TRIAL NATION 2020

# YEARLY REPORT FOR TRIAL NATION AND CENTERS

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# Executive Summary

2020 was the year of the COVID-19 pandemic, which made its mark also on Trial Nation. However, a very robust hospital sector and setup for clinical trials made it possible for patients in Denmark to continue participating in clinical trials, and new trials were initiated during the year. This is in stark contrast to the situation in many other countries.

2020 was also the year in which clinical trials made the headlines across the world. We eagerly anticipated the results of the vaccine studies that would give us back the world we used to know. Especially two of our centers, those for infectious disease and respiratory disease, have played a key role in the pandemic response. As a result of outstanding clinical capabilities, supported by direct investments in trial and research capacity, Denmark has been able to maintain sufficient clinical capacity while continuing to run and initiate new clinical trials in these two therapeutic areas. The investments were in the form of an Innovation Fund project and a COVID-19-related company donation.

The development in the number of ongoing clinical trials reported in Trial Nation Centers over the last three years is extremely positive, with an increase from 137 trials in 2018 to 209 trials in 2020. This is a result of Trial Nation centers and Denmark's capabilities growing in volume and visibility, as well as the development pipeline of new pharmaceutical products.

Due to the extraordinary circumstances of 2020, an overall response time for feasibility requests was not consistently documented in all centers. However, at the Centers for Dermatology and Infectious Disease, sponsor requests were usually addressed with exceptional efficiency within just one or two days.

Stronger media presence, both direct news channels and relevant social media, was a strategic priority for 2020. We have taken both a strategic and enterprising approach to communication. It has been our focus to increase our visibility to actors relevant for the overall clinical trial ecosystem. We produced the publication "Trial Nation – A healthier, smarter and wealthier Denmark", which is available in Danish and English. The publication has caused significant online media attention. Additionally, we have targeted communication to the general public as exemplified by four authored newspaper articles, 20 tailored newsletters, and a plethora of LinkedIn posts on both Trial Nation successes and those of others.

Trial Nation has enjoyed significantly more press coverage and press interaction in 2020 than in any of the previous years – more than 40 individual mentions in news media and partner newsletters. In addition to this, Trial Nation arranged and/or participated in two debates at *Altinget Sommermøde* in June.

We are happy to see that Trial Nation continues to attract members. At the start of 2020 the association had 29 members; January 1st, 2021 the number of members was 33, including the pro-bono members Danish Patients and the Danish Medical Societies.

Internally, Trial Nation has reviewed the secretariat functions and aligned the roles to support the board approved strategy.

The framework conditions for clinical trials were challenged and discussed in the Trial Nation Dialogue forum. The Danish Medicines Agency, the National Ethics Committee, The Danish Association of the Pharmaceutical Industry and MedTech Denmark engage in the forum. The forum met twice, as planned, during 2020.

It should be noted that 2020 marked the closure of the Innovation fund projects NEXT-1 as well as all aspects of NEXT-2 except the funds related to OPEN. Therefore, this is the last report related to these projects and next year only activities related to the OPEN funds will be reported in the yearly report.

We have a very inspiring and interesting year ahead in 2021 where we will continue executing on the strategy - for the health and wealth of Denmark.

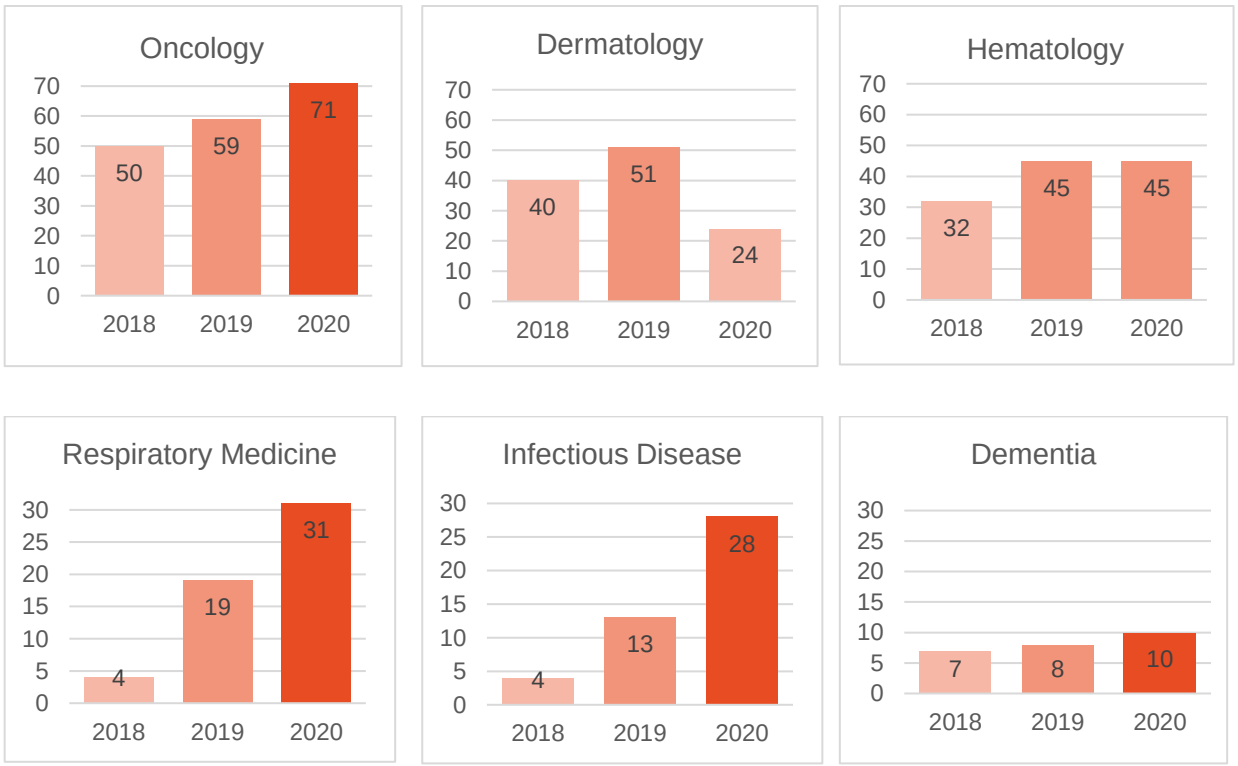
# Activities in 2020

A coordinated response is key to crisis management. Trial Nation contributed by acting as an intermediary, providing relevant clinical stakeholders with up-to-date knowledge of the latest developments on an ongoing basis. In addition to this, Trial Nation hosted meetings and a training for project personnel. The training for project personnel was developed and chaired by the Trial Nation pharma network and covered topics relevant to the impact of COVID-19 on clinical trials.

## Clinical activities

Our clinical centers have always formed the backbone of our contribution to the advancement of clinical trials in Denmark. They continue being a success, in 2020 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 2020.

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 is represented in the sections below. An overview of the development of each center is shown in Figure 1. below. Details on clinical trials are presented in the sections for each center.



