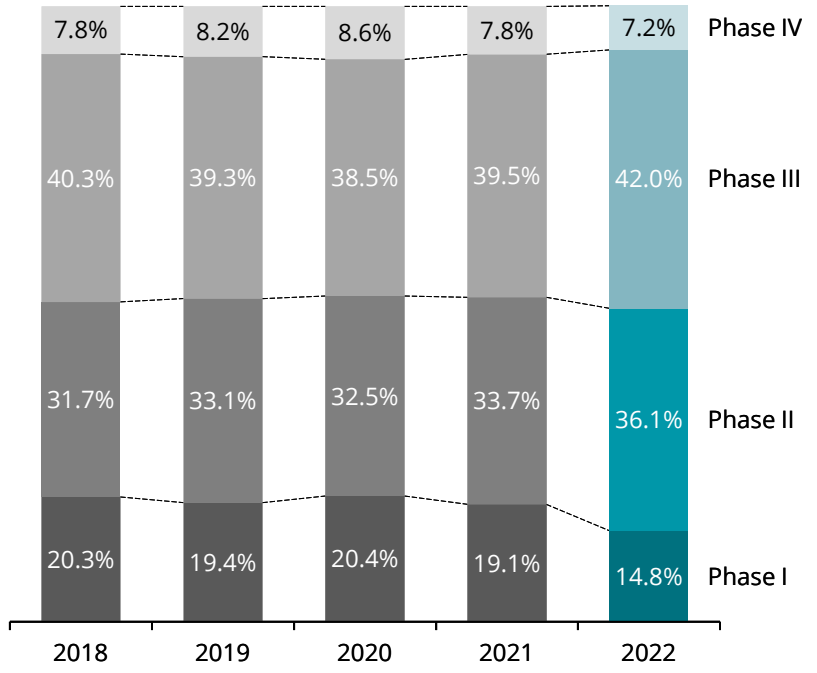
Percentage of CTAs per phase in Belgium (2016-2022) compared to European cohort (2018-2022)[10]

Belgium



European cohort

Large variation between countries for phase 1 (0.0%-23.2%);

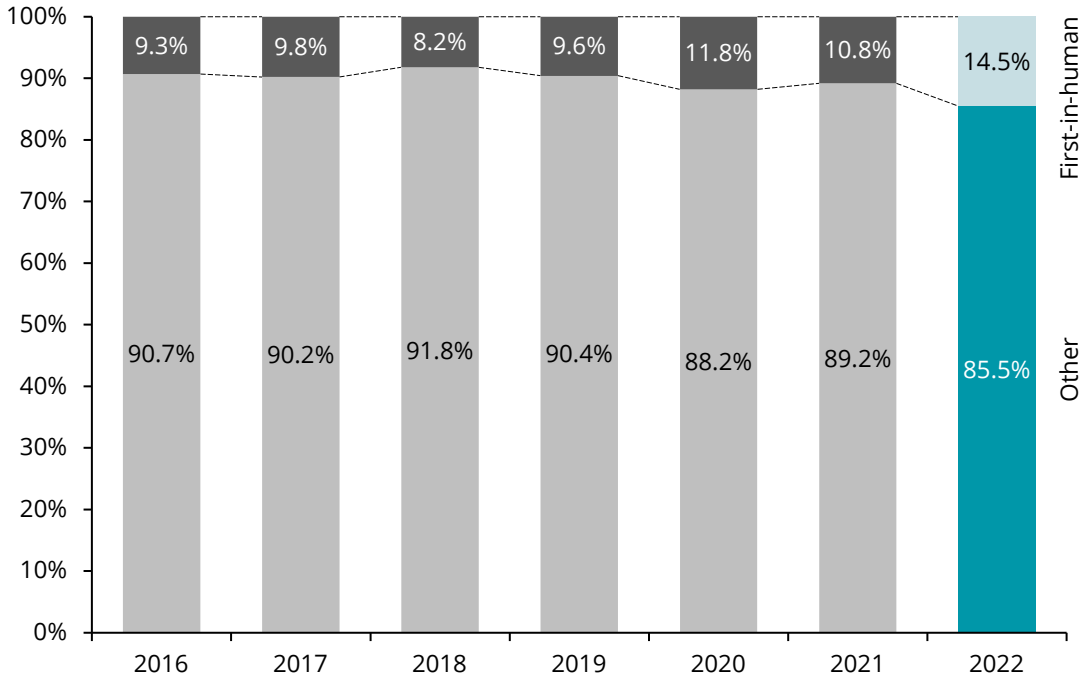


European evolutions in clinical trials

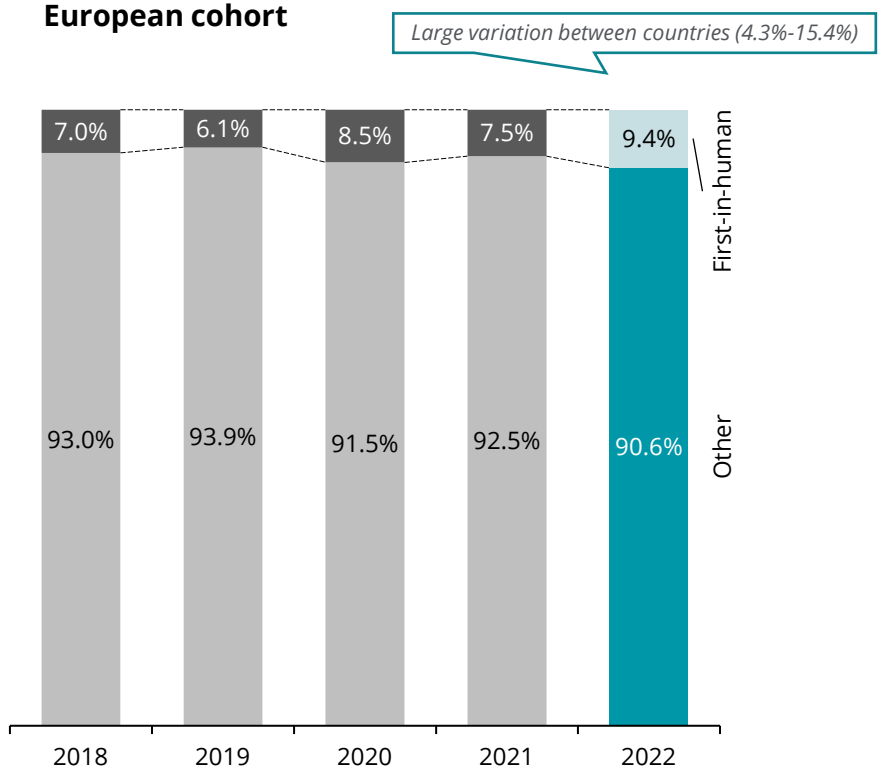
The proportion of first-in-human CTAs in Belgium is higher compared to the European cohort. While large variations are observed within the European cohort, Belgium is among the leading countries

Percentage of CTAs that are first-in-human in Belgium (2016-2022) compared to European cohort (2018-2022)[10]

