

Annual Report 2021

Trial Nation
Clinical Trials Denmark

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Executive Summary

The Danish Life science-strategy was presented in May 2021. It is an ambitious plan to develop and accelerate the relevance and positive impact of the life science-sector on Danish health, science, and wealth. Both Trial Nation as an organisation and clinical trials as a discipline was emphasised as pivotal to reach the goals of the Strategy.

The acute crisis management of the corona virus, that characterised 2020 evolved into crisis co-existence in 2021. The Danish healthcare system was challenged by this continued strain. Nurses, primarily, was at times sharing too much work between too few hands. The Danish clinical research departments maintained an impressive momentum, both initiating and attracting clinical trials while allocating resources to COVID-19 response capacities.

Feasibilities:

An ever-increasing number of feasibilities come in an electronic format that makes it difficult to share feasibilities and to have them registered correctly. The actual numbers are therefore likely to be substantially higher than reported.

During the year Trial Nation has worked on establishing a national overview of clinical trials to provide a more equal access for the individual patient to find trials which may be suitable for them. This is part of the overall digitalization and decentralization agenda in clinical trials as well as in the healthcare system which Trial Nation supports in different ways, such as being a project partner in the Virtual Clinical Trials project and active participation in the Decentralized Clinical Trials dialogue forum which has provided input to the Danish regulatory guideline on decentralized clinical trials. Trial Nation has also collaborated with national and international partners communicating on decentralized clinical trials and shared knowledge and experiences from the Danish context.

Trial Nation has in 2021 financially supported a project with the aim to describe the way to successful development and implementation of medical devices using artificial intelligence. The workshops have attracted a lot attention and participation has been subscribed in full. The project will be finalised with a half day conference in 2022. The medical device area is undergoing significant changes with regards to requirements for clinical documentation, starting with the new regulation on medical devices that come into effect in May 2021. It is expected that the number of clinical trials on medical devices will increase in the years to come. To support this development Trial Nation has ensured that key stakeholders supporting clinical environments in clinical trials on medical devices has received training on the new regulatory requirements.

2021 was the year where Trial Nation had more press coverage and, we believe, was at the heart and minds of more people, than ever. Stronger media presence, both direct news channels and relevant social media, was a strategic priority for 2021.

The large international public private partnership The Health Outcomes Observatory (H2O) provided a very promising opportunity for Denmark in 2021. A consortium of The Danish Medicines Agency, The Danish Health Data Agency and University Hospital Aarhus was selected to assume a pivotal role in the project. This will anchor the project in Denmark, but more importantly it merges the strong commitment of the Danish consortium, the demi century-long

Danish investment in health data and a patient-centered approach to health decisions of the future.

Overall, we are happy that, despite certain painful administrative challenges, 2021 was a great year for clinical trials in Denmark.

We look forward to 2022. You can dive into our focus for 2022 in the section “An Outlook for 2022”.

Activities in 2021

May 2021 brought us the Danish Life science-strategy. An ambitious plan to develop and accelerate the relevance and positive impact of the life science-sector on Danish health, science, and wealth. Both Trial Nation as an organisation and clinical trials as a discipline was emphasised as pivotal to reach the goals of the Strategy.

The two most discussed barriers to clinical trial execution in Denmark in 2021 have been administrative. Delayed ethics and legal processing have been reported by multiple stakeholders, as a severe and current Achilles heel of the ecosystem. From a Trial Nation perspective, a development that allow us to confidently expect a positive development going forward is seen.

The acute crisis management of the corona virus, that characterised 2020 evolved into crisis co-existence in 2021. The Danish healthcare system was challenged by this continued strain. Nurses, primarily, was at times sharing too much work between too few hands. The Danish clinical research departments maintained an impressive momentum, both initiating and attracting clinical trials while allocating resources to COVID-19 response capacities.

We continued a strategic and enterprising approach to communication and visibility. At the time, 2020 was our most visible year. 2021 gave us an increased visibility of more than 50%. From 40 individual mentionings in 2020 to at least 63 in 2021. This includes national and international interest organizations (21), national and international media (13), Danish Authorities and ministries (11), Industry (10), Clinics (4), Other public part, national and international (2) and national and international public private partnerships (2). Additionally, we have published regular LinkedIn posts and monthly newsletters on news from our world and both Trial Nation successes and those of others.

Clinical activities

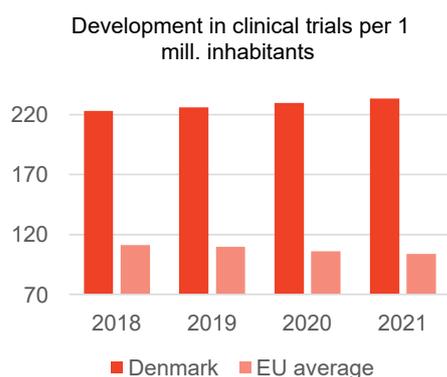


Figure 1: Denmark is #1 in trials per million inhabitants in EU. Not only is the Danish clinical trial ecosystem leading on this parameter. We are increasing the lead. The numbers are based on all ongoing trials in the year. Source: GlobalData January, 2022.

The Danish clinical trial ecosystem is both leading and defying a sad European trend (figure 1), where Europe see a decline in its share of clinical trials globally.

During 2021 Trial Nation worked towards the beginning of a new Trial Nation network, in psychiatry. This network was identified through a thorough analysis and stakeholder engagement and is expected to be formally started in 2022.

In addition to the existing Trial Nation Center and Network structure a third type of structure, called Trial Unions, was introduced in 2021. Trial Unions are made up of visionary clinicians who subscribe to the 'One for all and all for one' design that have proven successful in our centers and networks. Trial Nation will make all our experience in organizing strong research collaborations available to the Trial

Unions and we will include Trial Unions in relevant promotional initiatives, nationally, as well as internationally. Trial Unions do not receive financial funding from Trial Nation.

Our clinical centres have always formed the backbone of our contribution to the advancement of clinical trials in Denmark. They continue being a success, in 2021 perhaps more than ever. We have now witnessed the huge benefits of a structured approach to clinical trials organisation when immediate, coordinated response is required. This is evidenced by the figures for the clinical trials in 2021.

Please note that the aspects of what is important differs between clinical specialties and therapeutic areas. This means that there is a deliberate slight variance on how the visualisation of each area's work, such as unique clinical trials, is represented in the sections below. An overview of the development of each center is shown in Figure 2 below. Details on clinical trials are presented in the sections for each center.

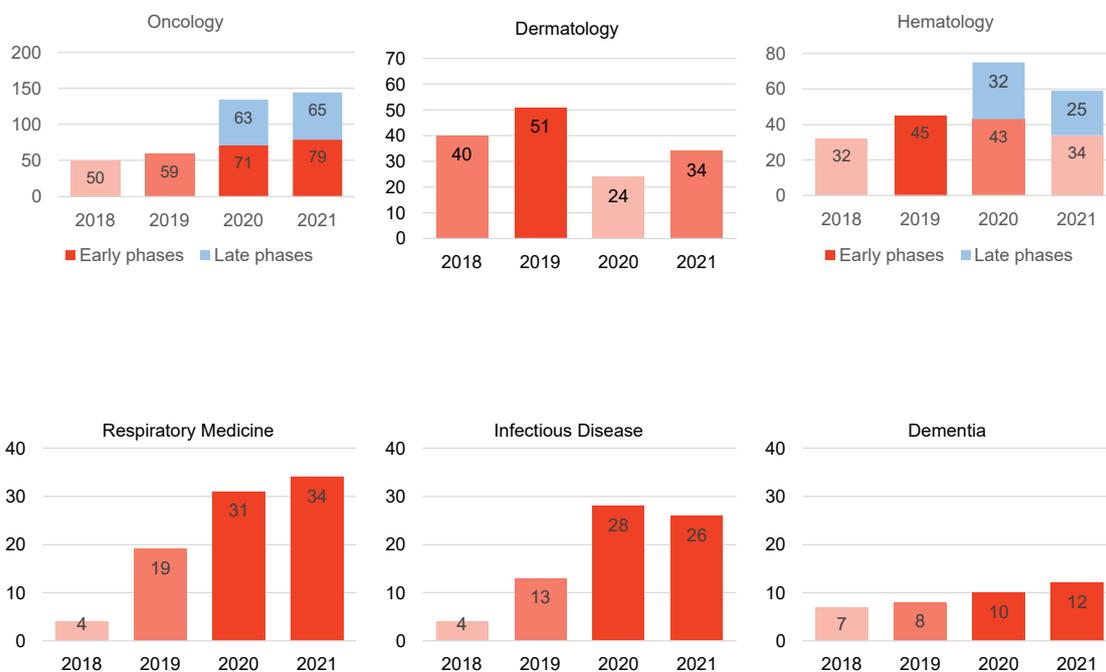


Figure 2. Development of number of ongoing trials in Trial Nation Centers from 2018 to 2021.

All centers experience that the trend of submitting feasibilities through web-questionnaires or web-portals is increasing. This poses a challenge keeping track of submitted information as the link is sent to an individual, and data is entered directly, i.e. there is no record locally of the submitted information.

In the Center of Dementia, we saw an increase in terms of trial activity in 2021, which confirms the positive growth in studies that the area is experiencing. Studies in this area often take place over several years and are often complex.

In the Center of Dermatology, a steady increase in open trials during 2018 and 2019 reached

a steadier state in 2020 and 2021, due to COVID-19. Furthermore, many of the long-running studies contributing to the high figures for 2019 and 2020 were also finalized in 2021. The center is proud of its activity, also for 2021.

In the Center of Hematology, the positive increase of new initiated trials continued in 2021 and with a high percentage in the early phase I+II. An increased numbers of the feasibilities were shared across the sites in the center.

In the Center of Infectious Disease and Immune Modulation, 2021 was again a remarkable year in the name of COVID-19. The center initiated one of the largest conducted trials in Denmark – a phase IV COVID19-vaccine trial. The Innovation Fund Denmark invested in capacity to mitigate the effects of COVID-19.

In the Center of Respiratory Medicine, the bulk of COVID-19 studies were finalized in late 2020. Even so, there was a slight increase in number of studies in 2021, and all sites were very active despite also being part of the Danish Covid-19 emergency response.

In the Center of Oncology, the center continued to increase its activities in 2021. The oncological research field is the most active both in Denmark and globally, measured by number of clinical trials. 51 new initiated trials in 2021 was a tremendous increase of 75% compared to 2020.

Within Pediatric medicine, the DanPedMed organisation have increased activities across its field. Following a more substantial, Trial Nation funded, coordinator role and a positive overall consolidation of the network, we can report an increase in network metrics. Based on a scientific publication, the network saw the pediatric agenda discussed by the Danish parliament.