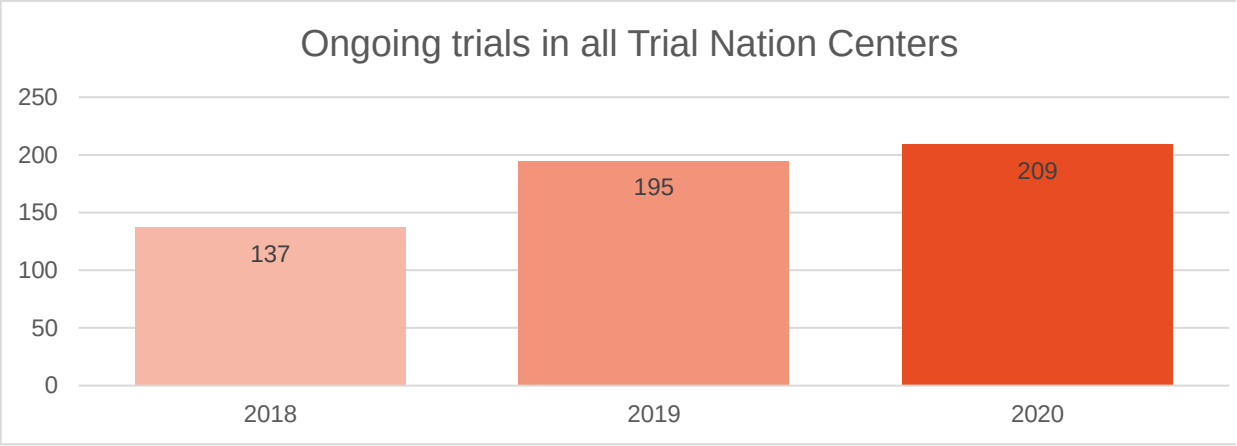



*Figure 1. Development of number of ongoing trials in Trial Nation Centers from 2018 to 2020.*

In the Center of Dementia, we saw a solid increase in terms of received feasibilities and trial activity. Positive response to feasibilities in 2020 creates good prospects for new studies ready to be initiated in 2021.

In the Center of Dermatology, a steady increase in open trials during 2018 and 2019 shifted downwards in 2020, due to COVID-19. Furthermore, many of the long-running studies contributing to the high figures for 2019 were also finalised in 2020.

In the Center of Hematology, clinical trial activity remained constant in 2020, which is a remarkable achievement in the face of a global pandemic. Additionally, the number of feasibilities received reached a record number of 78 in 2020, which makes for a promising 2021 in terms of trial initiations. The center was expanded with its 9th research site.

In the Center of Infectious disease, 2020 was a truly remarkable year. The center and its incredible clinicians juggled emergency treatment and emergency discovery. The Innovation Fund Denmark successfully invested in capacity increase following a Trial Nation application to the extraordinary call with the purpose to mitigate the effects of COVID-19.

In the Center of Respiratory Medicine, like in the infectious disease area, the sites were front and center in the initial, national response to the pandemic. The accomplishments at both centers are stellar examples of great infrastructure and collaboration. Novartis Healthcare A/S made a COVID-19 related donation which successfully increased respiratory research capacity.

In the Center of Oncology, the center increased trial activity substantially in 2020. The oncological research field is the most active both in Denmark and globally, measured by number of clinical trials. The number of ongoing trials increased, and the number of feasibilities rose from 65 to 115, thus introducing the hope that 2020 is not the last of the consecutive years of increasing activity. The center was expanded with its 8th and 9th research site.

Within Pediatric medicine, the DanPedMed organisation have started activities within the C4C framework during 2020 and updated its Site Description in the project, making Denmark more visible to collaborators. DanPedMed has also broadened the communication with the pediatric clinical community on participation in industry-sponsored clinical trials.

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 structures are facilitated by the regional coordinators within pharma and MedTech. During 2020, 46 feasibility requests were handled with an average response time of 2 working days.

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 year 2020 saw the start of the first fully decentralised trial in Denmark. To support the development of this field, the Danish regulatory authorities (DKMA) and Trial Nation collaborated in establishing a dialogue forum for digitalisation and decentraliation 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.

Development of MedTech is closely related to clinical investigations. This relationship will become increasingly manifest when the postponed European Medical Device Regulation will take effect, currently planned for May 2021. Trial Nation is promoting clinical development of MedTech directly by our AI MedTech call, in which DKK990,000 was distributed in support of a structured access to knowledge and experience. The call was launched late 2020 and results from grant recipient(-s) are expected from the late 2021.

### External activities

In 2019 Trial Nation became 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.

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 single-handedly and in collaboration with stakeholders such as Invest in Denmark (IiDK) and Healthcare Denmark (HCD). Key events include the following:

1. Together with IiDK, a Roundtable meeting was held in Boston, showcasing our clinical trials capabilities within oncology. The Trial Nation medical lead for Oncology presented to decision makers at US pharma companies to advocate placement of clinical trials in Denmark.

2. Together with HCD, Trial Nation learnt from and explored possible collaborations with South Korea and together with IiDK possibilities in the US was explored (Texas Medical Center).
3. Trial Nation was presented to the Interreg Europe MedTech 4 Europe, leading to inclusion as good practice in the project´s database.
4. Together with IiDK and alone, Trial Nation held face-to-face and virtual meetings between pharmaceutical companies and investigators within selected clinical specialties to facilitate the inclusion of Denmark and Danish sites in clinical trials.
5. Trial Nation presented its capabilities to interested organisations in Norway, Sweden, Ireland and Canada (Quebec).

### Infrastructure activities

Trial Nation has also 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 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.

## Center for Dementia

*In 2020, the Center for Dementia consisted of the following trial sites:*

Danish Dementia Research Center, Dept. of Neurology at Copenhagen University Hospital, Rigshospitalet. Clinical trial director, consultant neurologist, Kristian Steen Frederiksen was the medical responsible for the site in Trial Nation.

Regional Dementia Research Center, Dept. of Neurology at Zealand University Hospital, Roskilde. Consultant neurologist Peter Høgh was the medical responsible for the site in Trial Nation.

Dementia Clinic, Dept. of Neurology at Odense University Hospital, Svendborg. Senior Consultant neurologist Michael Oettinger was the medical responsible for the site in Trial Nation.

Dementia Clinic, Dept. of Neurology at Aarhus University Hospital. Consultant neurologist Hanne Gottrup was the medical responsible for the site in Trial Nation.

Dementia Clinic, Dept. of Neurology at Aalborg University Hospital. Specialist consultant neurologist Karsten Vestergaard was the medical responsible for the site in Trial Nation.

The Trial Nation Center for Dementia was established is 2018 and is coordinated by Professor Gunhild Waldemar, who served as the Trial Nation Medical Lead, and Dr. Kristian Steen Frederiksen, who coordinated the feasibility processes. Research administrator Jette Rasmussen served as the administrative coordinator. All are from the Danish Dementia Research Center, Rigshospitalet, Copenhagen. Kirsten Bødker from the Trial Nation secretariat was the facilitator of the center.

Apart from the above-mentioned Medical Lead and the coordinators from the five memory clinics, the steering committee for the Trial Nation Center for Dementia also included consultant neurologist Lena Hjermind, Danish Dementia Research Center, Dept. of Neurology at Copenhagen University Hospital, Rigshospitalet and consultant neurologist Anette Torvin Møller, Dementia Clinic, Dept. of Neurology at Aarhus University Hospital, who also served as contacts for trials in Huntington's disease.