Belgium



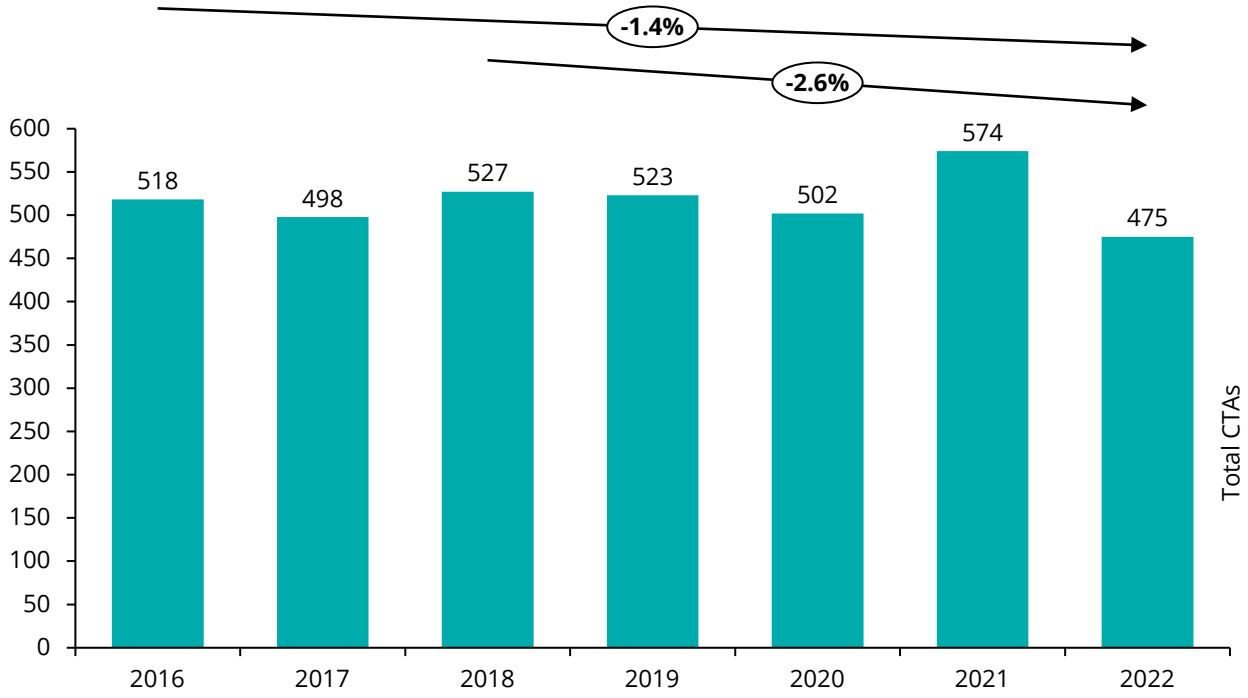
European cohort



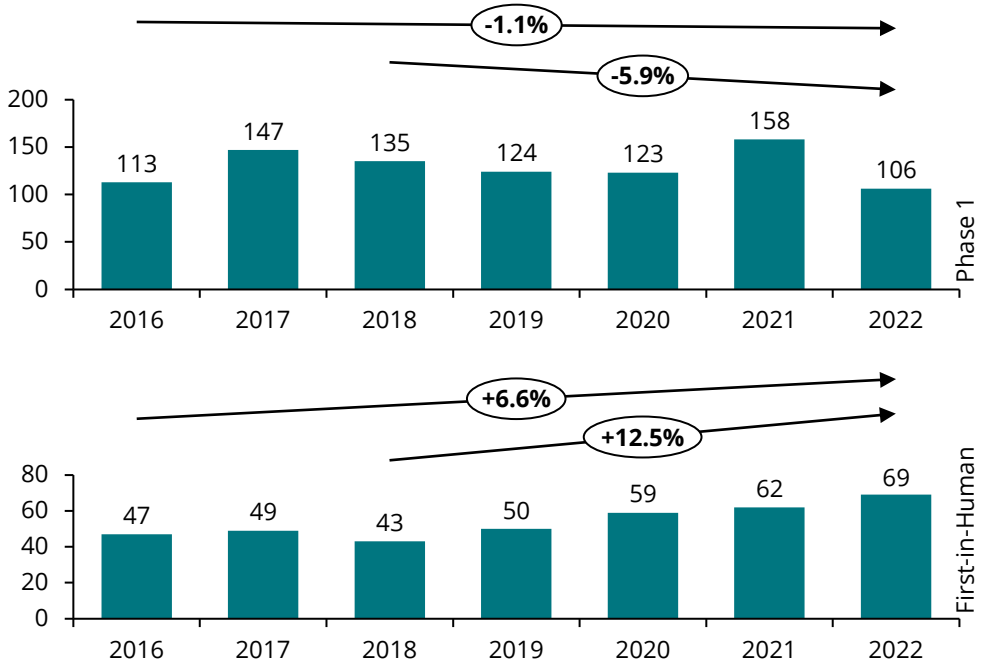
Belgian evolutions in clinical trials

The larger proportion of first-in-human trials is driven by an increase of first-in-human trials and a decrease in overall CTAs and this trend is more pronounced over a shorter time horizon

Growth in CTA volume in Belgium, absolute number of all CTAs[10]



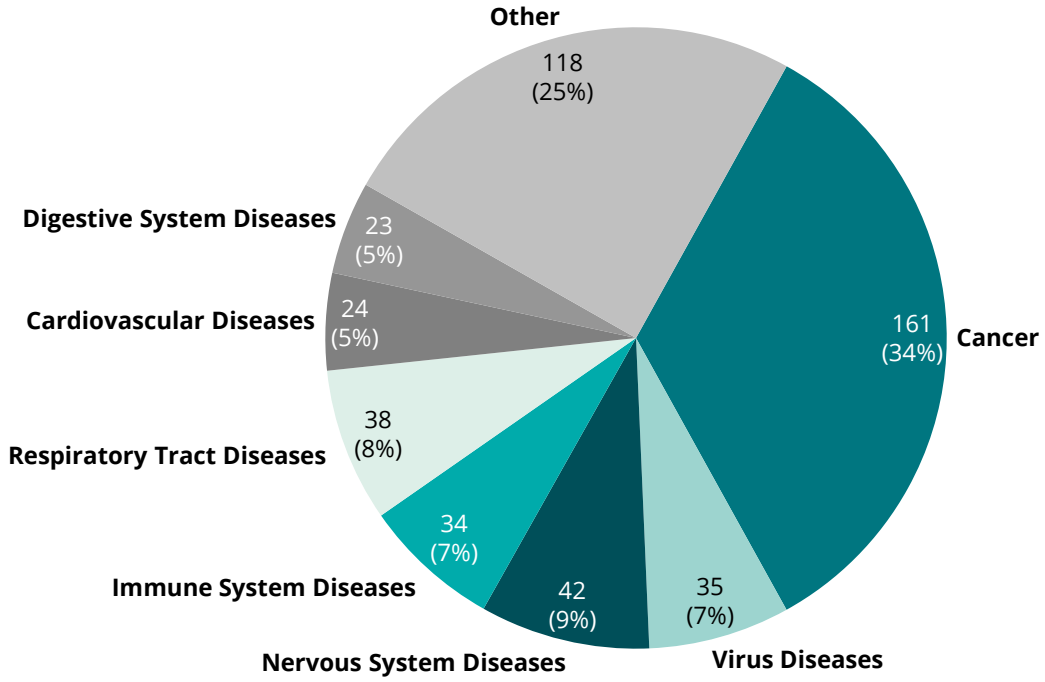
Growth in CTA volume in Belgium phase 1 CTAs and. first-in-human (2016-2022)[10]