An important point is that even though Trial Nation has a certain number of nationally coordinated centers and networks, our work covers all therapy areas in clinical research in Denmark. Clinical trial feasibilities for areas not covered by the national center structures are facilitated by the regional coordinators within pharma and MedTech. During 2021, 55 feasibility request-swere handled with an average response time of 2 working days, which is an increase of nine more feasibility requests compared to 2020.

Trial Nation is one of the project partners in the Decentralised Clinical Trials project. Decentralised clinical trials are very high on the clinical trials agenda, and the first fully decentralised trial in Denmark is live. To support the development of this field, the Danish regulatory authorities (DKMA) and Trial Nation collaborated in establishing a dialogue forum for digitalisation and decentralisation of clinical trials. Throughout the year, Trial Nation gathered structured information on identification of incentives, experiences, and barriers from patient associations, investigators, authorities, and big pharma.

MedTech had a good 2021, where clinical metrics and strategic activities increased. The impact of the new medical device regulation has not yet translated to an increase of the number of clinical trials. In 2021 9 feasibilities were performed. The center followed the work of the consortium chosen to carry out the AI-call. The aim of the call is to pave the way for future MedTech trials with AI components. This network orientated activity chose to tailor its activities to ensure the possibilities of meeting in person and results will therefore be published and disseminated with completion in early 2022.

External activities

Trial Nation is the first Danish associated partner to a EUR 18M, 5-year project within the IMI research initiative, the world's largest public-private research partnership in terms of budget. The project IMI H2O aims to create health outcomes observatories that will amplify the patient voice in individual healthcare as well as in the overarching healthcare systems. Trial Nation provides key insights regarding clinical trials obtained as a central intermediary. We continuously work to keep clinical trials high on the project agenda.

Our international public private partnership IMI-H2O delivered a very promising opportunity for Denmark in 2021.

The Health Outcomes Observatory (H2O) project will set up and operate national entities – “observatories” – in order to equip patients with digital tools that will allow them to monitor and document their outcomes in a standardised manner. To achieve this, the first national observatories will set up an umbrella observatory (the pan-European Observatory) whose main role will be to ensure this consistency in the overall approach.

A Danish consortium of The Danish Medicines Agency, The Danish Health Data Agency and University Hospital Aarhus won the public call for proposals. This will anchor the project in Denmark, but more importantly it merges the strong commitment of the Danish consortium, the demi century-long Danish investment in health data and a patient-centered approach to health decisions of the future.

Throughout the year, Trial Nation has initiated and participated in many activities with the purpose of increasing the number of clinical trials in Denmark both through activities strengthening the framework of clinical trials and to increase the visibility on clinical trial capabilities in Denmark. This has been done stand-alone and in collaboration with stakeholders such as Invest in Denmark (iIDK), Healthcare Denmark (HCD), member companies and other actors relevant to the eco-system around clinical trials. Key events include the following:

The Trial Nation Perspective

1. Panel discussion at “Nordic Life Science Strategies & Initiatives”. March
2. Key-note speech at Health Cluster Portugal's annual meeting. April
3. Presentation of Trial Nation to representatives from Danish hospital pharmacies. September.
4. “Trial Nation – A Part of the Danish Clinical Research Ecosystem” at Park Annual Life Science meeting. October
5. “Innovation through clinical research and private/public partnerships” at Medicon Valley Alliance Yearly Meeting. November
6. Presenting “Integrated partnerships to foster novel clinical trials” at Danish National Biobank symposium “Innovative approaches in large-scale research infrastructures. November
7. Presenting Trial Nation at Synapse event in Aalborg. November

Clinical and National promotion

1. Webinar ‘How to conduct clinical trials in EU after Brexit’ targeted towards Japanese companies together with the Foreign Ministry and LINK-J. May
2. Virtual Round Table meeting in Center of Hematology in collaboration with Invest in Denmark arranged for US companies. May

3. Webinar on Personalized Medicine in collaboration with the Foreign Ministry and Lif. May
4. China – Denmark seminar on “The innovation forum of Danish clinical research co-operation seminar”, in collaboration with the Foreign Ministry and Healthcare Denmark. September
5. Taiwan-Denmark Seminar on Co-development of New Drugs in collaboration with the Foreign Ministry. September
6. Delegation visit from Texas Medical Center in collaboration with the Foreign Ministry. September
7. DCT session at KONECT conference, South Korea. October

Knowledge liaison

1. Sessions on implementation Trial Management digital portals. January
2. Facilitation of two discussion meetings between Videnskabetiske Medicinske Komitéer and Trial Nation company members and CRO-network on informed consent in relation to DCT. September
3. Clinical Winter school. A symposium that introduces ambitious health students to key principles of clinical trials, presented by Danish thought leaders in their fields. The first of hopefully many. Realised in collaboration with Synapse student organization and Novartis. November.
4. Eight per year - Trial Nation themed industry member meeting. Updates from Board meetings and discussions on trends and barriers. Relevant guest speakers. Cross-member networking.
5. Three per year - Trial Nation themed CRO network meeting. Update on trends and barriers. Relevant guest speakers. Cross-member networking.
6. Four webinars for knowledge sharing on DCT during 2021, hosted by ICDK Silicon Valley

Training

1. Two- day training for project personnel on “Collaboration in Clinical Trials with commercial Sponsors” gathering 35+ participants. September
2. Training in new regulation on medical devices. October

Public debate

1. Altinget Summer Meeting debate. Advance the important agenda of Patient Reported Outcomes. Panelists: Marianne Nord Hansen, Chair, Late cancer effects; Lisbeth Nielsen, Director general, DHDA; Jørgen Schøler, Medical Director, AUH and HTA board co-chair; Jesper Kjær, Director of Data Analytics Centre, DHMA; Helle Pappot, Dr. Med, Prof. in Patient involvement. June
2. Panel debate at “The Future of Swedish and Danish Life Science”. September
3. Life science debate on “Concrete solutions to increase clinical research in Denmark” in collaboration with Merck, LIF, Aarhus University, Medicon Valley Alliance and Dansk Erhverv in October

Conference appearance

1. DCT session at the conference “INSIGHTS events Kliniske forsøg 2021”, Denmark in September.

Infrastructure activities

Trial Nation also has initiated two strategically very important projects.

The first is the project “National Overview of Clinical Trials”, a platform providing every Dane with the possibility of finding up-to-date relevant clinical trials in an easy way.

The second is a digital recruitment platform with the purpose of making it easier for individuals to be matched to relevant trials. The National Overview of Clinical Trials is funded partly via the Innovation Fund project NEXT-2, which ended 31st of December 2021, and partly by the government through the restart agreement for Life Science. The Digital Recruitment Platform has received funding from the Restart agreement for Life Science.

Furthermore, the Life Science strategy adopted by May 2021 supports the development of these platforms.

An outlook for 2022

Below is an overview of Trial Nation’s focus for 2022:

- Contribute to the implementation of the life science strategy
- Revisit Trial Nation strategy based on developments since 2019
- Establishment of a new network in psychiatry
- Establishment of Trial Unions in nephrology and neurology
- Implement and scale up the National Overview of Clinical Trials
- Decisions on design of Digital Recruitment Platform
- Build on the work with digitalization of clinical trials
- Continue building competencies to support to clinical trials in medtech
- Scout for opportunities, and establish strategic partnerships as relevant to strengthen Denmark’s position for clinical trials in medtech
- Actively scan for synergies and possibilities for partnership with Danish Life Science Cluster
- In partnerships, support the development of new clinical trials methodology, for instance in patient outcomes, with the purpose of being at the forefront of new approaches in clinical trials.
- Ensure Collaboration with the Foreign ministry and other parties to attract clinical trials to Denmark
- Increase awareness of Trial Nations activities and outcomes across relevant stakeholders nationally
- Launch new website

Center for Dementia

The dementia departments and our general Center presentation can be found online [here](#).

Key metrics and conclusions

2021 was a good year for the Center for Dementia. Six initiated trials in 2021 meant a 50% increase in newly initiated trials. And the total number of open trials increased to 12, thereby continuing the positive trend in the recent two years. The number of feasibilities received fell from ten to eight. All feasibilities received were deemed as very interesting studies for participation by the Center.

Medical Lead

Professor Gunhild Waldemar*

Feasibility coordinator

Clinical trials director Kristian Steen Frederiksen*

Center facilitator

Kirsten Bødker, Trial Nation.

*Danish Dementia Research Center, Rigshospitalet, Copenhagen.

“Overall, there will always be slight fluctuations from year to year, but in general we are seeing a growing interest from pharma companies in terms of interest in conducting trials within dementia in Denmark. It is likely due to a number of factors, but I would like to think that the quality we deliver and the unique network in the Trial Nation Center of Dementia is a part of this”.

Kristian Steen Frederiksen, Clinical trials director

All metrics, except received feasibilities, increased in 2021. A total of 8 clinical trial feasibilities involving one phase I feasibility, three phase II feasibilities, two

phase III feasibilities and one feasibility of undisclosed phase involving two or more of the clinical departments were evaluated and completed in Center of Dementia in 2021, see Figure 3. Most of the feasibilities were shared across participating memory clinics (i.e., sites) in the center – only one was not shared as specifically requested by the Sponsor.

“The COVID-19 pandemic is affecting our activities, but we have nevertheless managed to keep the network of trial-active memory clinics (the sites in Trial Nation Center for Dementia) open, and we have also started new studies in 2021”.

Professor Gunhild Waldemar, Medical Lead.

Center for Dementia	2018	2019	2020	2021
Feasibilities received	6	4	10	8
Initiated trials	2	2	4	6
Open Trials	7	8	10	12

Table 1. Overall activities of feasibilities, initiated and opened trials in Trial Nation Center for Dementia.

Feasibilities

In 2021, 7 of the 8 requested feasibilities covered Alzheimer’s disease and one covered spinocerebellar ataxia. The Center responded positively to all 8 feasibilities, see Figure 3.