The region of Southern Denmark has previously been present in the center with two departments. The organisation of dementia clinics in the region was changed from April 2020, meaning that there is now only one clinic (residing in Svendborg), and this memory clinic is a part of the network.

The yearly activities are summarised in Table 1 and described in detail below.

## Overall activities of feasibilities, trials and recruitment

All metrics, except those concerning enrolled patients, increased in 2020. A total of 10 clinical trial feasibilities involving two phase I-II feasibilities, four phase III-IV feasibilities, three open-label extension trials and one feasibility of undisclosed phase involving one or more of the clinical departments were evaluated and completed in Center of Dementia in 2020, see Figure 2. Most of the feasibilities were shared across participating memory clinics (i.e., sites) in the center – only a very few were not shared, if specifically requested by the sponsor.

| Center for Dementia | 2018 | 2019 | 2020 |
|---|---|---|---|
| Number of feasibilities received | 6 | 4 | 10 |
| Number of initiated trials | 2 | 2 | 4 |
| Number of trials open in year | 7 | 8 | 10 |
| Number of patients enrolled in trials | unknown | 71 | 57 |

*Table 1. Overall activities of feasibilities, trials and patients enrolled in Trial Nation Center for Dementia.*

### Feasibilities

Feasibilities were received from sponsors from big pharma, midsized pharma, smaller pharma and CROs. In 2020, eight of the 10 requested feasibilities concerned Alzheimer's disease and two concerned Huntington's disease. The Center replied positively to all 10 feasibilities.

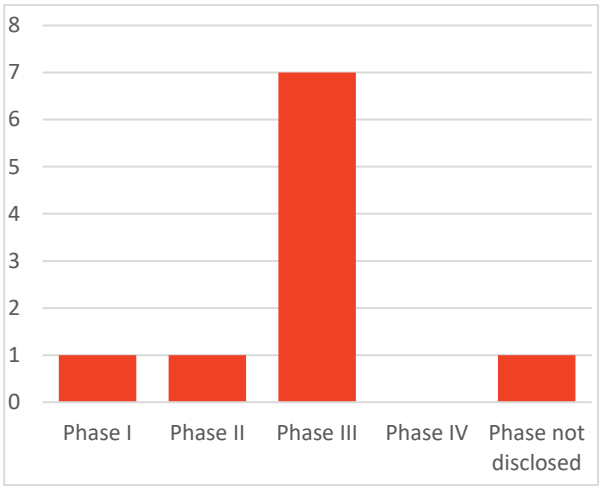



*Figure 2. Feasibilities, separated by phase, received in 2020 by Trial Nation Center for Dementia or reported by affiliated departments.*

Most of the feasibilities in Alzheimer's disease were shared across participating sites in the Center – only a very few were not shared, if specifically requested by the sponsor. Concerning Huntington's disease, not all sites participated in the feasibility process – either because the infrastructure was not in place, or because clinical trials in Huntington's disease are not conducted at all sites.

The Trial Nation Center for Dementia was chosen to participate in seven trials, not chosen in two trials due to low number of patients, and for one trial the Center is still waiting for a response. The number of feasibilities received shows an upwards trajectory (see table 1) and in the Trial Nation Center for Dementia, a continued effort to increase awareness of the Center within the Life Science industry is ongoing. Please refer to the paragraph "Focus in 2021".

## Clinical trials

In 2020, the Center for Dementia initiated a total of four commercial clinical trials, two in Huntington's disease and two in Alzheimer's disease. The two studies in Alzheimer's disease were initiated at the Clinical Trial Unit at Rigshospitalet. The two Huntington's disease trials were initiated at Aarhus University Hospital and Rigshospitalet. Overall, 10 clinical trials were ongoing in 2020, as six trials were initiated before 2020 and were still open in 2020, three in Alzheimer's disease and three in Huntington's disease. See distribution across trial phases in Figure 3 below. Five commercial trials are already planned for initiation in 2021.

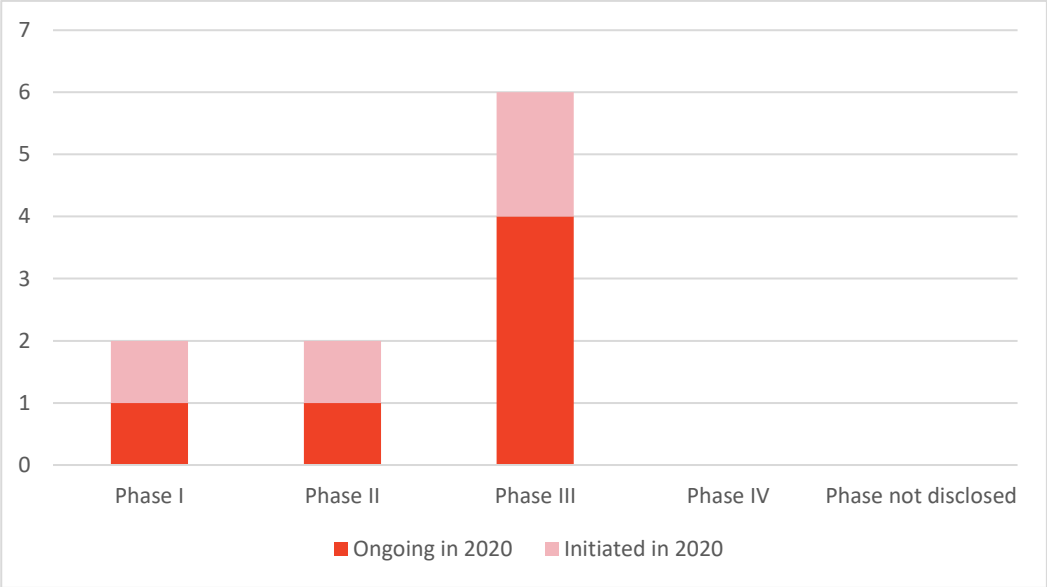



*Figure 3.* Number of clinical trials ongoing and initiated at the Trial Nation Center for Dementia in 2020

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

### Recruitment

The Center for Dementia has overall been able to maintain operations through the COVID-19 pandemic. All sites were able to remain open during the pandemic.

A total of 57 participants were actively enrolled or participated in the 10 ongoing trials in 2020. Thirty participants with Alzheimer's disease were enrolled in trials and 24 participants with Huntington's disease.

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

## Center activities

1. Activities in 2020 have to some degree been affected by the COVID-19 pandemic. The following activities were conducted in Center for Dementia in 2020:
2. Medical Lead Gunhild Waldemar presented the Center for Dementia to the board of Trial Nation.
3. Virtual steering committee meetings took place in March, October and December.
4. Furthermore, activities related to feasibilities, company meetings, grant administration and other organisational matters took place on an ad hoc basis.

## Cost summary

In 2020, each of the sites in Center for Dementia was supported by a grant of DKK186,000. 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.

**Danish Dementia Research Center, Dept. of Neurology at Copenhagen University Hospital, Rigshospitalet** spent the grant improving the patient flow together with a new patient database to optimise the identification of possible participants in clinical trials and increase recruitment to clinical trials. The Medical Lead chaired the four center meetings during the year and worked as an adviser for organisational and administrative questions from other sites in the center. The Clinical Trial Director coordinated feasibilities, pre-feasibilities and other requests from the pharma industry, taking responsibility for the feasibility log and trial log for the center, and worked closely with the facilitator of the center.