Belgian evolutions in clinical trials

A wide variety of therapeutic areas was covered in Belgium in 2022 with the largest proportion for oncology trials

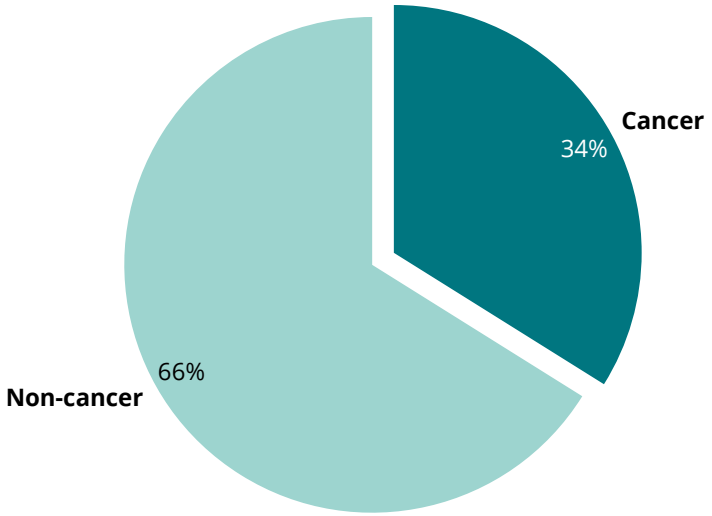
Proportion of CTAs for selected disease areas in Belgium (2022)[10]



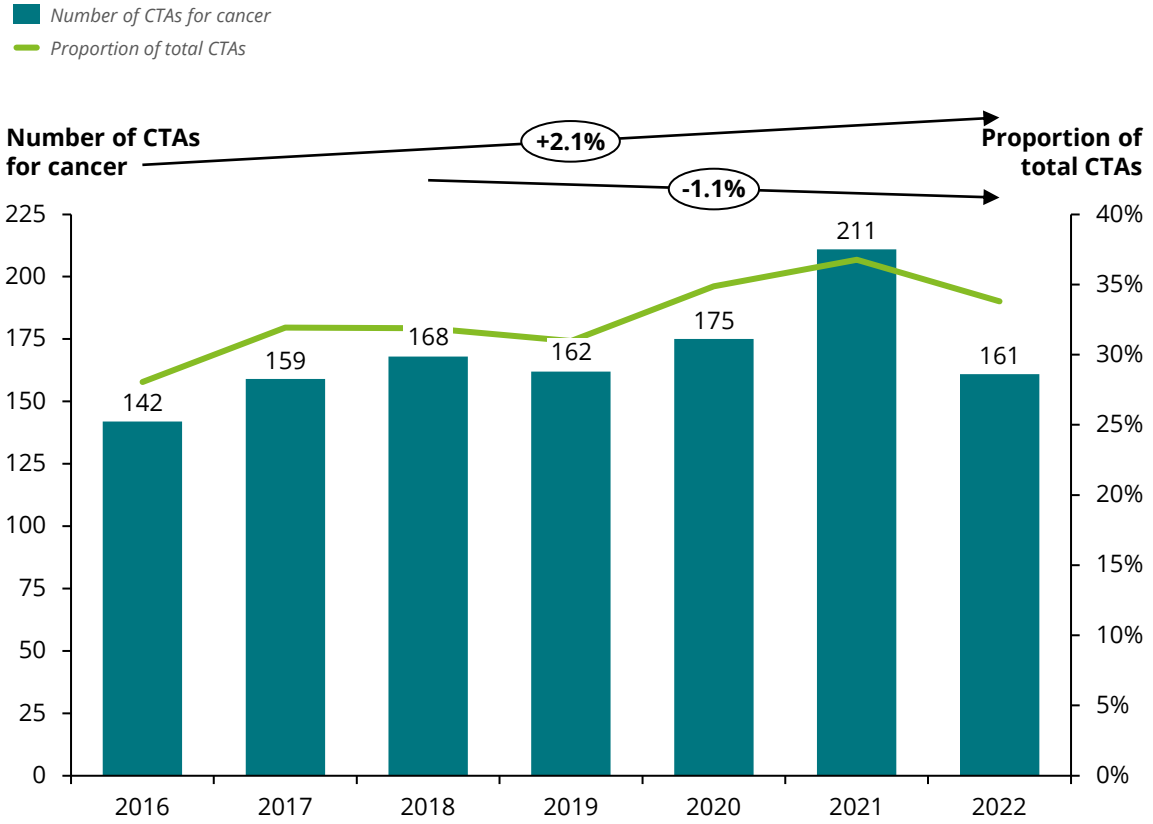
Therapeutic areas covered in clinical trial authorisations

34% of all Belgian CTAs is conducted in the domain of cancer. The 5-year CAGR is showing a small declining trend in volume of CTAs for cancer in Belgium, with a growing trends since 2016

Percentage of CTAs in cancer authorized by the FAMHP in Belgium (2022)[10]



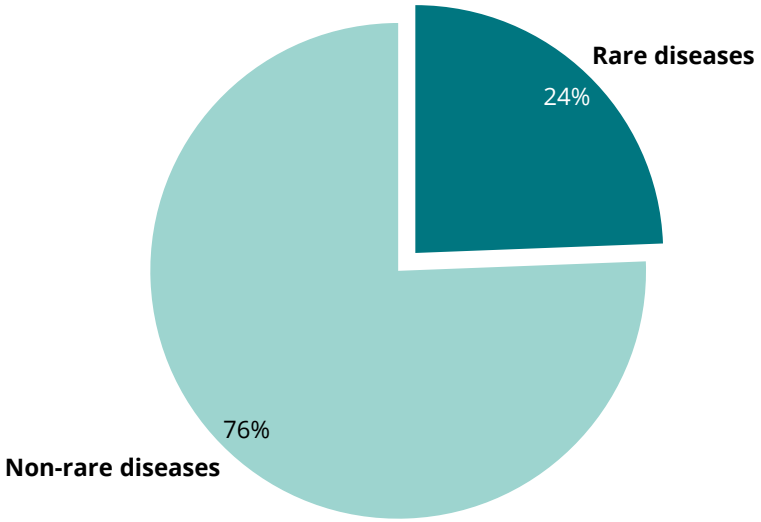
Percentage of CTAs in cancer authorized by the FAMHP in Belgium (2022)[10]