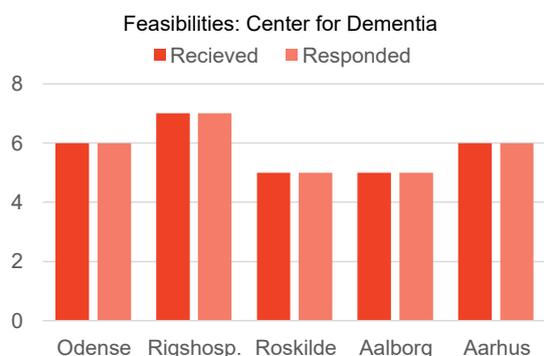


Figure 3. Feasibilities received and answered in 2021 by Trial Nation Center for Dementia reported by affiliated department

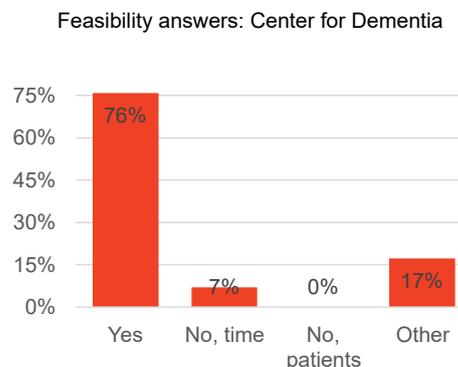


Figure 4. How the feasibilities were answered in 2021 by Trial Nation Center for Dementia reported by affiliated department

Clinical Trials

In 2021, the Center for Dementia initiated a total of six commercial clinical trials – an increase of 50% compared to 2020. Overall, 12 clinical trials were ongoing in 2021, see Figure 5, as six trials were initiated before 2021 and were still open in 2021. This constitutes an increase in open trials. Please refer to the distribution across trial phases in Figure 6 below.

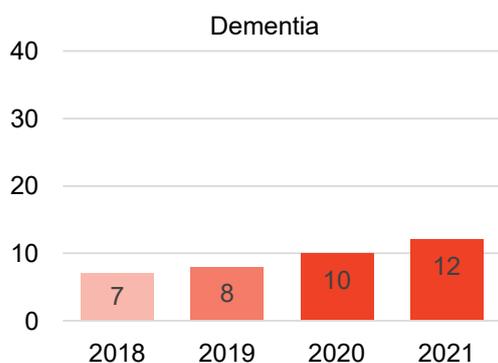


Figure 5. Number of open clinical trials at the Trial Nation Center for Dementia since 2018.

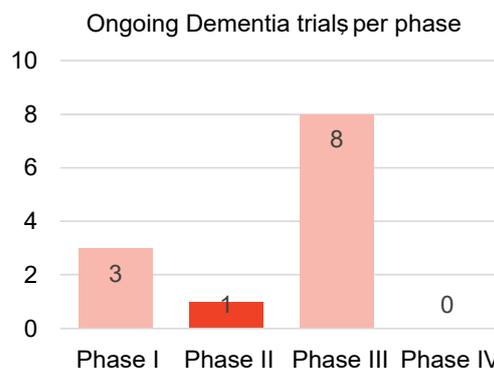


Figure 6. Number of open clinical trials at the Trial Nation Center for Dementia in 2021 distributed into phases.

Studies on patients suffering from Alzheimer’s and Huntington’s disease in general are very complex with regards to both in- and exclusion criteria (specific biomarkers and cognitive scales) and operational aspects, as the number of visits, tests and interventions is high often during a long period of time.

Alzheimer's disease and Huntington's disease are two diseases with severe unmet medical need, and no disease-modifying therapy is at present available.

"Going forward, it is important to ensure that investment is made in a more solid foundation for our memory clinics, so that they can always offer an appropriate treatment trial for our patients, for whom there are currently only a few other options."

Professor Gunhild Waldemar, Medical Lead

Recruitment

The Center for Dementia has been able to maintain operations through the COVID-19 pandemic. All sites were able to remain open during the pandemic, even for a very fragile patient population.

Some of the sites have been challenged in 2021 in terms of capacity due to a national strike affecting nurses, lack of project staff, neurologists, and other specialists. Nevertheless, it is expected that the sites will be able to run at full capacity again in 2022. The disease area is generally challenged by the lack of specialists, which results in long waiting times for diagnosis, and which also influences the capacity to run clinical trials.

Center activities

The center distribution and documentation of feasibilities and activities in 2021 has to some degree been affected by the COVID-19 pandemic. The following activities were conducted in Center for Dementia in 2021:

1. The Annual meeting in Trial Nation Center for Dementia took place in March in Odense with the steering committee and research personell from all sites in Denmark
2. Virtual steering committee meetings took place in March, October, and December.
3. Furthermore, activities related to feasibilities, company meetings, grant administration and other organizational matters took place on an ad hoc basis.
4. Regular meetings between study coordinators from all sites has been started to strengthen the collaboration between the sites and to support new research staff. One face-to-face meeting and two virtual meetings took place in 2021.
5. The Trial Nation Center of Dementia leaflet for external use available through the Trial Nation homepage has been updated.

Cost Summary

In 2021, each of the sites in Center for Dementia was supported by a grant of DKK185.400 by Trial Nation to ensure preparedness and infrastructure for clinical trials. In addition to this, Danish Dementia Research Center, Dept. of Neurology at Copenhagen University Hospital, Rigshospitalet was granted DKK50.000 for the role as Medical Lead and DKK175.000 in support of the role as feasibility coordinator for the Center.

The annual report for each individual site for 2020 was approved by the Trial Nation Board December 2021.

Focus in 2022

In 2022, the center will focus on:

1. Continue to attract trials in Alzheimer's disease and Huntington's disease and other indications within the area of dementia by:
 - 1.1. Ensuring efficient feasibility handling with one point-of-contact for sponsors and focusing on close collaboration with the sponsors or CROs to facilitate entry into, and understanding of, the trial environment in Denmark regarding trials within the dementia area.
 - 1.2. Increasing visibility of the competencies in the center towards the industry.
 - 1.3. Arrange one-to-one meetings with selected companies.
2. Continue the improvement of collaboration across the sites and with the Trial Nation secretariat. Building competencies and capacity will still be in focus on both departmental and management level.
3. Ensuring the competencies and capacity in each of the sites to be able conduct the relevant trials.
4. Develop patient databases that can also be used for patient selection for commercial clinical trials. This is a part of the action plan in several departments.
5. Continue the development of collaboration between the study coordinators.

Center for Dermatology

All departments and our general Center presentation can be found online [here](#).

Medical Lead

Professor Simon Francis Thomsen*

Feasibility coordinator

Stine Ørts Pedersen*

Center facilitator

Annette Buusman, Trial Nation.

**Department of Dermato-venerology, Bispebjerg Hospital*

Key metrics and conclusions

2021 was a good year for the Center for Dermatology. 11 initiated trials in 2021 meant a small increase in new, initiated trials (table 2 below), hereby continuing the positive trend in the recent two years. The number of feasibilities received reached 56, counted as the total of feasibilities at all sites; in 65% of the cases, response to the feasibilities was positive. The number of ongoing clinical trials increased with 4% compared to the previous years.

In the words of Professor Simon Francis Thomsen, Medical Lead: "COVID19-studies have had priority with the authorities and Ethics committees. This may

have added to the bulk of delayed approvals within dermatological studies". Please refer to table 2 and figure 7 for details.

There is a high number of feasibilities in the therapeutic area. In 2021 56 feasibilities were received, of which 65% were deemed suitable and possible by the departments. The number of feasibilities in combination with the increased number of open trials, testifies to a solid overall research activity of the Center.

The center for Dermatology continues the important contribution to national and international research in dermatology, allergology and venereology. Four of five Danish regions are currently represented in the Center, and the possibilities of including Region North will be further explored in 2022.

The Center for Dermatology has been substantially involved in and contributed to providing researcher perspectives to the implementation of Decentralized Clinical Trials in Denmark in close collaboration with the DKMA.

The yearly activities are summarized in Table 2 and described in detail below.

Center for Dermatology	2019	2020	2021
Number of feasibilities received	19	22	56*
Number of initiated trials	14	10	11
Number of trials open in year	51	24	34

*Table 2: Overall activities of feasibilities and trials. *Please note that as a consequence of the increased digitalization of feasibilities, the calculation of the number of feasibilities has been adapted and the number of feasibilities received in 2021 is not directly comparable with previous years.*

Feasibilities

A total of 56 feasibilities were handled by the coordinator and the departments in Center for Dermatology in 2021. Please note that as a consequence of the increased digitalization of feasibilities, the calculation of the number of feasibilities has been adapted. This means that a direct comparison to previous years is not possible, i.e., the number for 2021 is not directly comparable to the 22 feasibilities the previous year, as it reflects the fact that all feasibility activity has been registered for each site, as opposed to only the unique feasibilities shared by the coordinator. Most of the feasibilities concerned phase II trials, following the trend of previous years. Feasibilities were answered within 5 days to the Sponsor. 65% of the feasibilities were answered positively. The main reasons for declining participation were lack of time, resources, or patients.

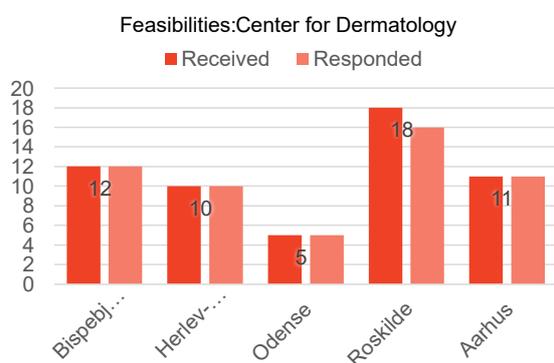


Figure 7. Feasibilities received in 2021 by Trial Nation Center for Dermatology by affiliated departments.

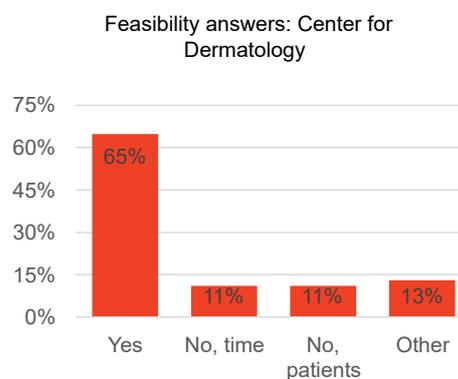


Figure 8. How the feasibilities were answered in 2021 by Trial Nation Center for Dermatology reported by affiliated department

Clinical trials

A total of 34 clinical trials were ongoing in 2021 across the Center departments, compared to 24 studies in 2020 (figure 9). This increase is particularly impressive in light of the setbacks following COVID-19, which impacted patient recruitment as well as organization of staff. Like previous years, apart from participating in clinical trials, resources were also spent strengthening the qualifications of research staff in the Center and improving administrative procedures. The distribution of trials across trial phases was like that of previous years (figure 10).

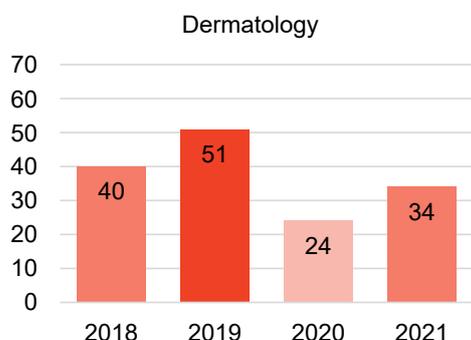


Figure 9. Ongoing and initiated clinical trials in Center for Dermatology in 2020, distributed across trial phases.