**Dementia Clinic, Dept. of Neurology at Odense University Hospital, Svendborg** received the rest of the grant from the dementia clinic in Odense, when the two clinics were merged in Svendborg. They spent part of the grant on a seminar to develop a research strategy for the new organisation in the new clinic areas in Svendborg. Other priorities included an educational research course for two medical doctors, a new freezer and a new refrigerator for the new research lab, to be used for commercial clinical trials, and the ward nurse and research secretary being compensated for working with commercial clinical trials some hours a week. The rest of the grant (DDK561,356) will be transferred to the 2021 budget and spent on further education of the research staff.

**Regional Dementia Research Center, Dept. of Neurology at Zealand University Hospital, Roskilde** spent the grant educating the research nurse and a PhD student to be able to help conduct the commercial clinical trials. A new medical specialist has begun training to be able to work as a co-investigator.

**Memory Clinic, Dept. of Neurology at Aalborg University Hospital** spent part of the grant on the development of a new database to support commercial clinical trials and GCP-training courses for the physicians. The clinic was partly closed in the spring, and some of the planned research training sessions were postponed due to COVID-19. The rest of the grant will be transferred to the 2021 budget and spent on database development and fee for a new research nurse.

**Dementia Clinic, Dept. of Neurology at Aarhus University Hospital** spent part of the grant on training and supervision of a new research nurse and a nurse for back-up tasks, to compensate administrative staff for research administration in relation to commercial clinical trials. In addition to this, they spent the grant developing workstreams for the research group and answering feasibilities from commercial sponsors, as well as participating in Trial Nation related meetings. The rest of the grant (DKK83,714) will be transferred to the 2021 budget.

## Focus in 2021

In 2021, the center will focus on

1. Continuing to attract new 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 competences in the center towards the industry.
1.3. Participating in international conferences with the goal of establishing contacts with life science industry to attract clinical trials.
1.4. Arranging an International Roundtable meeting with selected company headquarters to present the center and Trial Nation.
1.5. Arranging one-to-one meetings with selected companies.

2. Continuing improvement of collaboration across the sites and with the Trial Nation secretariat. Building competence and capacity will still be in focus on both departmental and management level.
3. Developing 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.

## Center for Dermatology

The Center for Dermatology was established in 2015 and is led by Professor Simon Francis Thomsen from Bispebjerg University Hospital. Four of the five Danish regions are currently represented in the center, with the Capital region being represented by two sites (the possibilities for collaboration with research sites in Region North will be explored in 2021). Pia Nørrisgaard and (since late 2020) Annette Buusman from the Trial Nation secretariat were facilitators of the center.

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

*In 2020, the Center for Dermatology consisted by the following trial sites:*

Department of Dermato-Venereology at Bispebjerg University Hospital. Professor, Senior Consultant Simon Francis Thomsen

Department of Dermato-Venereology at Bispebjerg University Hospital. Professor, Senior Consultant Simon Francis Thomsen

Department of Dermatology at Zealand University Hospital Roskilde. Professor, Senior Consultant Gregor Jemec

Department of Dermatology and Allergy Center at Odense University Hospital. Professor, Senior Consultant Carsten Bindslev-Jensen

Department of Dermatology and Venereology at Aarhus University Hospital. Professor, Senior Consultant Lars Iversen

### Overall activities of feasibilities, trials and recruitment

A total of 22 clinical trial feasibilities involving six phase I-II feasibilities, eight phase III-IV feasibilities and eight feasibilities of undisclosed phase involving one or more of the clinical departments were performed in Center for Dermatology in 2020 (see Table 2 below).

| Center for Dermatology | 2018 | 2019 | 2020 |
|---|---|---|---|
| Number of feasibilities received | 29 | 19 | 22 |
| Number of initiated trials | 15 | 14 | 10 |

| | | | |
|---|---|---|---|
| Number of trials open in year | 40 | 51 | 24 |
| Number of patients enrolled in trials | 62 | 171 | N/A |

*Table 2: Overall activities of feasibilities, enrollment and trials. The number of recruited patients is not available for 2020.*

## Feasibilities

A total of 22 feasibilities were handled by the coordinator in Center for Dermatology in 2020; this is a slight increase compared to the previous year (see distribution across trial phases in Figure 4 below). As expected, most of the feasibilities concerned phase II and III trials. Since information about the trial phase was not disclosed in all feasibility requests, it is possible that some of the feasibilities did concern trials in phase I, which would be a distribution similar to that of previous years.

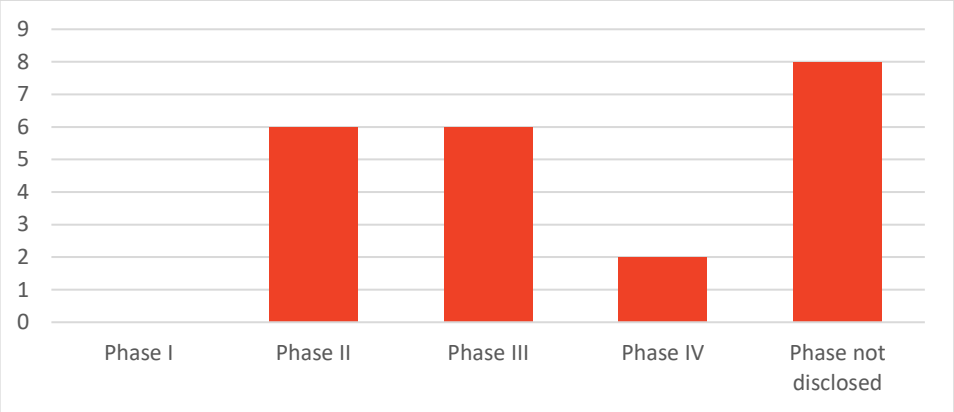



*Figure 4. Number of phase I-IV feasibilities received in Center for Dermatology in 2020.*

Regarding sharing of feasibilities in the center, this is becoming increasingly difficult to document and track, as companies and CROs continue to use proprietary online feasibility requests processes. Furthermore, feasibilities are also shared via some of the electronic shared investigator portals used by several companies and CROs. Finally, several companies have longstanding working relationships with the individual investigators and still prefer sending feasibility requests directly to a particular research site. As a consequence of this, it is not always possible for the center feasibility coordinator to intercept all feasibility requests.

Sponsors were primarily big pharma companies; about 10% of the requests were coordinated by CROs.

## Clinical trials

In 2020, the Center for Dermatology initiated a total of 10 commercial clinical trials involving one or more of the clinical trial sites. Two trials are already planned for initiation in 2021. Overall, 24 clinical trials were ongoing in 2020, as 14 trials initiated in 2019 were still open in the first half of 2020.

The number of documented commercial clinical trials in phase I-IV was reduced by more than half, compared to 2019. This reduction should be seen in light of the many challenges brought on by COVID-19 in the year of 2020. Furthermore, many of the long-running studies contributing to the high figures for 2019 were also finalised that year.