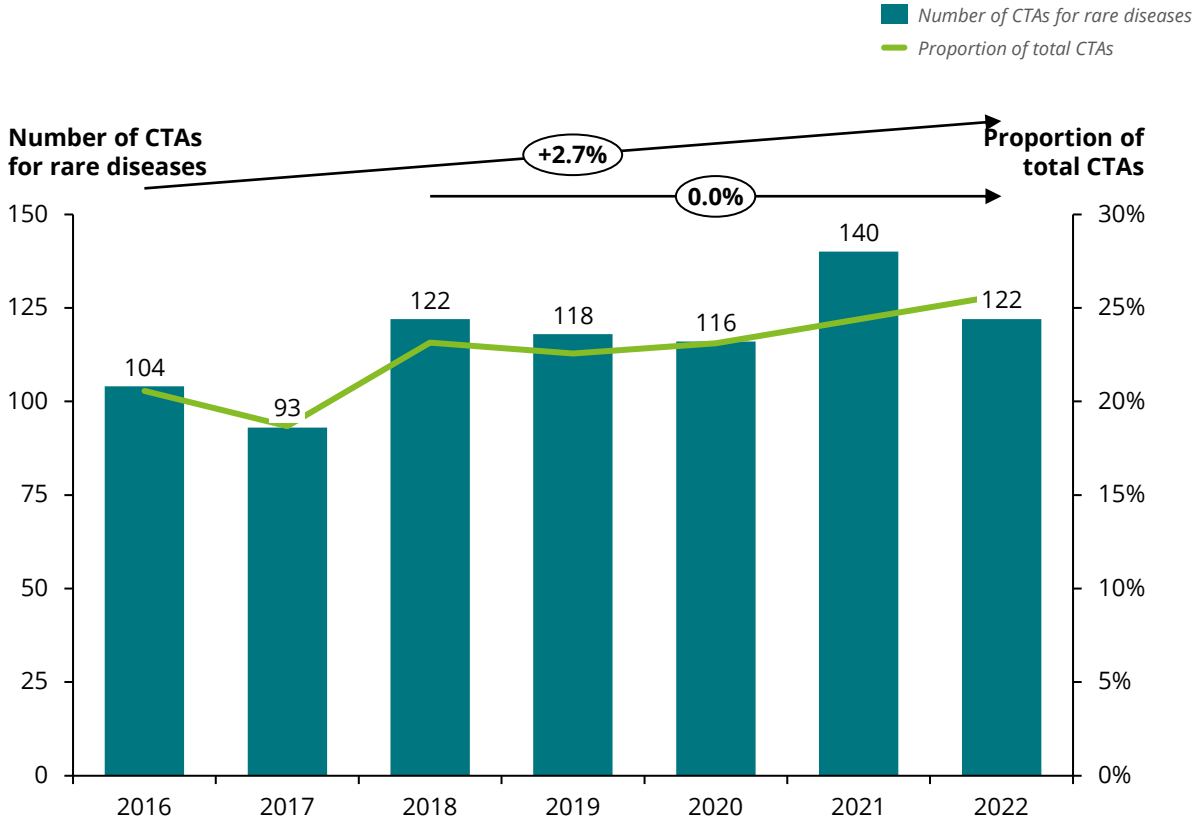
Therapeutic areas covered in clinical trial authorisations

24% of all CTAs in Belgium is conducted in the domain of rare diseases. The 5-year CAGR is showing a stable trend in volume of CTAs for rare diseases in Belgium, with a growing trends since 2016

Percentage of CTAs in rare diseases authorized by the FAMHP in Belgium (2022)[10]



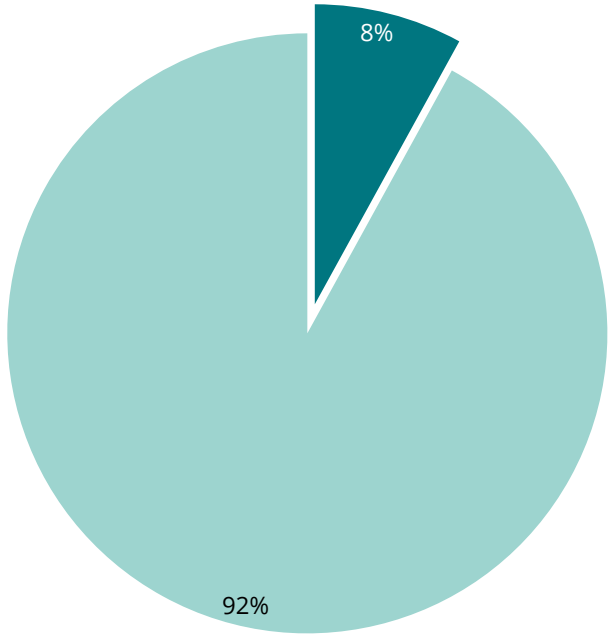
Evolution of CTAs for rare diseases in Belgium (2016-2022)[10]



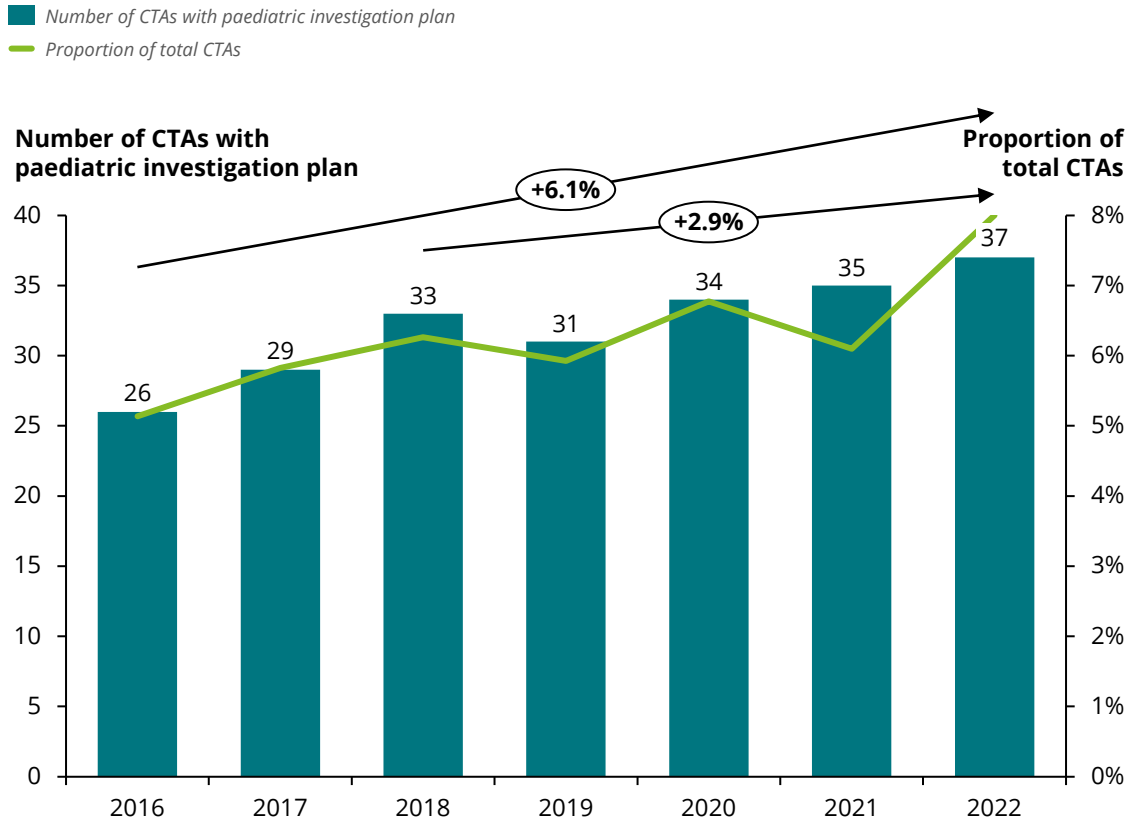
Therapeutic areas covered in clinical trial authorisations