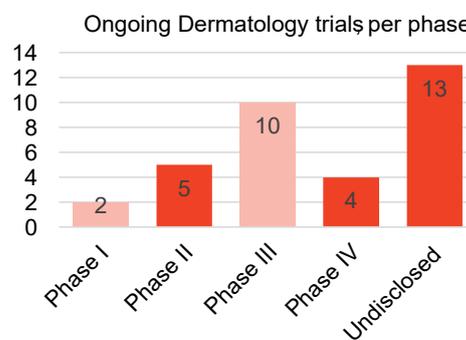


Figure 10. Number of open clinical trials at the Trial Nation Center for Dermatology in 2021 distributed into phases.

Recruitment

In 2021, 102 patients in total were recruited in commercial clinical trials across the five dermatology research sites.

Center activities

Decentralised Clinical Trials (DCT) took center stage in 2021. Trial Nation and Professor Simon Francis Thomsen worked closely with the Danish Medicines Agency (DKMA) to facilitate implementation of DCT in Danish research and provided input both to the current DKMA guideline on DCT and to the Strategic Research Council in Capital Region of Denmark.

In 2016 the development of a national patient recruitment database in dermatology was started and put into use. Since the project was initiated, a lot has happened within both technology and legal requirements. This led to the decision to use the learnings to feed into a more current approach, and a decision was taken in 2021 to retire the database. Starting the project in 2016 showed considerable foresight and has yielded invaluable learnings which are fed into relevant Trial Nation projects, and a manuscript published in a peer reviewed dermatology journal in 2021.

The goals for 2021 concerning collaboration internally as well as with companies and patient organizations were met – patient empowerment has been a focus point and has resulted in increased patient involvement in trial designs and guideline committees. The Center has also been heavily involved in the planning of HudSagens conference at Christiansborg, planned for April 2022.

Feasibility metrics are still challenging to document, as described earlier – this will be a focus point also in 2022.

Cost summary

In 2021, each of the clinical departments in Center for Dermatology was supported by a grant of DKK209.000. In addition to this amount, the department at Bispebjerg Hospital was granted DKK50.000 for the role as Medical Lead, and DKK175.000 in support of the role as coordinator for the center.

Each individual sites' annual report has been approved by the Board of Trial Nation in December 2021.

Focus in 2022

1. Initiate the first Decentralized Clinical Trial within dermatology in Denmark.
2. Establish relevant treatment research databases.
3. Host the Nordic Dermatology Congress in Copenhagen in April 2022.
4. Follow up on feasibilities in each department in a way that allows for deeper understanding and consolidation of the data.
5. Continue the existing collaboration with relevant patient organizations.

Center for Hematology

All departments and our general Center presentation can be found online [here](#).

Key metrics and conclusions

Medical Lead

Professor Niels Abildgaard*

Feasibility coordinator

Sally Grant*

Center facilitator

Ask Aabenhus, Trial Nation

* Dept. Hematology, Odense University Hospital

2021 was a good year for the Center for Hematology. Twenty-five initiated trials in 2021 meant an increase in new, initiated trials, thereby continuing the positive trend in the recent three years. 129 feasibilities in total were received by sites in the Center. As a consequence of the increased digitalization of feasibilities within hematology, the calculation of the number of feasibilities has been adapted. This means that a direct comparison to previous years is not possible. The feasibilities received were of interest for the Center. Many of the feasibilities were shared across the sites in the center.

"As the data indicate it has been as busy year in clinical research, many new feasibilities and new studies to be initiated as a consequence of increasing interest from pharmaceutical companies to do clinical trials in Denmark. The corona pandemic has not affected this, rather contrary, probably because the Danish health care system has been rather robust during the pandemic".

Professor Niels Abildgaard, Medical Lead.

The yearly activities are summarised in Table 3 as described below.

Center for Hematology	2018	2019	2020	2021
Number of feasibilities received	32	63	78	129*
Number of initiated trials (phase I-II/all)	8/ -**	11/ -**	8/14	10/25
Number of trials open in year (phase I-II/all)	32/ -**	45/ -**	43/75	34/59

Table 3: Overall activities of feasibilities and trials.

*The number of feasibilities received in 2021 is not directly comparable with previous years

**In 2018 and 2019 only phase I-II trials were registered.

Feasibilities

The sites in The Center for Hematology received a total of 129 commercial hematologic feasibilities in 2021, documented by each of the hematologic departments forming part of the Center for Hematology. Almost half of them were related to early phase trials. Figure 7 describes feasibilities received at each site in the Center and table 3 above shows the development

over time. Please be aware of a reporting bias as most feasibilities are shared directly with investigators, meaning clinical research sites are not consistently informed of all feasibilities.

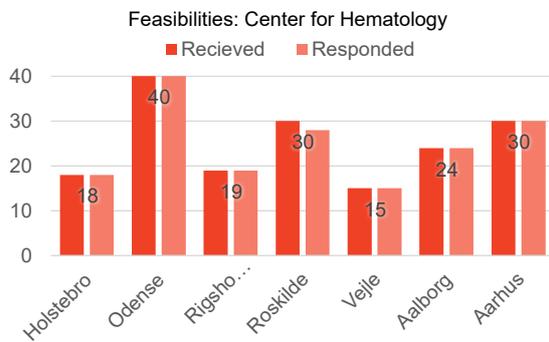


Figure 11. Feasibilities received in 2021 by Trial Nation Center for Hematology by affiliated departments.

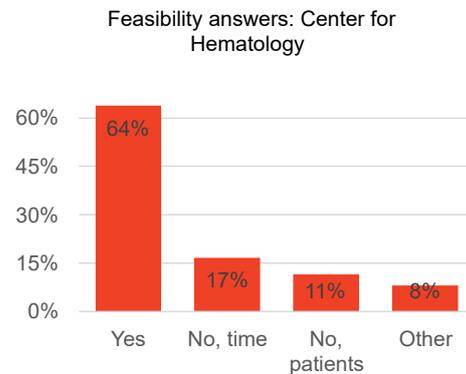


Figure 12. How the feasibilities were answered in 2021 by Trial Nation Center for Hematology as reported by affiliated department

Clinical Trials

In 2021, 59 commercial clinical trials involving one or more of the clinical departments in the center were reported as active. Of these, 34 phase I-II trials were reported as ongoing in 2021 compared to 43 the year before. Six of the ongoing trials were pediatric hematology trials. As in previous years, the numbers are subject to uncertainty and should be seen as minimum estimates.

25 commercial clinical trials were initiated involving one or more of the clinical departments, of which ten trials were phase I-II. This is an increase in the number of documented new, initiated trials from fourteen the year before.

Figures 13 and 14 provide a visual representation of the data.

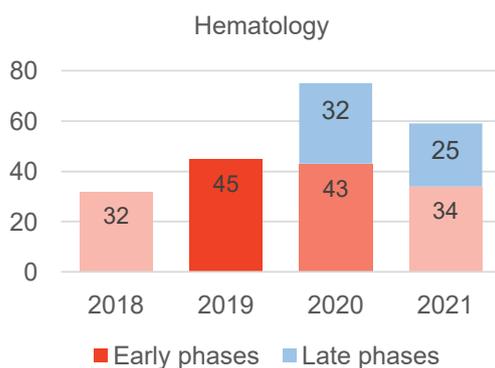


Figure 13. Number of open clinical trials at the Trial Nation Center for Hematology since 2018.

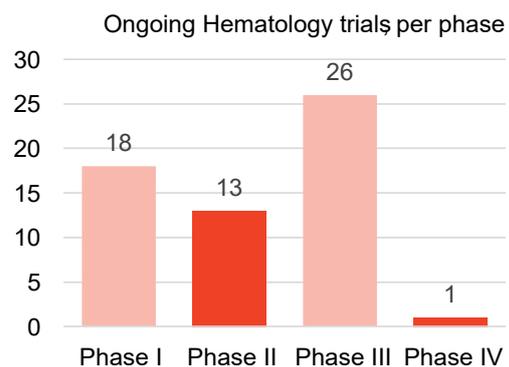


Figure 14. Number of open clinical trials at the Trial Nation Center for Hematology in 2021 distributed into phases.

Recruitment

The Phase I Unit at Rigshospitalet recruited 46 patients in 2021. This is an increase compared to 2020 where 38 patients were recruited. And at Odense University Hospital they initiated two FIH trials.

Center activities

In 2021 the Danish hematology sites managed to remain open all the time during COVID-19. Recruitment was impacted by the pandemic, albeit reporting to Trial Nation indicate that hematologic clinical trials in Denmark have been less impacted compared to many other European countries.

Furthermore, some meetings and conferences were converted to web-meetings, and planned large, physical meetings and conferences were postponed.

"Somehow, COVID-19-canceled international meetings has changed the focus to make things the best possible internally in our clinics and in our clinical research departments".

Professor Niels Abildgaard, Medical Lead

The following joint activities took place in Trial Nation Center for Hematology:

1. National sharing and handling of feasibilities.
2. Consolidation of the number of sites participating in clinical trials that target few patients and rare diagnoses.
3. Referral of patients for clinical trials at other departments in the center.
4. In collaboration with Medical Lead, other research experienced chief physicians and Invest in Denmark a web-based Roundtable meeting took place in May, presenting Denmark, the Center for Hematology and their research competences for affiliate and headquarter representatives from US-based companies.
5. Web-based center meetings.

Cost Summary

In 2021, each department in Center for Hematology was supported by a grant of DKK216.375 by Trial Nation to ensure preparedness and infrastructure for clinical trials. The Department of Pediatrics and Adolescent Medicine at Rigshospitalet received its grant via Trial Nation Center for Oncology. Medical Lead and National Feasibility Coordinator/Center Coordinator which are placed at Odense University Hospital and are compensated accordingly (DKK50.000 and DKK175.000 respectively).

Each individual sites' annual report has been approved by the Trial Nations Board in December 2021.

"I believe that we in 2022 will see increasing activity as we did in 2021; globally, the corona pandemic will still affect the health systems. In Denmark, our situation is quite good in that respect, and we will be an attractive country for performing clinical trials. Also, the establishment of Trial Nation is in process to fulfil its full potential".

Professor Niels Abildgaard, Medical Lead.

Focus in 2022

In 2022, the Center for Hematology will focus on attracting new trials plus improving the national collaboration across departments. This will be accomplished by:

1. Single company marketing activities towards the industry of the competences in the center and at the departments. The activities will be conducted in collaboration with Invest In Denmark and Copenhagen Capacity.
2. Improved sharing and handling of feasibilities.
3. Ensuring support of capacity for clinical trials
4. Support of the development and implementation of a national database on clinical trials, thereby improving referral of patients for clinical trials and providing patients with an opportunity to seek participation in clinical trials.
5. Improving the national collaboration across departments in general and specifically regarding:
 - 5.1. The number of departments participating in specific clinical trials with fewer patients
 - 5.2. Referral of patients for clinical trials at other departments in the Center
 - 5.3. Patient involvement in clinical trials
 - 5.4. Clinical trial deliverables
6. A seminar on patient involvement in clinical trials is to be planned in 2022

Center for Infectious Disease and Immune Modulation

All departments and our general Center presentation can be found online [here](#).