By the end of 2020, all departments were involved in the conduct of between one and 12 clinical trials, meaning that the 24 ongoing trials were performed with all five sites involved (see Figure 5 for an overview of number of trials at each department). Where the number of clinical trials was lower than expected, resources were spent strengthening the qualifications of the research staff involved and improving administrative procedures.

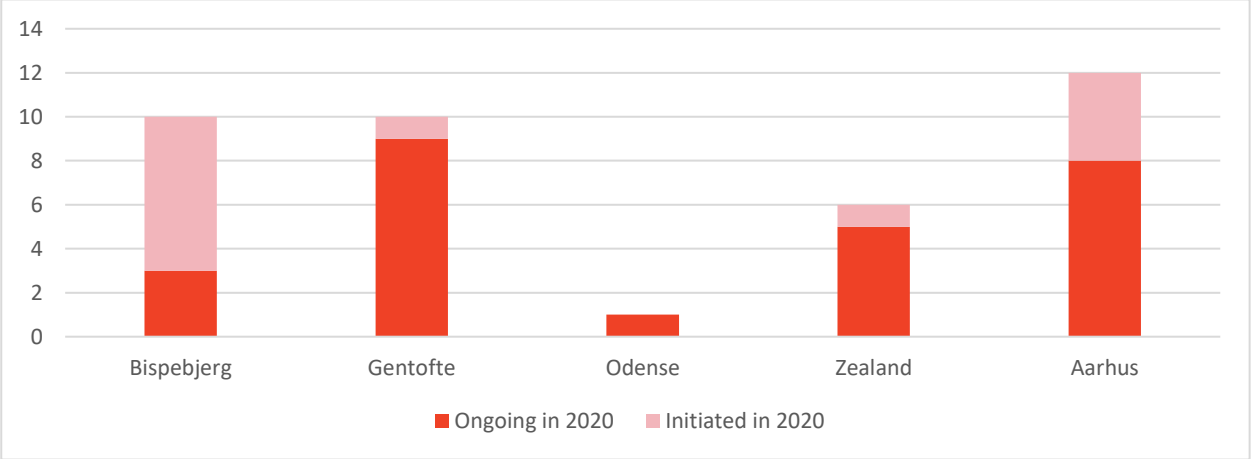



*Figure 5. Number of clinical trials ongoing and initiated in Center for Dermatology in 2020.*

The distribution of trials across trial phases was similar to that of previous years (see Figure 6).

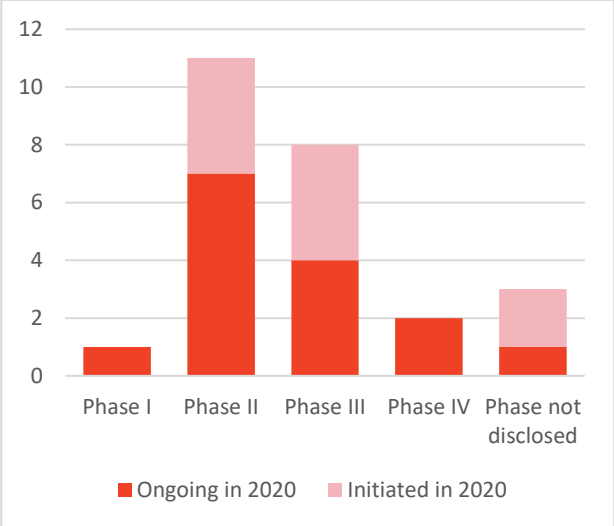



*Figure 6. Ongoing and initiated clinical trials in Center for Dermatology in 2020, distributed across trial phases.*

Apart from the commercially funded clinical trials, 2020 saw considerable activity in the field of non-commercial clinical research. One of the departments in the Trial Nation center for Dermatology is a partner in an Innovation Fund Denmark-project on decentralised clinical trials. Trial Nation is also a partner in this project, and an overview of the project activity is provided in a separate section of this report.

## Recruitment

Patient recruitment continued to be a priority in 2020, as exemplified by the development of a national patient database (described in the paragraph below). The number of recruited patients is not available for 2020.

## Center activities

1. As for all clinical sites, the consequences of the COVID-19 pandemic put many of the planned activities in the Center for Dermatology on hold. This also means that recruitment has been impacted by the pandemic, even though clinical research in Denmark reportedly has been less impacted than in many other European countries.
2. In 2020, the center had one physical meeting, which was the annual meeting at the premises of Trial Nation. Three patient organisations were represented at the meeting: The Psoriasis association, the AE association (Atopic Eczema), and HS association (Hidradenitis Suppurativa). The three organisations have formed an alliance called "HudSagen" with the purpose of increasing awareness and improve lives for patients living with chronic skin diseases. There is considerable interaction between this alliance and the investigators in the Center for Dermatology, with the common goal to increase patient involvement/influence in clinical trials. Sanos Clinic, a CRO, also participated in the annual meeting to discuss potential collaboration and patient recruitment.
3. Furthermore, two virtual meetings were held (in September and November), one of them with the participation of the pharma company sponsoring many of the clinical trials within dermatology at the sites. The company's pipeline and continued collaboration with the investigators was discussed.
4. The Medical Lead at the center continued to drive the development of a national patient database, which will facilitate recruitment of patients in future clinical trials. The Center for Dermatology, represented by each site, prepared a draft manuscript submitted to a peer reviewed dermatology journal describing the aims and scope of the Trial Nation Database.

## Cost summary

In 2020, each of the clinical departments in Center for Dermatology was supported by a grant of DKK222,000. 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.

At **Department of Dermato-Venereology, Bispebjerg University Hospital**, the primary focus was to maintain the planned patient recruitment to the clinical trials despite three months on hold due to the COVID-19 pandemic. The site succeeded in this because of staff flexibility and goodwill in the clinical department. The research site expanded with a new Principal Investigator, adding to the existing scientific qualifications. In four national commercial clinical trials, the site was the first to include patients.

Holding the function as feasibility coordinator of the center, the site managed to send out 22 feasibilities, typically receiving an answer from other center departments and responding to sponsor within an

impressive three days. The Medical Lead was actively participating in the forum for Decentralised Clinical Trials, in collaboration with the Danish Medicines Agency.

Furthermore, the Medical Lead participated in several national advisory boards.

At **Department of Dermatology and Allergy, Gentofte University Hospital,** the primary focus was the successful hiring and training of an additional study coordinator. In addition to this, the Trial Nation grant was spent on keeping the research site up to date in terms of GCP-certificates, equipment and most importantly: adaptation of ways of working to accommodate for the consequences of COVID-19. Several studies were closed down or cancelled by the sponsors, in many cases after a considerable amount of resources had already been spent on planning and initiation. Overall, the adapted recruitment goals were met to the extent possible.

At **Department of Dermatology, Zealand University Hospital Roskilde**, the grant was spent primarily on maintaining the staffing, i.e., a part-time study assistant and a part-time study nurse. The patient recruitment numbers were initially impacted by the pandemic but improved as the knowledge and experience with COVID-19 related prophylaxis and risks increased. Negotiations to participate in several new trials are ongoing.