8% of all CTAs are conducted with a paediatric investigation plan. The 5-year CAGR indicates a modest growth for this type of CTAs, significantly increasing since 2016

Percentage of CTAs with a paediatric investigation plan authorised by the FAMHP in Belgium (2022)[10]



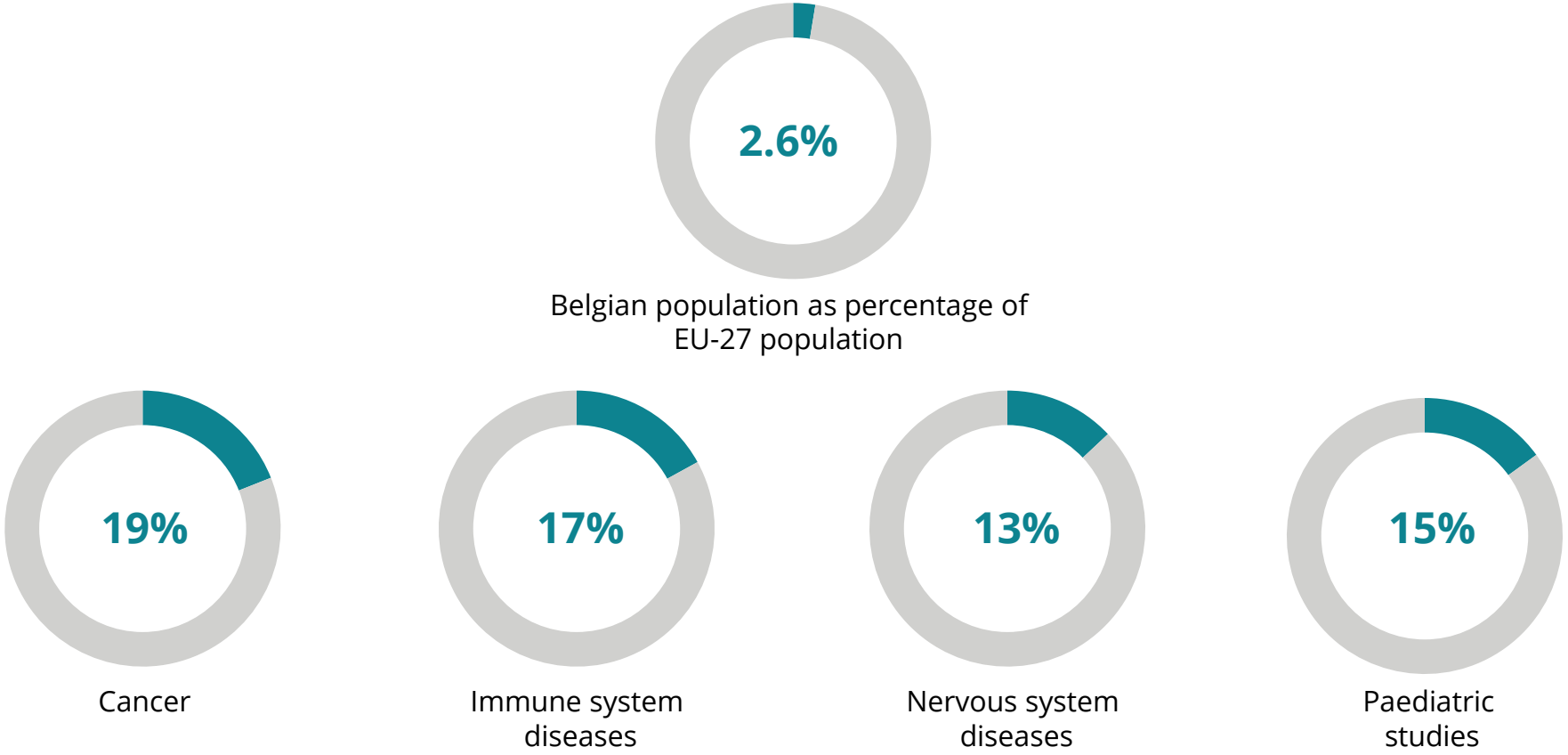
Evolution of CTAs with a paediatric investigation plan in Belgium (2016-2022)[10]



Overall clinical trials footprint of Belgium at European level

Belgium holds a strong clinical trials footprint at European level with a relatively high percentage of clinical trials in Europe conducted in Belgium

Proportion of European clinical trials conducted in Belgium for selected type of studies compared to the proportion of the Belgian population in Europe (2022)[10]



Overall clinical trials footprint of Belgium at European level

Strong regulatory, scientific expertise and quality of trials centres remain key drivers for the attractiveness of Belgium; start-up timelines and the adoption of new technologies remain attention points

Average rate of Belgium on the following drivers for clinical trial location selection (2017 versus 2022)[11]

Rating scale of 0-10 with 10 being “extremely good”

Enhancing diversity, equity, and inclusion in clinical trials

Understanding Diversity, Equity, and Inclusion in clinical trials

Diversity, equity, and inclusion encourages the representation of diverse populations e.g., varying gender identities, races, ethnicities, religions, socio-economic backgrounds, cultures, and sexual orientations[12,13]

What is diversity, equity, and inclusion in clinical trials?

Diversity, equity, and inclusion in clinical trials refer to efforts and principles aimed at ensuring that the participants in clinical research represent a broad range of demographics, including factors such as race, ethnicity, gender, age, socio-economic status, and other relevant characteristics.

The goal is to promote fair and equal access to and representation in trials, thereby improving the generalizability and applicability of research findings to the population most applicable for using the product in real life setting.

DIVERSITY

... refers to the traits and characteristics of all people

E.g. adequate representation of ethnic groups, gender, ...

EQUITY

... refers to equitable policies striving to ensure that all individuals have equal access to the same opportunities, regardless of background or identity

E.g. fair access to clinical trial information

INCLUSION

... refers to the behaviors and practices that ensure those individuals and groups are valued, permitting diversity to flourish

E.g. inclusive enrollment strategies

Balancing between standardization and real-world relevance[13]

When deciding who can participate in a trial, researchers face a choice: should a group of people be selected that is very similar to each other to reduce bias, or should a more diverse group be chosen that represents the real-world patients who might use the treatment?