2021 was a very busy year for the Center for Infectious Disease and Immune Modulation - another year in the name of COVID-19.

Key metrics and conclusions

Eleven new trials were initiated in 2021 continuing the high level of activity of 2020, compared to previous years. One, very large, COVID-19 vaccine trial enrolling 7000 participants caused significant expansion of the Clinical Trial Units and a non-precedented level of collaboration across the country. The number of new trials in 2021 was a result of a high number of received feasibilities receiving a positive response in 2020. For 2021, the number of feasibilities received was reduced from 28 to 17. The high numbers of feasibilities received in 2020 reflected the acute COVID-19 situation, and numbers for 2021 may be more representable. This is described in table 4 and figure 15.

Center for Infectious diseases	2017	2018	2019	2020	2021
Number of feasibilities received	13	18	9	28	18
Number of initiated trials	3	2	4	15	11
Number of trials open in year	3	4	13	27	26

Table 4: Overall activities of feasibilities and trials.

Feasibilities

Eighteen feasibilities were evaluated and completed by the sites in Center of Infectious Disease and Immune Modulation in 2021. Nine were for phase I-II studies, eight were phase III-IV studies and one feasibility was of undisclosed phase. 13 trials were commercial trials and five were international trials funded by the EU or NIH. Figure 15, below, shows the feasibilities received and responded to by affiliated department.

“We saw an explosion in new studies and feasibilities in 2020 due to COVID-19. That development naturally flattened out in 2021 as both treatments and vaccines were developed, and we got more hold on covid. We would expect to see a slight decline again in 2022, and a stabilization at a higher level than before the pandemic.”

MD, Nina Breinholt Stærke, Feasibility coordinator

Four of the 18 feasibilities were declined by all sites due to lack of trial population. For seven of the trials the Center was not selected for different reasons such as long approval times in Denmark, the covid-19 vaccination program does not match all cohorts in a trial, or a non-disclosed reason by Sponsor. Currently two feasibilities are pending response. A visual representation is shown in Figure 16.

Medical Lead

Professor Lars Østergaard*

Feasibility coordinator

MD, Nina Breinholt Stærke*

Center facilitator

Kirsten Bødker, Trial Nation.

*Infectious Department, Aarhus University Hospital

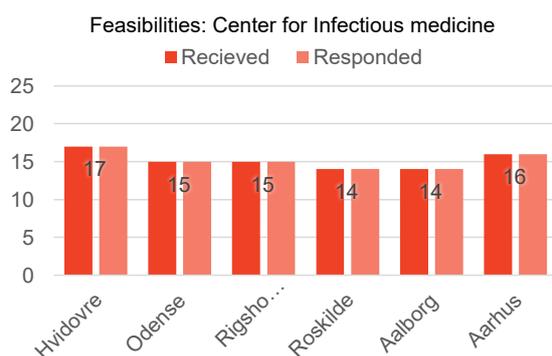


Figure 15. Feasibilities received and answered in 2021 by Trial Nation Center for Infectious Disease and Immune Modulation reported by affiliated department

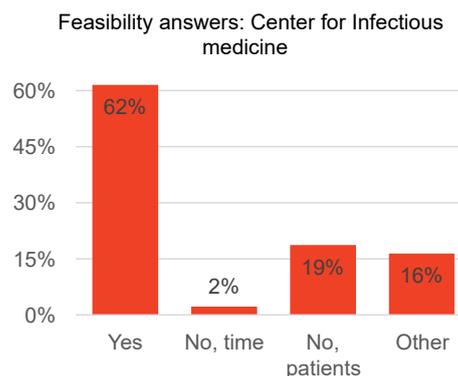


Figure 16. How the feasibilities were answered in 2021 by Trial Nation Center for Infectious Disease and Immune Modulation reported by affiliated department

All feasibilities, except those where Sponsor have specifically requested exception, has been shared in the center, a reflection of a well-established, close collaboration in the center. All feasibilities are responded to within the agreed five days – and often much shorter - within a day or two.

Clinical trials

In 2021, the Center for Infectious Diseases and Immune Modulation initiated a total of 11 clinical trials. Seven were commercial trials. The sites in the Center of Infectious Disease and Immune Modulation have a long history of collaboration with Center of Excellence for Health, Immunity, and Infections (CHIP), who runs several NIH and EU funded international trials. In 2021 two trials funded by NIH were started, and two trials funded by the Danish Ministry of Health were started. The Danish Ministry of Health and NIH-funded trials are included here as they are externally funded high profile trials.

Overall, 26 clinical trials were ongoing in 2021, as seen in Figure 17. Fifteen trials with trial initiation before 2021 were still open in 2021. Eleven were commercially funded trials and 4 were investigator-funded trials. Investigator-initiated clinical trials are included in this report, when they were of a certain size, involving 4 to 6 of the six sites in the Center and are of high scientific importance.

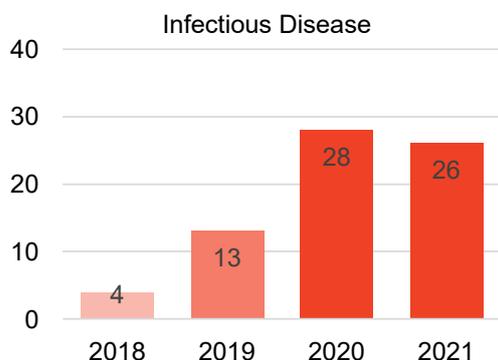


Figure 17. Number of open clinical trials at the Trial Nation Center for Infectious Disease and Immune Modulation in 2021

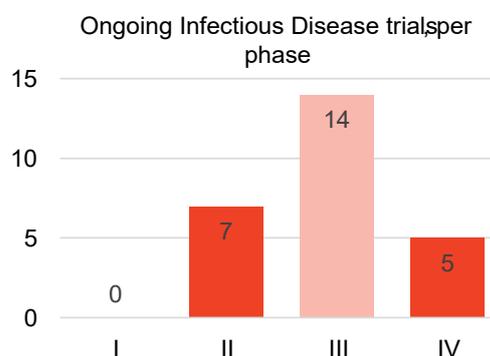


Figure 18. Number of open clinical trials at the Trial Nation Center for Infectious Disease and Immune Modulation in 2021 distributed into phases.

The center has seen an increase in activity over the years and 2021 is about the same level

as 2020. The increase in activity during the last two years is mainly driven by COVID-19 trials. About half of the clinical trials were COVID-19 treatment trials and the other half were other indications in infectious disease.

Recruitment

In 2021 the Center for Infectious Diseases and Immune Modulation have enrolled an extraordinary number of patients. This is primarily driven by the ENFORCE trials. ENFORCE and ENFORCE plus are two trials funded by the Danish Ministry of Health to evaluate the COVID-19 vaccines used in Denmark. Approximately 7000 participants, who will be followed for two years, have been enrolled in the ENFORCE trials.

Center activities

1. The Center for Infectious Disease and Immune Modulation collaboration has been expanded by a Network for Infectious Disease. The Network consists of an additional 6 sites, on top of the sites in the center. The Network has received all relevant feasibilities since its inception.
2. In April a two-day meeting for research coordinators from Center for Infectious Disease and Immune Modulation was arranged to bring learnings from the COVID-19 pandemic into the daily practice. It also prepared the coordinators for the next COVID-19 wave and has helped in strengthening the collaboration between the sites.
3. In September a Center meeting with the Swedish research group, ACTION, took place. The purpose was to discuss research collaboration and clinical trials.
4. In November a face-to-face meeting took place to strengthen the collaboration between the center and the new network and share best practice on how to establish a research unit with regards to staff, funding, and research agreements.
5. The Innovation Fund Denmark, as part of their efforts to combat COVID-19, invested in a project increasing the clinical trial capacity at the Center for Infectious Diseases and Immune Modulation. The project started May 2020 and finished end July 2021. The steering group met every month to follow up on issues such as ongoing and planned trials. Additionally, the study coordinators from all six sites, the feasibility coordinator and the facilitator from the Trial Nation secretariat met every week to discuss operational aspects and share best practice on COVID-19 trials. The project report is approved by Innovation Fund Denmark and has been a great success.

After the end of the COVID19-MITC project, the weekly meetings for study coordinators and the facilitator from the Trail Nation secretariat has continued. The study coordinators from the Network for Infectious Disease are also invited into these meetings.

Cost Summary

In 2021, each of the clinical departments in Center for Infectious Disease and Immune Modulation was supported by a grant of DKK209.000 from Trial Nation to ensure preparedness and infrastructure for clinical trials. In addition to this amount, the site at Aarhus University Hospital was granted DKK50.000 for the role as Medical Lead, and DKK175.000 in support

of the role as feasibility coordinator for the Center.

The annual report for each site for 2021 was approved by the Trial Nations Board of Directors in December 2021.

“The efforts that have been made in the center over the last few years have been noticed by the pharma companies. We expect more people will choose to place e.g. vaccine studies in Denmark in the future.”

Professor Lars Østergaard, Medical Lead

Focus in 2022

1. Continue to attract vaccine trials and trials within the area of infectious disease and immune modulation by:
 - i. Ensuring efficient feasibility handling with one point-of-contact for sponsors and focusing on close collaboration with the sponsors or CROs to facilitate entry into, and understanding of, the trial environment in Denmark regarding trials within the infectious disease and immune modulation area.
 - ii. Increasing visibility of the competencies in the center towards the industry.
 - iii. Arrange one-to-one meetings with selected companies
 - iv. Arrange Round Table meetings in collaboration with Invest in Denmark
2. The Center will continue to strengthen the collaboration to the new Infectious Network and to support the new Network sites in their abilities to participate in clinical research.
3. The center will specifically focus on attracting vaccine trials as it is gaged that these are an important part of the center’s activities in the future.
4. Bring the attention to experiences gained through the logistically highly complex and high patient number vaccine trial, ENFORCE, to boost Denmark’s readiness for future large-scale vaccine trials.
5. The center will further extend collaboration with other specialties, e.g., pediatrics, respiratory, and hematology as the center see a trend in trials which require a broader collaboration across disease.
6. The center will continue to work proactively towards establishing collaboration with new industry partners and to expand their capability to conduct clinical trials in new areas within the field of infectious disease and immune modulation.