At **Department of Dermatology and Allergy Center, Odense University Hospital**, the grant was spent supporting clinical trial activities and training of research staff, strengthening the qualifications to perform clinical trials at the site. Furthermore, the grant helped fund administrative tasks like archiving patient consents and entering data from patient journals in relevant databases. In the second half of 2020, the role of Trial Nation-responsible investigator transferred to a professor in the field of dermato-allergology.

At **Department of Dermatology and Venereology, Aarhus University Hospital**, the primary focus was to strengthen the cross-sectional collaboration with other therapeutic areas about optimising procedures related to clinical trials. This resulted in improved procedures for budget negotiations and updating of the SOPs at the site, and the information material to patients has been updated. The site increased the focus on recruiting to the extent possible, e.g., the pre-screening function available via Refhost (a web portal used for electronic referrals from general practitioners) and was proactively reaching out to the patients to boost recruitment. Several pre-feasibility investigations from sponsors were handled by the site.

### Focus in 2021

In 2021, the center will focus on attracting new trials and improving the national collaboration across departments, ensuring effective feasibility handling, sufficient capacity for clinical trials, and predictable deliverables including capture of relevant trial performance data. Patient empowerment will continue to be a priority in 2021, as well as investigating potential collaboration with other Trial Nation centers such as the Center for Respiratory Disease.

Marketing of the competences in the center to the industry will still be in focus. The following specific activities will help achieve this goal:

1. Ensuring go-live and maintenance of the Derma database and continuing the work on other relevant local patient databases.
2. Improving the national collaboration across departments, including sharing of feasibilities.
3. Following up on feasibilities in each department in a way that allows for deeper understanding and consolidation of the data.
4. Recruitment metrics will be obtained for 2021 and onwards.
5. Identifying and collaborating with relevant private research clinics.
6. Continuing the existing collaboration with the relevant patient organisations.
7. Investigating possibilities for collaboration with other research clinics in the dermatological therapeutic area in Denmark.

## Center for Hematology

Medical Lead for the center was Niels Abildgaard from Department of Hematology at Odense University Hospital. Clinical Research Unit Manager Sally Grant from Odense University Hospital was responsible for national feasibility handling and center coordination and Ask Aabenhus from the Trial Nation secretariat was responsible for center facilitation.

The nine hematology departments treat almost all Danish hematological patients and cover all phases of clinical trials.

The department of Hematology at Holstebro Hospital joined the center from January 1st, 2020, thereby further broadening the geographic reach of the center.

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

*In 2020, the Center for Hematology consisted of the following trial sites:*

Department of Hematology at Copenhagen University Hospital (Rigshospitalet). Senior Consultant & Clinical Research Unit (CRU) Leader Peter Brown (phase II-IV) Senior Consultant & Phase I lead Martin Hutchings (phase I clinical trials)

Department of Pediatrics and Adolescent Medicine at Copenhagen University Hospital (Rigshospitalet). Senior Consultant & CRU Leader Karsten Nysom

Department of Hematology at Holstebro Hospital (Hospital Unit West). Senior Consultant & CRU Leader Stanislaw Pulczynski

Department of Hematology at Herlev and Gentofte Hospital. Senior Consultant & CRU Leader Lars Møller Pedersen

Department of Hematology at Odense University Hospital. Clinical Professor & CRU Leader Niels Abildgaard

Department of Hematology at Vejle Hospital. Clinical Professor & CRU Leader Torben Plesner.

Department of Hematology at Zealand University Hospital. Senior Consultant & CRU Leader Christian Bjørn Poulsen.

Department of Hematology at Aalborg University Hospital. Senior Consultant & CRU Leader Henrik Gregersen

Department of Hematology at Aarhus University Hospital. Clinical Professor & Research Leader Francesco D'Amore

## Overall activities of feasibilities, trials and recruitment

### Feasibilities

A total of 78 commercial hematologic feasibilities were received in 2020, either via Trial Nation or documented by hematologic departments forming part of the Center for Hematology. See distribution across trial phases in Figure 7. The figure shows an increase of feasibilities compared to 2019 where 63 feasibilities were documented, even when all the feasibilities documented by the new department at Holstebro Hospital are subtracted and Zealand University Hospital did not report on feasibilities. However, as in previous years, the figures are subject to substantial uncertainty as most of the feasibilities are shared directly with investigators, leaving the clinical research sites uninformed in several cases and resulting in reporting bias. The true number of feasibilities is therefore likely to be higher.

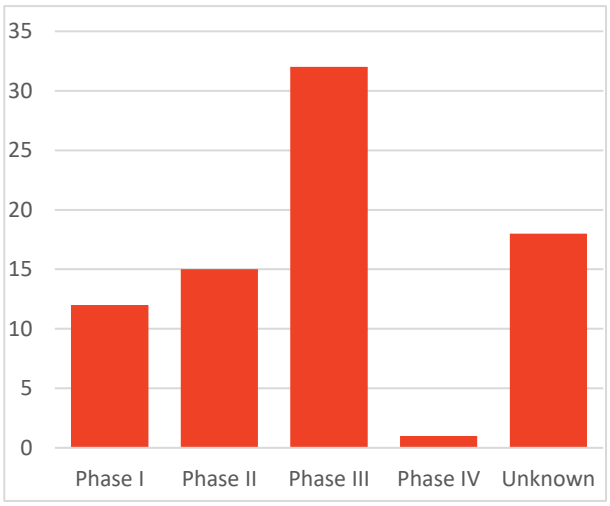



*Figure 7. Feasibilities received in 2020 by Trial Nation Center for Hematology or documented by affiliated departments.*

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

*Table 3: Overall activities of feasibilities and trials.*

### Clinical trials

In 2020, 75 commercial clinical phase trials were reported as active involving one or more of the clinical departments in the center. Of these, 43 phase I-II trials were reported as ongoing in 2020 compared to 45 the year before. Four of the ongoing trials were pediatric hematology trials. As in previous years, the numbers are subject to uncertainty and likely to be minimum estimates.

14 commercial clinical trials were initiated in involving one or more of the clinical departments, of which eight trials were phase I-II. This means that despite the many challenges brought on by COVID-19 in 2020, the number of documented commercial clinical trials initiated in phase I-II was reduced only by three compared to 2019.

As in the past years all departments were involved in commercial clinical trials. See Figure 8.