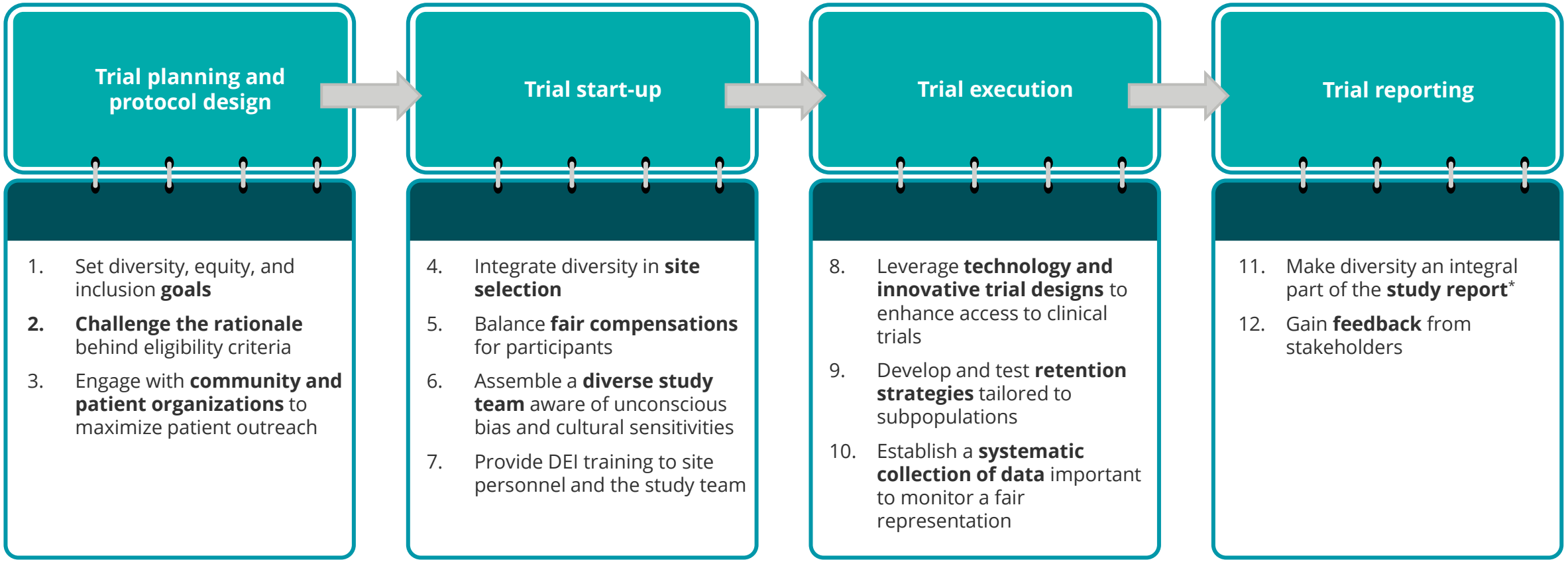
If the focus is on similarity, control for factors that might temper the study results can be achieved. On the other hand, this could mean missing out on important insights about how the treatment might help or harm a broader group of patients who are likely to use it if it is approved.

It always requires a balancing act between precision and real-world relevance.

A multifactorial approach throughout the clinical trial life cycle

Highlighting diversity, equity, and inclusion in clinical trials presents an opportunity for diverse stakeholders to collaboratively work on various steps across the entire clinical trial lifecycle

Clinical trial life cycle and opportunities for accelerating diversity, equity, and inclusion[12,14]



* As part of today's good clinical research practice, a demographic breakdown of the study population is included in the study report

1. Set diversity, equity, and inclusion goals

Establish clear recruitment goals that are aligned with post-approval product users allows monitoring diversity during the trial

Aiming to recruit a study population that maximally reflects the population likely to use the product after approval, setting diversity targets upfront will facilitate the monitoring during the study and will help to take actions accordingly. This is also suggested in the FDA's guidance (see use case on the right) and will support sponsors, researchers, and regulators in monitoring and attracting the right people for the right study.

Unlike the mandatory demographic breakdown to be reported in the study, an in-depth knowledge of the targeted population is a prerequisite when designing the study protocol. This understanding will have an impact on multiple elements, including eligibility criteria, site selection, and participant outreach.

FDA's Race and Ethnicity Diversity plan to ensure equitable participation in clinical trials[15]

With the Diverse and Equitable Participation in Clinical Trials (DEPICT) Act having been signed into U.S. law as part of the 2023 omnibus spending bill, clinical trials under American jurisdiction must now comply with the FDA diversity plan to achieve racial and ethnic inclusiveness in trials.

The FDA published a guideline with recommendations focusing on race and ethnicity on how to compile a diversity plan. Elements discussed in the guideline are:

- Overview of the disease/condition
- Scope of medical product development program
- Goals of enrolment of underrepresented racial and ethnic participants
- Specific plan of action to enrol and retain diverse participants
- Status of meeting the enrolment goals

2. Challenge the rationale behind eligibility criteria

Challenge the rationale behind eligibility criteria to broaden recruitment potential and align study participants with real-world population and trends

Tendency to control study population in clinical trials

Generally, eligibility criteria are formulated based on information that is available regarding the indication (e.g. prevalence and incidence) and need to accurately represent the population likely to be treated with the product.

In practice, researchers often encounter the natural inclination to select a narrow group of subjects who are very similar to each other, aiming to control confounding factors that could potentially affect the study results. However, this approach may lead to a mismatch between the study population and the real-world population that could benefit from the treatment[16].

Challenging the rationale behind eligibility criteria for improving access to clinical trials

One approach for aligning the study population and the real-world population is challenging the eligibility criteria so that more diverse people can be engaged for participating in clinical trials.

For example, does the age limit of healthy volunteers need to equal less than 65 years old? Or could it be defined based on different criteria? It is observed that expanding the eligibility criterion age for healthy volunteers beyond 65 years has a positive effect in recruiting more women in phase 1 clinical trials[17]. This decision reflects the commitment to inclusivity, aligning with the demographic trend of an aging population in society.

3. Engage with community and patient organizations

Active community engagement will help to build trust, foster awareness and improve knowledge by the broader public

Active community engagement is essential to maximize participant outreach and improve the likelihood of recruiting a diverse study population.

The degree of community engagement can range from a fully collaborative model like community-based participatory trials to less engaged approaches that involve community input for specific study needs, such as participant recruitment[18].

Build trust

Lack of trust in clinical trials and the healthcare system in general is recognized as one of the major barriers for trial participation. Multiple factors can contribute to patient distrust including cultural values and communication barriers, the documented historical discrimination in trials, the fear of improper data use and the complexity of the healthcare system[19].

Offering transparent communication and partnering with public organizations such as patient advocacy groups or community organizations can contribute to the establishment of a trustworthy relationship between trials staff and the broader public[20, 21].

Foster awareness of clinical trials and improve knowledge

A study by the National Institutes of Health (NIH) indicated that 85% of patients were either unaware or unsure that participation in clinical trial was an option at the time of diagnosis[22]. This is often linked to the knowledge level of clinical trials, defined as the understanding of the purpose of certain trials.