Center for Oncology

All departments and our general Center presentation can be found online [here](#).

Key metrics and conclusions

2021 was a very positive year for the Center for Oncology in relation to clinical trials. 51 new initiated trials in 2021 was a tremendous increase of 75% compared to 2020, thereby continuing the very positive trend in the recent years.

The yearly activities, including feasibilities are summarized in Table 5 below.

Medical Lead

Senior Consultant Kristoffer Rohrberg*

Feasibility coordinator

Laurine Harsløf*

Center facilitator

Ask Aabenhus, Trial Nation.

* The Phase I Unit, Copenhagen University Hospital

“In recent years, through Trial Nation and other stakeholders, an enormous effort has been made to promote Denmark as a country where it pays off to conduct trials in. The figures give the impression that the effort has been successful. My impression is that COVID-19 has shown to many that Denmark has a robust and reliable healthcare system. And it has been easier to perform research in DK than in many other countries through the pandemic.”

Senior Consultant Kristoffer Rohrberg, Medical Lead

Center for Oncology	2018	2019	2020	2021
Number of feasibilities received	83	65	115	221 ¹
Number of initiated trials (phase I-II/I-IV)	16/ ⁻²	18/ ⁻²	10/29	28/51
Number of trials open (phase I-II/I-IV)	50/ ⁻²	59/ ⁻²	71/134	79/144

Table 5. Overall activities of feasibilities and trials.

¹Please note that as a consequence of the increased digitalization of feasibilities, the calculation of the number of feasibilities has been adapted and the number of feasibilities received in 2021 is not directly comparable with previous years.

² In 2018 and 2019 only phase I+II trials were registered.

Feasibilities

All the sites in The Center for Oncology received a total of 221 commercial oncologic feasibilities in 2021, documented by each of the oncology departments forming part of the Center for Oncology. A large proportion of feasibilities are for early phase trials. As a consequence of the increased digitalization of feasibilities within oncology, the calculation of the number of feasibilities has been adapted. This means that a direct comparison to previous years is not possible. Twenty-three of the feasibilities were directed towards The Phase I Unit at Rigsho-

spitalet. An additional nine were handled by the Pediatric Oncology Department. Please refer to figures 19 and 20 respectively.

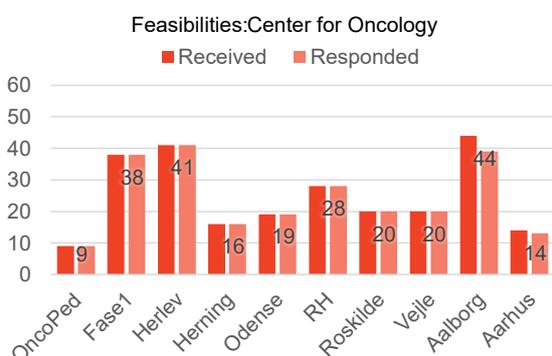


Figure 19. Feasibilities received and answered in 2021 by Trial Nation Center for Oncology reported by affiliated department

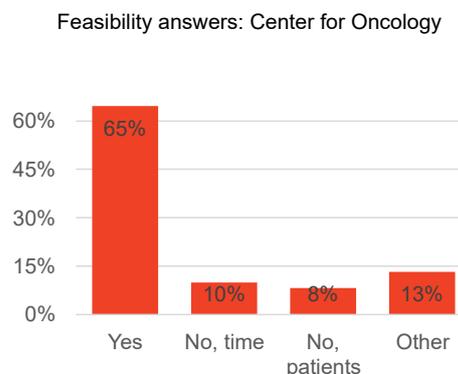


Figure 20. How the feasibilities were answered in 2021 by Trial Nation Center for Oncology reported by affiliated department

Clinical trials

In 2021, 144 commercial clinical phase trials were reported as open, an increase of ten compared to 2020. Of these, 79 were phase I-II trials compared to 71 the year before. 51 new commercial clinical trials were initiated involving one or more of the clinical departments, an increase of 75% compared to 2020. Twenty-eight of the trials were phase I-II, an increase from ten the year before.

Thirteen of the ongoing trials were pediatric oncology trials. Four of these were initiated in 2021, all in early phases, including one first-in-human trial.

As in previous years, the numbers are subject to uncertainty and should be seen as minimum estimates.

All departments were involved in the conduct of commercial clinical trials which is in line with previous years. Figures 21 and 22 respectively describes the development of trials over time and distribution of clinical trials phases.

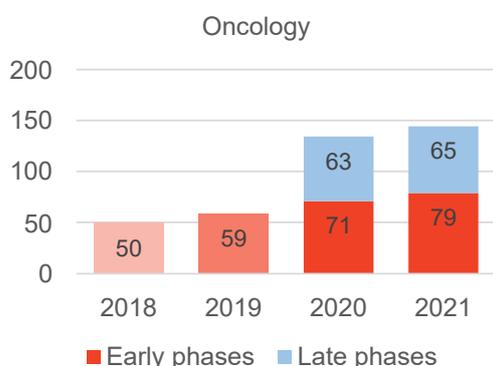


Figure 21. Number of open clinical trials at the Trial Nation Center for Oncology in 2021

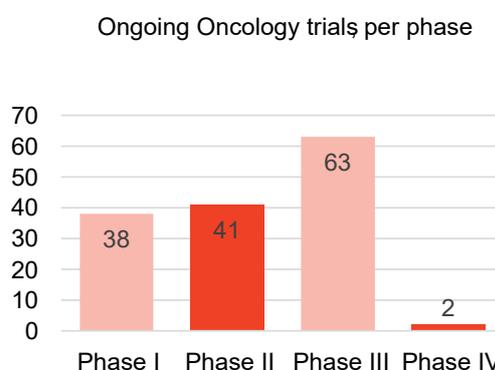


Figure 22. Number of open clinical trials at the Trial Nation Center for Oncology in 2021 distributed into phases.

Recruitment

88 patients received experimental treatment at the Phase I Unit at Rigshospitalet in 2021, numbers being very stable from 2020.

Despite the COVID-19 pandemic, all sites remained open in 2021 and reportedly, oncology trials in Denmark have been less impacted compared to many other European countries.

“The general confidence in the Danish handling of COVID-19 and the fact that we have been able to include patients throughout the pandemic has made Denmark attractive to sponsors. For periods, we have been the only site worldwide in several phase 1 trials that have actively recruited patients.”

Senior Consultant Kristoffer Rohrberg, Medical Lead.

Center activities

Due to the COVID-19 pandemic meeting activities and conferences were converted to web-meetings, and other activities were put on hold. The following joint activities took place in Trial Nation Center for Oncology:

1. National sharing and handling of feasibilities.
2. Referral of patients for clinical trials at other departments in the center.
3. Web-based Center meeting on the direction and organisation of the center
4. Supported to the project of the national overview of clinical trials.
5. Continued improvement of the collaboration with relevant patient organisations on clinical research

Cost summary

In 2021, each of the clinical departments in Center for Oncology was supported by a grant of DKK346.667 by Trial Nation to ensure preparedness and infrastructure for clinical trials. In addition to this amount, the Phase 1 Unit at Copenhagen University Hospital, Rigshospitalet was granted DKK50.000 for the role as Medical Lead, and DKK175.000 in support of the role as feasibility coordinator for the Center.

The individual sites' annual report has been approved by the Board of Trial Nation in December 2021

“2021 was a busy year with increased interest in Denmark as a preferred country to perform clinical studies within oncology. We have thus seen a marked increase in the number of clinical studies that are opened, and our impression is that the number of patients treated in clinical oncology studies is increasing. This has led to bottlenecks in the research infrastructure in several places in the country. This would benefit from being supplemented with additional resources if this positive trend is to be maintained in the coming years.”

Senior Consultant Kristoffer Rohrberg, Medical Lead

Focus in 2022

In 2022, Center for Oncology will focus on attracting new trials plus improving the national collaboration across departments. This will be accomplished by:

1. Single company and round table activities, marketing the competences in the center and at the departments to the industry. The activities will be conducted in collaboration with liDK and Copenhagen Capacity.
2. Effective sharing and handling of feasibilities.
3. Ensuring support of capacity for clinical trials.
4. A center meeting to set the direction and organisation for the center.
5. Improving the national collaboration across departments in general and specifically regarding.
 - a. The number of departments participating in specific clinical trials with fewer patients.
 - b. Referral of patients for clinical trials at other departments in the center.
 - c. Patient involvement in clinical trials.
 - d. Clinical trial deliverables.
6. A seminar on patient involvement in clinical trials was postponed and is planned to take place in 2022.
7. Raising awareness on the importance of prioritisation of clinical research with regional and national decision makers.

Center for Respiratory Medicine

All departments and our general center presentation can be found online [here](#).

Key metrics and conclusions

2021 was a productive year in the Center for Respiratory Medicine. 34 ongoing trials in 2021 meant an increase in activity compared to the previous year, thereby continuing the positive trend despite COVID-19 related challenges. The number of feasibilities received was 64, all of which were answered and in 64% of the cases, departments responded with an interest in participating.

Regarding the number of open trials in 2021, this is an increase compared to 2020, despite the fact that a large bulk of COVID-19 studies were finalized in 2020.

The most noteworthy figure this year is the large number of feasibilities received and responded to between sites, which in combination with the increased number of clinical trials reflects a solid overall activity throughout 2021.

Center facilitator Annette Buusman says, "Reflecting on 2021, what stands out to me is the strong sense of obligation to the Danish research community among members of the Center for Respiratory Medicine. This was exemplified by performing on-site training of new/inexperienced staff from other Trial Nation Centers. Members of the Respiratory Center also played a key part in the Trial Nation-arranged training course for research staff in all regions."

Center for Re- spiratory Medi- cine	2018	2019	2020	2021
Number of feasi- bilities received	18	24	22	64*
Number of initia- ted trials	2	13	10	12
Number of trials open in year	4	19	31	34

Table 6: Overall activities of feasibilities and trials.

*Please note that as a consequence of the increased digitalization of feasibilities, the calculation of the number of feasibilities has been adapted and the number of feasibilities received in 2021 is not directly comparable with previous years.

Medical Lead

Professor Charlotte Suppli Ulrik*

Feasibility coordinator

Eva Brøndum*

Center facilitator

Annette Buusman , Trial Nation.

*Respiratory Research Unit, Dept. of Respiratory Medicine, Copenhagen University Hospital-Hvidovre

Feasibilities

A total of 64 commercially funded feasibilities were received in the Center for Respiratory Medicine in 2021. Please note that as a consequence of the increased digitalization of feasibilities, the calculation of the number of feasibilities has been adapted. This means that a direct comparison to previous years is not possible, i.e., the number for 2021 is not directly comparable to the 22 feasibilities the previous year, as it reflects the fact that all feasibility activity has been registered for each site, as opposed to only the unique feasibilities shared by the coordinator.