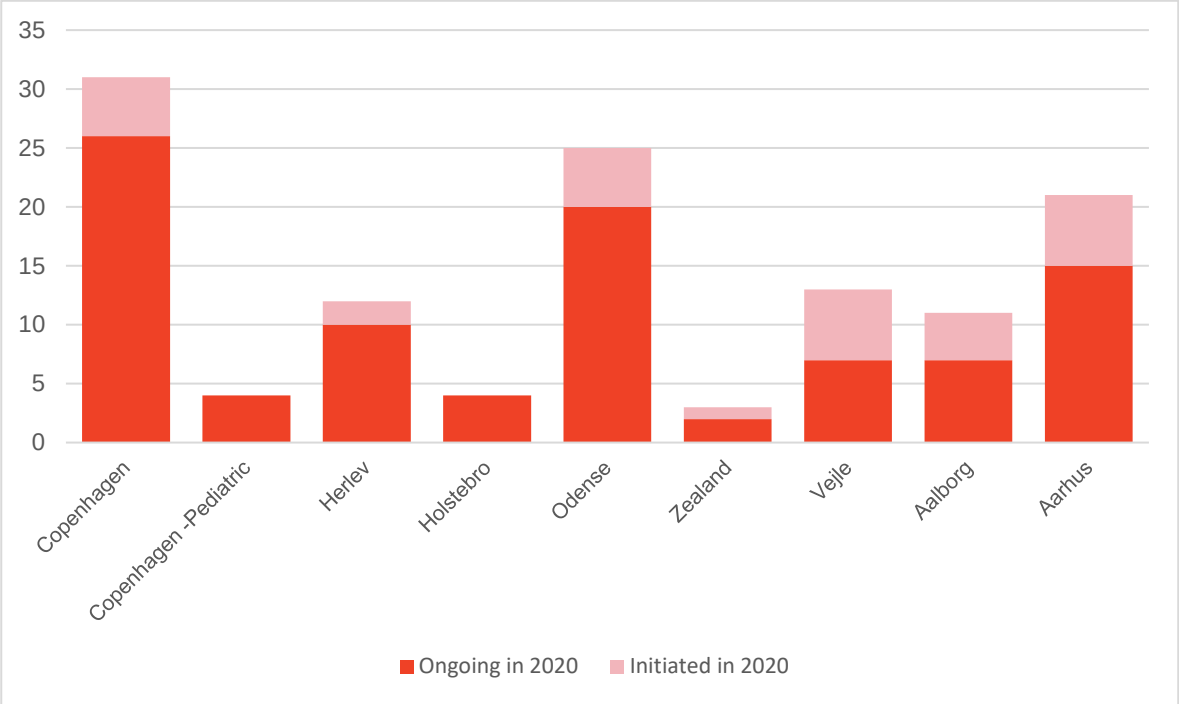



*Figure 8: Number of clinical trials ongoing and initiated in Trial Nation Center for Hematology in 2020.*

## Recruitment

The Phase I Unit at Rigshospitalet recruited 38 patients in 2020 across 10 clinical trials in phase I. The site recruited the first three patients worldwide for a first-in-human trial in acute myeloid leukemia and the first two patients worldwide for another first-in-human trial in multiple myeloma, both initiated in 2020.

Based on the available data and data capture tools, further elaboration on recruitment figures is not possible.

## Center activities

Due to the COVID-19 pandemic, 2020 was a truly special year for the Danish hematology sites. At most clinical departments, recruitment was paused for a short period during spring, and at some departments in part again in December. This also means recruitment was impacted by the pandemic, although it has been reported to Trial Nation that hematologic clinical trials in Denmark have been less impacted compared to many other European countries.

Furthermore, some meeting activity was converted to web-meetings, but planned, large, physical meetings and conferences were postponed, and other activities paused. Still, 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. Web-meetings with affiliate and headquarter representatives from relevant companies.
5. Supporting the Trial Nation CRO Network web-meetings.
6. Web-based center Meeting.

Issues to consider:

1. National sharing of feasibilities was challenged by use of electronic feasibility platforms and electronic clinical management platforms. The challenges include, but is not limited to, the number of platforms to be supported, suboptimal user-friendliness, use of legal language (e.g., confidential disclosure) not approved by the hospitals legal counsel. This was highlighted to the commercial sponsors, however in many cases it was beyond the immediate control of local subsidiaries. In other cases, companies preferred to conduct the feasibility process on their own and seek Trial Nations advice as to which departments and consultants to contact.
2. Precision medicine protocols reduced the potential patient pool due to narrow selection criteria. Consequently, improved structures for referral of patients for all phases between hospitals for clinical trials within Denmark and within the Nordics are needed. The barriers identified so far are mainly administrative, however complex of nature.
3. A national database on clinical trials is needed to support clinicians' and patients' knowledge of clinical trials open for recruitment in Denmark, which is a prerequisite to improving referral of patients for clinical trials.
4. A seminar on patient involvement in clinical trials was postponed several times during 2020 due to COVID-19.

## Cost summary

In 2020, each department in Center for Hematology was supported by a grant of DKK217,500 by Trial Nation to ensure preparedness and infrastructure for clinical trials, except Department of Pediatrics and Adolescent Medicine at Rigshospitalet, which received its grant via Trial Nation Center for Oncology. Odense University Hospital was further supported with an additional DKK50,000 and DKK175,000 in support of the department's roles as Medical Lead and National Feasibility Coordinator/Center Coordinator, respectively.

**Herlev Hospital** spent the grant on the establishment of an office to improve the facilities for monitors and project nurses, updating SOPs for clinical trials and updating the department's budget negotiation tool plus creation of a "site presentation". The grant has further been spent on courses for project nurses, and on findings ways to ensure clinical trial performance during the COVID-19 pandemic and the resulting changes to visit schedules and laboratory tests.

**Holstebro Hospital** spent the grant on training activities and updates of GCP certificates, updating procedures and SOPs (including patient recruitment procedures) for clinical trials, IT implementation and training. The department further spent the grant on feasibility handling and management and coordination meetings in relation to clinical trials.

**Odense University Hospital** spent the grant on improving the infrastructure and the clinical preparedness for clinical trials. Physical and organisational changes have been made in the ambulatory/day section to support phase I-II trials. The grant was further spent preparing for an upcoming accreditation in the field of hematopoietic stem cell transplantation (HSCT) and cellular therapy (JaCie accreditation). The department also coordinated the national sharing and handling of feasibilities and took part in the center meeting and planning of the postponed seminar on patient involvement.

**Rigshospitalet** spent the grant on training activities, updates of CVs and GCP certificates, development of a procedure book, professional coordination of clinical trials with medicinal products, feasibility handling, quality evaluations, authority approvals and budget negotiations.

**Zealand University Hospital** spent the grant on improving the preparedness for clinical trials, training and knowledge sharing through feasibility process optimisation, coordination of clinical trials and visualisation of the Clinical Trial Units tasks, updates of the CVs, certificates, GCP training and training more generally, process optimisation and development of a trial management system. Additionally, the possibility for developing a phase I unit at Zealand University Hospital has been investigated further.

**Vejle Hospital** spent the grant on maintenance of patient databases, CVs and SOPs, training and knowledge sharing with other clinical trial sites and Trial Nation, development of a protocol assessment tool and research budget maintenance.

**Aalborg University Hospital** spent the grant on feasibility handling and optimising the feasibility and confidential disclosure agreement (CDA) process, increasing awareness of clinical trial protocols at the site, GCP and protocol training. CVs and SOPs have been updated. The site also continued working with recruitment improvement and participated in Trial Nation meetings.

**Aarhus University Hospital** spent the grant on feasibility handling and coordination of new treatment regimens like bi-specific antibodies and CAR-T, activities related to clinical trials with expensive hospital medicine and COVID-19. Furthermore, the grant was spent on Trial Nation- related meetings and workshops, and support of Holstebro Hospital with regards to budget negotiations.

## Focus in 2021

In 2021, 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 and round-table marketing activities (web-based) 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. Improving the national collaboration across departments in general and specifically regarding:
    4.1. The number of departments participating in specific clinical trials with fewer patients
    4.2. Referral of patients for clinical trials at other departments in the Center
    4.3. Patient involvement in clinical trials
    4.4. Clinical trial deliverables
5. Support of the development 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.