Various initiatives can improve awareness and knowledge about clinical trials in Belgium including community-embedded media campaigns (e.g. flyers, videos, or study websites).

The launch of the Belgian Clinical Trial Portal[23]

The Belgian Clinical Trial Portal is a database that facilitates easy access to information about clinical trials and is the result of a collaborative effort involving patients, patient organizations, physicians, and the industry.

4. Integrate diversity in site selection

Selecting sites near the target population reduces practical obstacles for participants, providing better access to trials and innovative treatments

Choosing trial sites near the target population can simplify the recruitment of underrepresented groups. This approach not only reduces practical obstacles for participants, such as travel time and mobility challenges, but also enhances equal access to innovative treatment options.

The feasibility assessment and site selection process for a study involve evaluating various factors (see figure), such as investigator expertise, approval processes, ease of patient recruitment, and data quality[24,25]. To enhance inclusivity, it is crucial to actively incorporate diversity considerations into the site selection criteria during the feasibility assessment.

Environment driven	Investigator driven	Hospital/unit driven	Costs
• Size of market/eligible patients in region • Speed of Ministry of Health/Ethics approvals • Government financial/tax incentives • Cost of running trials in relevant market • Disease management system/networks • Country on Institution's 'core country list'	• Investigator interest • Previous experience in similar studies • Concurrent trial workload • Recruitment and retention track record in prior trials • Publication track record	• Site personnel study experience and training • Site personnel language capabilities • Facilities required by trial (labs, imaging) • Hospital quality assurance process • Hospital institutional approval system/contracts • Respondent's previous experience with hospital	• Costs of running a trial in the relevant market for phase II • Costs of running a trial in the relevant market for phase III

5. Balance compensation for participants

Lowering the financial burden in participating in clinical trials by providing financial compensation for taking part in the study can contribute to diversity, equity, and inclusion in clinical trials

Balance between covering costs and financial gain

Compensating participants for taking part in the clinical trial can help alleviate the financial burden that often leads patients to decline involvement in clinical trials[26,27]. The overarching goal of compensation is to look for a delicate balance: ensuring that the reimbursement is sufficient to cover associated costs without creating a situation where individuals are motivated solely by financial gain.

This compensation can take different forms, such as monetary payments or vouchers, as long as it is easy to use for all patients. Reimbursement of expenses needs to go beyond solely covering expenses related to travel and food. A list of possible compensations is provided in the table.

Clear guidelines delineating which costs are eligible for reimbursement and which are not, published by ethics committees, can further support investigators in their decision-making process.

Potential reimbursement expenses incurred by research participants and caregivers[14]

Transportation	Examples
Transportation	• Car, train, bus, bike for traveling • Care mileage • Parking
Accommodation	• Hotel • AirBnB
Food	• Breakfast, lunch, dinner, snacks • Supplemental food
Other out-of-pocket expenses	• Childcare expenses • Eldercare expenses • Ancillary medical expenses incurred because of research participation (e.g. needles or over-the-counter-medication) • Medical supplies (e.g. disability supports) • Reimbursements for caregivers or family

6. Assemble a diverse study team

Assembling a diverse study team and providing them with strategies to acknowledge and address false judgements regarding minorities will maximize the recruitment of a diverse group of participants

Diversity in study teams positively impact diversity in clinical trials

A clinical research workforce that is diverse itself excels in prioritizing, connecting and successfully recruiting participants from diverse backgrounds [28,14].

While multiple factors will play a role, it is believed that providers sharing the same background as participants can better understand cultural considerations and beliefs and thereby facilitating a more trustworthy relationship.

7. Provide diversity, equity, and inclusion training to workforce

Diversity, equity, and inclusion training for healthcare workers reduces implicit bias that may shape participants enrolment

Study teams and healthcare workers participating in diversity, equity, and inclusion trainings will heighten their awareness of unconscious (or implicit) biases that detrimentally impact minorities[22].

Unconscious bias, also known as implicit bias, is commonly described as the presence of preconceived notions or unsupported judgments that favour or disfavour one thing, individual, or group over another, typically perceived as unjust[29].

Healthcare workers exhibit implicit bias when they mistakenly assess patients, making judgments rooted in race, ethnicity, gender, or other characteristics. This leads them to deem patients unsuitable for clinical trials or perceive potential heightened risks associated with including them in such trials.

Gaining awareness of the implicit bias among healthcare workers and acquiring strategies to address this false judgment will maximize the chances of minorities in the recruitment process and thereby enhancing diversity, equity, and inclusion in clinical trials.

8. Leverage technology and innovative trial designs

Digital transformation in healthcare can support diversity of clinical trial participants by facilitating remote and hybrid trial execution and streamlining data collection

Decentralized clinical trials can act as an enabler for diversity

Decentralized clinical trials can revolutionize trial inclusivity by leveraging digital technologies (e.g. remote consent, electronic surveys, and remote patient monitoring) to eliminate transportation barriers for potential minority participants[30]. A systematic review underscores that virtually recruited samples exhibit greater geographic diversity and faster recruitment than traditional methods[31].

While decentralized trials promise enhanced diversity, careful consideration of ethical concerns is required[32]:

- Physical safety confronts challenges due to reduced interaction with study personnel.
- Privacy and data protection concerns need to be addressed as digital tools capture and store all data.
- The risk of self-selection bias looms as decentralised trials demand a certain digital literacy level, potentially favouring more tech-savvy yet eligible participants.

To facilitate technology adoption, an innovative mindset and allowing flexibility in implementing technologies is recommended.

One example that can ease the adoption of decentralized clinical trials is enabling the direct shipping of investigational medicine products to trial participants from their associated sites—a practice allowed in the Netherlands but prohibited by law in Belgium[33].

Creating a memorandum of understanding together with the different stakeholders providing recommendations on how to further enhance the uptake of decentralized clinical trials can positively impact the diversity, equity, and inclusion in clinical studies.

9. Establish a systematic collection of data

Linking of data enriches datasets, providing valuable insights into the influence of diversity on clinical trials

The need for standardization of DEI data metrics

Collecting data metrics in a standardized format is critical to enable statistical validity, data linkage, and interoperability. However, collecting data on variables such as age, race, ethnicity, sex, gender, and socio-economic status is culturally sensitive and constantly evolving.

Over time, the Clinical Data Interchange Standard Consortium (CDISC) has made substantial efforts to establish standard data collection for clinical trials[34]. Nevertheless, no standards have been created yet for gender or socio-economic status. Future work is necessary to standardize these endpoints in order to evaluate the influence of these factors on health and treatment.

Balance between collecting data and meet GDPR-conditions

To track diversity among participants in clinical trials, it is crucial to gather specific data metrics during studies.

The overarching principle guiding data collection is that it must be pertinent to the study and comply with GDPR conditions. As a result, ethics committees consistently request justification for the selection of particular data metrics. Further details on navigating the regulatory balance between GDPR and clinical trials are found on page 35.