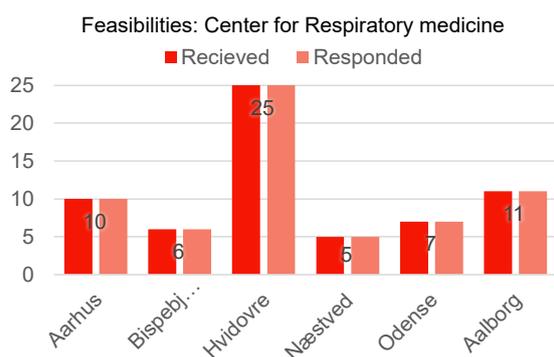


Figure 23. Number of feasibilities received in Center for Respiratory Medicine in 2021.

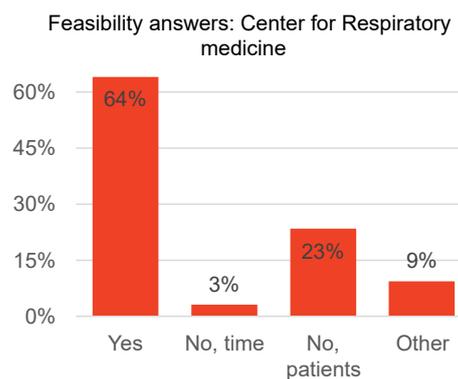


Figure 24. Reasons for declining participation in clinical trials – all sites

Professor Charlotte Ulrik, Medical Lead, explains that the high number of responses to feasibilities from Copenhagen University Hospital-Hvidovre reflects the fact that the team at Hvidovre provide a coordinated response to Sponsor on behalf of the sites in the Center and network.

In figure 24, the reasons for declining participation are listed.

It is noteworthy that 23% of the feasibilities had to be declined because the sites did not have patients who would fulfill the inclusion criteria. This reflects the fact that for some diseases, the patient selection criteria, not least regarding pharmacological treatment, are not in compliance with current treatment guidelines in Denmark. In the words of Professor Charlotte Suppli Ulrik, Medical Lead: “Selection criteria like these potentially put the patient at risk of receiving a treatment which is inferior to the current standard of care.”

Clinical trials

In 2021, a total of 12 studies were initiated across the departments in the center, enrolling 119 patients in total. In addition to this number, some studies initiated in both 2019 and 2020 were still ongoing in 2021.

COVID-19 related studies continued to have strong focus in 2021, and most departments have continued their participation in trials related to COVID-19. Together with re-starting studies paused due to the pandemic and start-up of studies postponed due to the pandemic, this has turned 2021 into an extremely busy year for all departments within respiratory medicine. Additionally, many departments have had staff temporarily transferred to COVID-units, and the requirement to comply with the many fast changing restrictions related to the pandemic added to the challenge.

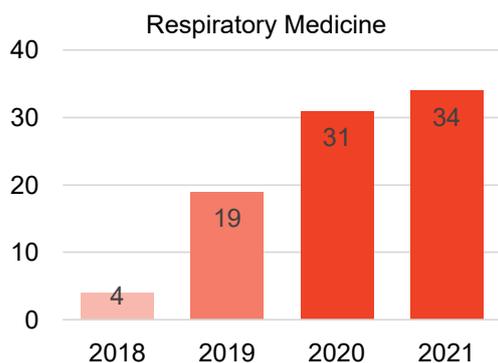


Figure 25. Number of open clinical trials at the Trial Nation Center for Respiratory Medicine in 2021

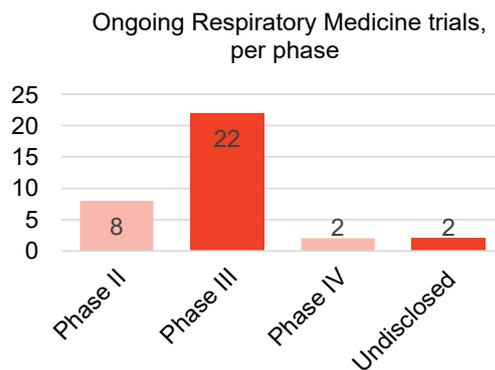


Figure 26. Number of open clinical trials at the Trial Nation Center for Respiratory Medicine in 2021 distributed into phases.

For an overview of distribution of clinical trials by phase, see figure 26.

Recruitment

Patient recruitment continued to be a challenge in 2021 due to the COVID-19 pandemic, as described above. Despite this, a total of 119 patients were enrolled in clinical trials in the center.

Center activities

The collaboration within respiratory center worked, and still works, smoothly. All clinicians work together, looking for opportunities to further make the collaboration better and stronger and improve the clinical study process - from the first contact from the sponsor to the close-out visit.

2021 saw the following main activities:

1. Annual meeting (discussing strategy, networking, future collaboration)
2. Respiratory network collaboration (also on a daily basis between departments)
3. Recurrent virtual meetings with sponsors/CROs to discuss study inclusion criteria
4. Ongoing contacts between PIs related to budgets, ethical approvals, legal issues etc.
5. Onsite training of new staff from other departments (within the respiratory speciality)

The targets for 2021 concerning collaboration both internally and with industry and patients were met, as were the goal to follow up on feasibilities and ensure understanding of data. With regards to optimizing key deliverables in clinical trials, including time from site initiation to First Patient First Visit, the sites succeeded to a very large extent, and will probably be fully optimized when the pandemic no longer has an impact on the daily work.

Cost summary

In 2021, each of the clinical departments in Center for Respiratory Medicine was supported by a grant of DKK209.000 to ensure preparedness for clinical trials. The Department of Respiratory Medicine at Hvidovre Hospital received an additional DKK50,000 to support the role of Medical Lead, as well as DKK160.417 to support the national feasibility handling and coordination of network activities from February to December 2021, during the sick leave of the permanent feasibility coordinator.

Each individual sites' annual report has been approved by the Board of Trial Nation in December 2021

Focus in 2022

Primarily due to the pandemic, the targets for 2022 will not differ substantially from the targets for 2021. In 2022, the center will therefore continue to focus on attracting new, especially early phase trials and improving the national collaboration across sites. This will ensure effective feasibility handling, sufficient capacity for clinical trials, predictable deliverables (including capture of relevant trial performance data) and patient empowerment.

Marketing of the competences in the center towards industry will further be intensified. Furthermore, based on learnings from the pandemic, we will seek to facilitate collaboration across the centers/disease areas/specialties.

Danish Pediatric Network (DanPedMed)

DanPedMed has increased its activities in 2021. DanPedMed collaborates with all 17 pediatric departments in Denmark, including direct contact to 160 clinicians in various pediatric subspecialties.

DanPedMed corresponds to similar networks in the other Nordic countries, who work together through NordicPedMed. DanPedMed is also a member of the Pan-European network Conect4Children (C4C).

The network was established in 2016 through a collaboration between the Danish Pediatric Society and the Danish Society of Clinical Pharmacology. A grant from Trial Nation made it possible to hire three part time research nurses, who today work across the country in close cooperation with the steering committee and the National Coordinator to strengthen the sites' readiness to conduct clinical trials.

Governance and Cost summary

The national coordinator ensures contact to relevant clinicians at the pediatric departments to facilitate participation in research collaborations, including clinical trials.

Since January 2021, the National Coordinator has increased her weekly hours from six to 32 thereby increasing the focus on clinical trials within the pediatric field. DanPedMed has during 2021 received a Trial Nation grant of DKK 450.000. The expanded role of the national coordinator is additionally financed with a grant from C4C.

The Pediatric Network DanPedMed, 2021:

Chair: Pernille Mathiesen, Member of the Danish Society of Pediatrics. Consultant at the Department for Pediatric and Adolescent Medicine. Herlev Hospital

National Coordinator: Pernille Skovby, Nurse at Research Unit for Pediatric and Adolescent Medicine, Rigshospitalet, University Hospital Copenhagen.

Clinical activities

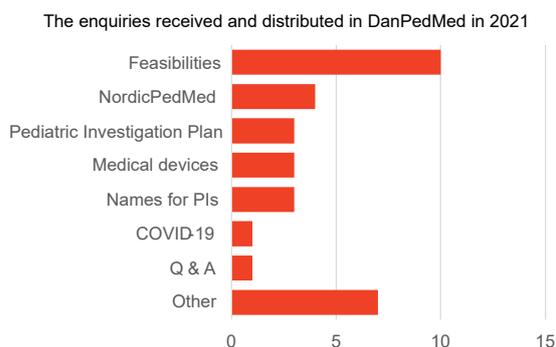


Figure 27. DanPedMed activities in 2021, summarized.

All feasibilities were circulated to all relevant sites and in 2021 the number of both feasibilities (8 to 11) and studies increased (1 to 4). 35 inquiries were received and distributed in the network. The inquiries divide into different types as follows in Figure 16. The network is very content with the documented and experienced increase in activity.

Furthermore, it has been possible to initiate clinical studies for children with respiratory syncytial virus (RSV). In addition, there is a good workflow with C4C, there is a strengthened attention to pediatric clinical trial units around the country and the collaboration with the Danish Paediatric Society (DPS) regarding a national center of knowledge for pediatric medicine is now receiving national political attention.

The Department of Neonatology, Rigshospitalet, Denmark is included as a site in one of four investigator-initiated clinical trials running under C4C. Denmark is also participating a study from Bayer with three sites as one of the four Industry proof of viability studies.

Other activities in 2021

An article (Greater vigilance in medication for children and adolescent is warranted in Denmark) was published in The Danish Medical Journal, 'Ugeskrift for Læger' in 2020, and brought attention to the discussion about children and medicine. This topic has reached public interest and was raised as a question in the Danish parliament in 2021.

Trial Nation and DanPedMed is part of the large, pan-European Innovative Medicines Initiative (IMI) project Connect4Children (C4C). In 2021 the grant to Denmark has increased (€50,000 to €65,000 yearly) and as a National Hub DanPedMed is today seen as a relevant and eligible partner in the C4C. DanPedMed contributes to several tasks in the C4C project description.

DanPedMed is also an active partner in NordicPedMed, with Pernille Skovby (in the role of secretary) arranging monthly meetings. DanPedMed was the main applicant in a proposal to: The Nordic Trial Alliance, where we, in 2021, was acknowledged with a grant of 1 mio NOK Kr for a two-year project in NordicPedMed (Establishment of Network for Nordic Pediatric Clinical Trial Units).

Focus in 2022

1. In 2022, DanPedMed will continue strengthening national collaboration on medicines for children and continue to be an attractive member of the C4C network.
2. Furthermore, DanPedMed will continue to focus on improving the national collaboration across departments of pediatrics and adolescent medicine in Denmark to increase awareness about DanPedMed and focus on outcome of enquiries.
3. In March 2022 DanPedMed is the host for a one-day international conference on children, adolescents and medicine.
4. In September 2022 DanPedMed is hosting a conference on: Establishing Nordic PedMed Clinical Trial Unit (CTU) network

DCT – Decentralised Clinical Trials

Background

Supporting the implementation of digitalization of clinical trials is of strong strategic interest for Trial Nation, Denmark is one of the most digitalized countries in the world, and there are strong synergy possibilities between the digitalization of clinical trials and digitalization of the healthcare system.

Trial Nation has in 2021 continued the participation in the Innovation Fund supported project on Decentralised Clinical Trials (DCT), contributed in the DCT Dialogue forum hosted by the DKMA and worked on papers related to DCT.

Furthermore, Trial Nation has during 2021 supported the development of a unique National Overview of Clinical Trials that can provide patients and health care personnel with a first of a kind, day-to-day updated overview of all clinical trials performed in Denmark, their status and location. This initiative is funded by means from the Innovation Fund Denmark as part of the NEXT-2 project as well as by the governmental restart agreement and is described in more detail under “Infrastructure activities”.

Trial Nation continued during 2021 to contribute to the Innovation Fund Denmark project Decentralised Clinical Trials (DCT) where progress is made in exploring ways of performing clinical trials in which patients and trial staff are not necessarily at the same physical location. During 2021 significant steps has been taken in additional elements that has been digitalized, which are described in Figure 28 below.

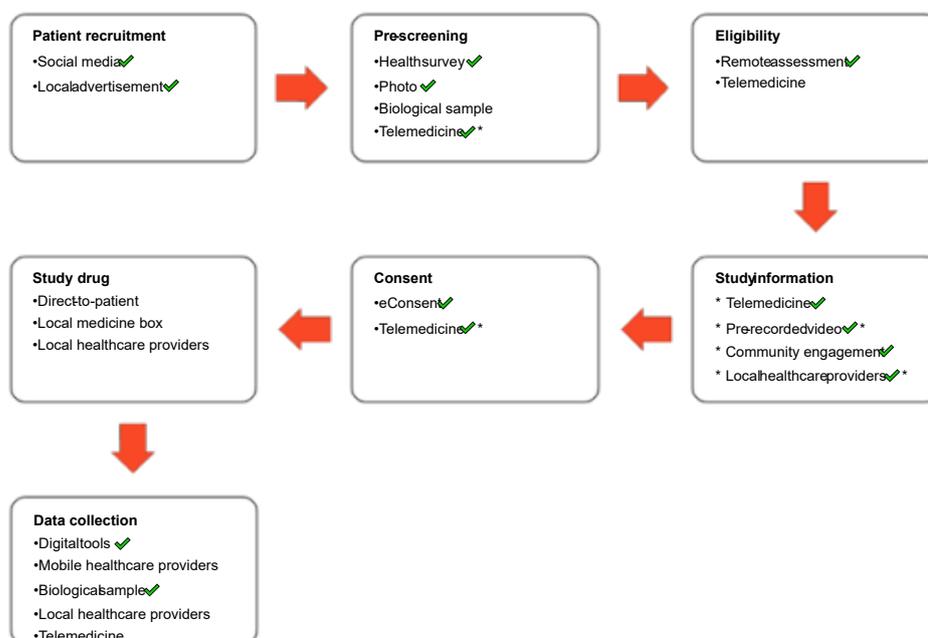


Figure 28. The boxes reflect the patient-involving elements in a traditional clinical study. The subpoints show a decentralized approach to the elements. The decentralized elements deployed in the Denmark is indicated with a green checkmark. An asterisk indicates elements which have been implemented during 2021.

Importantly, The Medical Scientific Ethical Board will accept decentralized informed consent procedures, adhering to published guidelines for a period of two years. After the two years the novel approach will be evaluated, and hopefully made permanent. In preparation for this process, Trial Nation facilitated meetings between life-science companies and the ethics committee (De Videnskabsetiske Medicinske Komiteer) in order to provide inputs and discussions in the development of the process.

Framework activities

Trial Nation has contributed actively into the DCT Dialogue forum, which was set-up jointly by Trial Nation and the Danish Medicines Agency (DKMA) and is now hosted by the DKMA. The forum, gathers authorities, patients, researchers, the industry, DKMA and Trial Nation and meets several times per year. It provides opportunity for discussion of views, barriers, and experiences with DCT and of regulatory processes, to give input to the advancement of the DCT agenda in Denmark. The collaborative approach and outcomes from this forum have fed into the globally first (May 9th 2021) issued regulatory guideline on decentralized clinical trials ("Guidance on the implementation of decentralised elements in clinical trials with medicinal products") – a guideline which is very much alive and updated regularly.

Trial Nation, the Danish Medicines Agency, and the Danish Association of Pharmaceutical Industry established a collaboration with Innovation Center Denmark (ICDK) Silicon Valley with the purpose of bringing the latest insights and knowledge from Silicon Valley to the forum for dialogue on decentralised clinical trials. The collaboration was established in the end of 2020 and from this collaboration four webinars for knowledge sharing has been held during 2021, hosted by ICDK Silicon Valley, and an Outlook report is in production.

Focus in 2022

1. Trial Nation will continue to work with collaboration partners from pharmaceutical companies, hospitals and regions, regulatory authorities, and patient organisations to support driving the implementation of trials with decentralized elements in Denmark.
2. Trial Nation will continue to contribute into the DCT Dialogue forum
3. A paper to showcase DCT in Denmark will be released together with Healthcare Denmark
4. An Outlook report on DCT developed by ICDK Silicon Valley, where Trial Nation has contributed, will be released early 2022.
5. The National overview of Clinical Trials will start its implementation phase.
6. Overarching design decisions will be produced for the Digital Recruitment Platform, and these will guide the next steps in the project.

Trial Nation MedTech Center

The MedTech Center is not a typical Trial Nation Center as it covers all therapeutic areas and technologies.

Clinical activities

Clinical trial feasibilities for areas not covered by the national center structures are facilitated by the regional coordinators within MedTech. During 2021, 9 feasibility requests were handled in MedTech, a welcome increase from the three feasibilities processed in 2020.

The number of initiated clinical trials in 2021 is compared to 2020 and 2010-2019 to illustrate the development in selected parameters for clinical trials over time. This is visualised in Table 7. We note that not only the number of multi sponsor trials, but in particular their proportion of all trials are on the rise in 2021. This could indicate that both public-private- and SME-corporate collaboration is increasingly seen as attractive.

	Historic (2010-2019)		2020	2021
	Cumulative	Average per year		
Single Sponsor	317	(53%) 32	(46%) 26	(36%) 19
Multiple Sponsor	281	(47%) 28	(54%) 30	(64%) 34
Total	598	60	56	53

Table 7. Ongoing and completed clinical trials on medical devices. Data source: Global Data January 2022.

When looking at trial activity broken down into indications, the contribution of COVID-19 trials can be seen in the figures. An increase in non-COVID-19 related trials from 46 in 2020 to 51 in 2021 is observed as shown in figures 29 and 30 below.

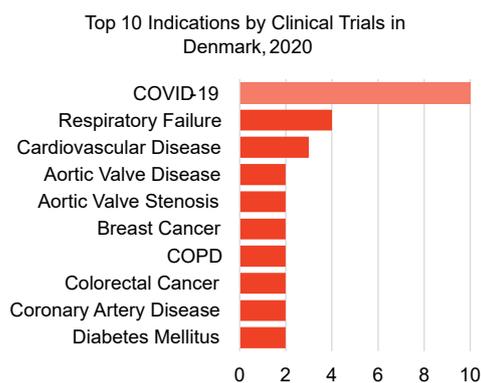


Figure 29. Top 10 Ongoing and completed clinical trials on medical devices by indication in 2020. Note the large number of COVID-19 trials. COPD: Chronic Obstructive Pulmonary Disease

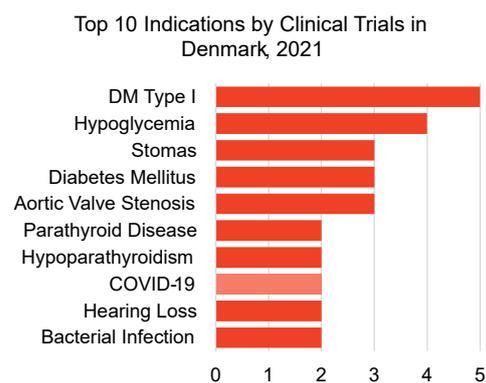


Figure 30. Top 10 Ongoing and completed clinical trials on medical devices by indication in 2021. Note the much less prominent position of COVID-19 trials, #8 in 2021, compared to #1 in 2020.

Strategic activities

The Center has worked on strategic activities that will lead to increased clinical trials for medical devices. These activities include a full-day medical device regulation (MDR) course, a national AI-call and establishing and maintaining strategic partnerships.

In October 2021, the Center arranged a full-day MDR course for regional MedTech coordinators, GCP monitors specialised in medical device trials, regional legal advisors, and regional health innovation employees. In total 20 people participated on the day. The feedback was very positive and several participants stated that the course was very relevant and appropriately timed, as the new EU Regulation has come into effect in May 2021.

The project group which received funding from the AI call initiated their work in April 2021. Activities in this project have on several occasions been affected by the COVID-19 situation in Denmark. Thus, the conference reporting the results from this work has been postponed until March 2022. The project group will report its findings to the MedTech Center in Q1 2022.

In October 2021, representatives from MedTech Center met with the Norwegian initiative Nordic Proof to share experiences and knowledge on feasibility enquiries and early collaboration with start-ups who expect to conduct clinical trials. Furthermore, representatives from MedTech Center met with both representatives from Texas Medical Center, USA in connection with the BioBridge initiative and representatives from the French office both part of the Ministry of Foreign Affairs, Invest in Denmark.

COVID-19 has also had its influence on activities this year. Both national restrictions and a Danish healthcare system under pressure, has led to the decision to postpone meetings with local clinical and project personnel working with clinical trials of medical devices.

Cost summary

Budget approved: DKK 1,800,000	
Personnel	DKK 180,000
AI call	DKK 1,260,000
MDR Course	DKK 38,500
Total	DKK 1,478,500
Transferred to 2022 budget	DKK 321,500

Focus for 2022

The Center will continue working on two remaining strategic topics selected by the board; medical devices with AI and improved infrastructure. To support this, communication material on the services Denmark can provide for clinical trials on medical devices will be produced in the beginning of 2022. In late 2022, a two-day course for project personnel will be held. This will enable more departments to partake in commercial trials. Lastly, the results from the AI project will be analysed and together with collaborators implemented as appropriate.

Trial Nation

Clinical Trials Denmark