Create sustained linkage between data sources

Enriched datasets have the potential to further direct research and public health. Linking several datasets is a prerequisite for leveraging the added value of collecting a plethora of data. In the context of clinical trials, linking available data (e.g. demographics and socio-economic data) together with study data can provide insights for researchers and other stakeholders to evaluate the effects of diversity on clinical trials and research in general. For example, it will enhance the ability to conduct real-world evidence studies to evaluate the long-term effects of a product in a specific environment (mainly during post-surveillance studies).

10. Develop and test different retention strategies for subpopulations

Proactively retaining participants throughout the entire study life cycle and fostering trust through transparency are crucial for the successful completion, credibility, and cost-effective trial execution

Addressing diverse needs across varied study populations

Keeping participants engaged and committed to the study protocol is crucial for successfully completing the research and ensuring the credibility of the results. It plays a pivotal role in the timely and cost-effective execution of the trial. The retention of patients holds significant importance as a high rate of participant attrition can negatively impact the project schedule and its overall quality, potentially leading to a temporary pause in the entire process.

To mitigate these challenges, it is essential to make every effort to retain participants throughout the entire study life cycle, minimizing any inconvenience or burden they may face. Understanding and addressing the specific needs of participant groups are key components in achieving successful retention.

Reported challenges to access in clinical trials[14]

Challenges	Reported examples by stakeholders
Interpersonal	• Lack of awareness of clinical trials • Health literacy and knowledge • Language issues • Cultural beliefs associated with participation in clinical trials • Digital literacy (and the ability to use technology)
Operational	• Travel expenses and mobility capacity, availability of childcare, time off from work • Complex trial protocols that are difficult for participants to adhere to • Inconvenient trial schedules or inflexible appointment times • Rigid eligibility criteria that may disqualify a significant portion of the population • Access and use of any technology

11. Make diversity an integral part of the study

Promote inclusive reporting by avoiding microaggressions while writing and by making use of subgroup analysis to generate further personalized evidence in clinical trials

Avoid microaggressions in reporting results and communication with trial participants

Microaggressions are often defined as brief, every day, intentional or unintentional verbal and non-verbal behavioural expressions that communicate hostile, derogatory or negative racial slights and insults to the targeted person or group43. Examples of microaggressions in healthcare are displayed on the right[35].

In the context of clinical trial reporting, microaggressions may appear in the language used to describe individuals or groups, assumptions made about their abilities or characteristics or in the description of certain results. It's essential to be aware of these forms of bias and try to avoid any language or content that may containing any form of stereotypes.

Make use of subgroup analysis[14]

Once the diversity hypothesis is defined in a study, further analysis of different subpopulations can aid in understanding the risk-benefit profile of a specific product within a particular population or environment. This strategy aligns with the trend of precision medicine, aiming to gather personalized insights for diverse and meaningful subgroups.

An outstanding question is how to establish criteria for determining when meaningful differences between subgroups exist, thereby reducing the subjectivity of conclusions drawn from the data. A guideline providing recommendations on specific decision criteria for subgroup analysis can contribute to objectively assessing certain parameters for future use in subgroup analysis.

Examples of microaggressions in healthcare[36]

Microassault
A program director repeatedly mispronounces an Asian resident's name despite being informed of the correct pronunciation by other faculty and staff

Microinsult
A black psychiatry resident is confused for a care companion by a nurse

Environmental microaggression
Posters show solely heterosexual couples in the office waiting room

12. Gain feedback from stakeholders on training and recruitment initiatives

Actively collecting lessons learned and tracking initiatives that have the most impact can help further shape strategies for fostering DEI in clinical trials[14]

Gaining feedback from stakeholders is paramount in the ongoing effort to accelerate diversity in clinical trials. Stakeholders, including patients, healthcare professionals, advocacy groups, regulatory bodies, and sponsors provide unique perspectives that are essential for evaluating the effectiveness and inclusivity of initiatives implemented.

By actively seeking and incorporating feedback, researchers and organizations can identify potential barriers, address unmet needs, and refine strategies to enhance diversity and representation in clinical trials. This iterative process not only ensures that the initiatives align with the diverse needs of the population but also builds trust and engagement within communities.

The insights gathered from stakeholders contribute to the continuous improvement of protocols, recruitment strategies, retention strategies, and communication approaches. It facilitates a more equitable and inclusive landscape in clinical research. Ultimately, incorporating stakeholder feedback serves as a critical step towards achieving more meaningful, representative, and impactful clinical trials.

Regulation as enabler in enhancing diversity, equity, and inclusion

Guidance and regulations on privacy, compensation of participants, and the adoption of innovative trial design may help the ecosystem in delivering qualitative and safe clinical trials at a competitive pace

GDPR and privacy

Collecting data regarding age, race, ethnicity and other characteristics must be aligned with GDPR-regulation and clearly motivated during clinical trial applications.

Compensation for participants

Compensations can reduce financial barrier for participants. However, balance between compensating participants without financial gain is necessary.

Adoption of DCT design

The adoption of Decentralized Clinical Trials (DCTs) can lower practical barriers identified by stakeholders. However, ethical considerations as outlined on page 33 must be reflected on when designing clinical trials.

Opportunity for the whole ecosystem

To further deliver qualitative and safe clinical trials at a competitive and attractive speed, there is a need for **clear guidance and consistency in regulations** made by consulting all the different stakeholders involved

Appendix

Methodology

Data collection

Quantitative data used to assess Belgium as a clinical trial location in Europe was obtained from following data sources:

- Federal Agency for Medicines and Health Products (clinical trial authorisations)
- Eurostat (demographic statistics)
- pharma.be member survey

Regarding the need and call to action for more diversity, equity, and inclusion in clinical trials, information was gathered from different stakeholders: industry sponsors, FAMHP, and ethics committees. This was done through semi-structured interviews as well as written communication and served as input to substantiate and nuance the observations described in the report. In turn, this allowed to explore concrete pathways to enhance diversity, equity, and inclusion in clinical trials.

Information verification

As it is crucial to ensure that observations and recommendation put forth in this report are accurate and correctly depict the situation in Belgium, PubMed database and grey literature were consulted to complement the information communicated in interviews.

Assumptions

A clinical trial is considered authorized if approved by the National Competent Authority. For the information on the phase and the non-commercial status of clinical trials in Belgium, available data in the FAMHP's internal database is used. The correctness of all figures depends on the quality of the data provided by the sponsors and the actions of all Competent Authorities to keep the European database up-to-date.

Disclaimer

As of 31 January, 2020, the United Kingdom no longer provides data to the European database. Consequently, the UK is excluded from the EU cohort. The number of CTAs assessed per month in 2021 and 2022, which is publicly available on the MHRA website, was utilized as a key indicator for CTA characteristics in the UK in this report.

As of 31 January, 2022, the EU Clinical Trials Regulation 536/2014 has replaced the EU Clinical Trials Directive 2001/20/EC. During the ongoing transition from the Clinical Trials Directive to the EU Clinical Trials Regulation, there may be some inconsistencies in the reporting of Clinical Trial Applications that have inadvertently occurred in the reported data.

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