# Center for Infectious Disease and Immune Modulation

The Center for Infectious Disease and Immune modulation was established in 2016 and is coordinated by Trial Nation Medical Lead, Professor Lars Østergaard. Feasibilities were coordinated and managed by MD, PhD stud. Nina Breinholt Stærke, also from Aarhus University Hospital. Kirsten Bødker from the Trial Nation secretariat was the facilitator of the center. Six infectious disease departments in Denmark are included in the center. In January 2020, the Department of Infectious Diseases at Zealand University Hospital, Roskilde, joined the center, which means that now all five Danish regions are represented the center. The yearly activities are summarised in Table 4 and described in detail below.

*In 2020, the Center for Infectious Disease and Immune Modulation consisted of the following trial sites:*

Department of Infectious Diseases at Aarhus University Hospital. Professor, Senior Consultant Lars Østergaard was the Trial Nation responsible medical doctor at the department.

Department of Infectious Diseases at Odense University Hospital. Professor, Senior Consultant Isik Somuncu Johansen was the Trial Nation responsible medical doctor at the department.

Department of Infectious Diseases at Copenhagen University Hospital, Rigshospitalet. Professor. Senior Consultant Jan Gerstoft was the Trial Nation responsible medical doctor at the department.

Department of Infectious Diseases at Zealand University Hospital, Roskilde. Consultant Lothar Wiese was the Trial Nation responsible medical doctor at the department.

Department of Infectious Diseases at Aalborg University Hospital. Professor, Senior Consultant Henrik Nielsen was the Trial Nation responsible medical doctor at the department.

Department of Infectious Diseases at Copenhagen University Hospital, Hvidovre. Professor, Senior Consultant Thomas Benfield was the Trial Nation responsible medical doctor at the department.

## Overall activities of feasibilities, trials and recruitment

A total of 28 feasibilities involving eight phase I-II feasibilities, 18 phase III-IV feasibilities and two feasibilities of undisclosed phase involving one or more of the sites were performed in Center of Infectious Disease in 2020 (see Table 4 below).

| Center for Infectious diseases | 2017 | 2018 | 2019 | 2020 |
|---|---|---|---|---|
| Number of feasibilities received | 13 | 18 | 9 | 28 |
| Number of initiated trials | 3 | 2 | 4 | 15 |
| Number of trials open in year | 3 | 4 | 13 | 27 |
| Number of patients enrolled in trials | 260 | 38 | 674 | 952 |

*Table 4: Overall activities of feasibilities, trials and patient inclusion.*

### Feasibilities

28 feasibilities were evaluated and completed by the sites in Center of Infectious Disease and Immune Modulation in 2020. 19 trials were commercially driven and eight were investigator-driven trials. *Figure* 9, below, shows the feasibilities received in 2020 separated by trial phase. The distribution between the phases was as excepted. Feasibilities were received from sponsors from big pharma, midsized pharma, smaller pharma and CROs.

Of the 28 feasibilities received, only one feasibility was declined by sites. This was due to lack of potential participants. One feasibility was declined by all six sites due to lack of patient population.

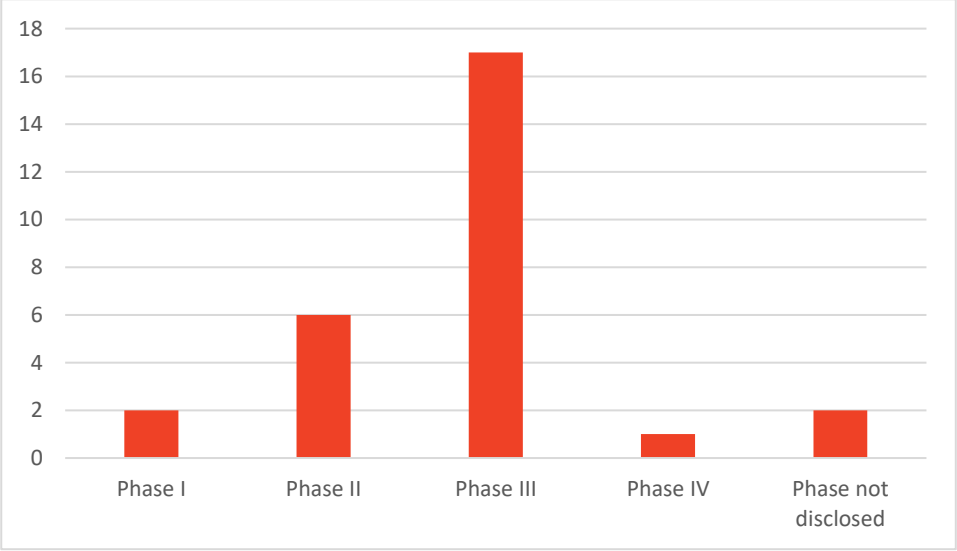



*Figure* 9. Feasibilities received in 2020 by Trial Nation Center for Infectious Disease and Immune Modulation or reported by affiliated departments divided into phases.

The Center for Infectious Disease and Immune Modulation was chosen to participate in 17 trials, not chosen in two trials due to a low number of COVID-19 positive patients hospitalised in the summer period, and for nine trials the center is still waiting for a response.

Most of the feasibilities have been shared in the center – only a very few have not been shared, in these cases upon specific request by the sponsor. This showcases the very close collaboration in the center. The response time has been within the agreed five days – and often within an impressive day or two.

## Clinical trials

In 2020, the Center for Infectious Diseases and Immune Modulation initiated a total of 15 clinical trials. The sites in the Center of Infectious Disease and Immune Modulation have a history of participating in National Institutes of Health (NIH) funded clinical trials, due to the collaboration with Center of Excellence for Health, Immunity, and Infections (CHIP), who runs several of the NIH funded international trials. 10 of the fifteen initiated trials were either funded commercially or by the NIH, and. five trials were investigator-initiated trials. The NIH-funded trials are included here as they are externally funded.

Most of the trials were conducted in more than three of the six sites in the center; only two studies were conducted at a single site. The majority of the clinical trials were COVID-19 treatment trials, and several other vaccine trials were also initiated in 2020. Most of the clinical trials were COVID-19 treatment trials, and several other vaccine trials were also initiated in 2020. Additionally, the sites initiated five investigator-initiated clinical trials, of which one trial includes all six sites and four trials includes five sites. The five investigator-initiated clinical trials are included in this report as they were of a certain size, involve several sites and are of scientifical importance, showcasing how a national network increases collaboration. Local investigator driven clinical trials are not included in this report.

Overall, 27 clinical trials were ongoing in 2020, as 12 trials initiated before 2020 were still open in 2020, as seen in Figure 12. Eighteen were commercially funded trials and nine were investigator-funded trials. By the end of 2020, the sites were involved in between five and 19 commercial clinical trials.

The center has seen an increase in activity over the years and 2020 is no exception. The increase in activity is mainly driven by vaccine trials and in 2020, approximately half of these were COVID-19 trials. Four commercially funded or NIH-funded trials are already planned for initiation in 2021, involving from three to six of the sites in the center.

Departments involved

By the end of 2020, the sites were involved in the conduct of between five and 19 clinical trials, see Figure 10, below, and four ongoing trials had all six sites involved.

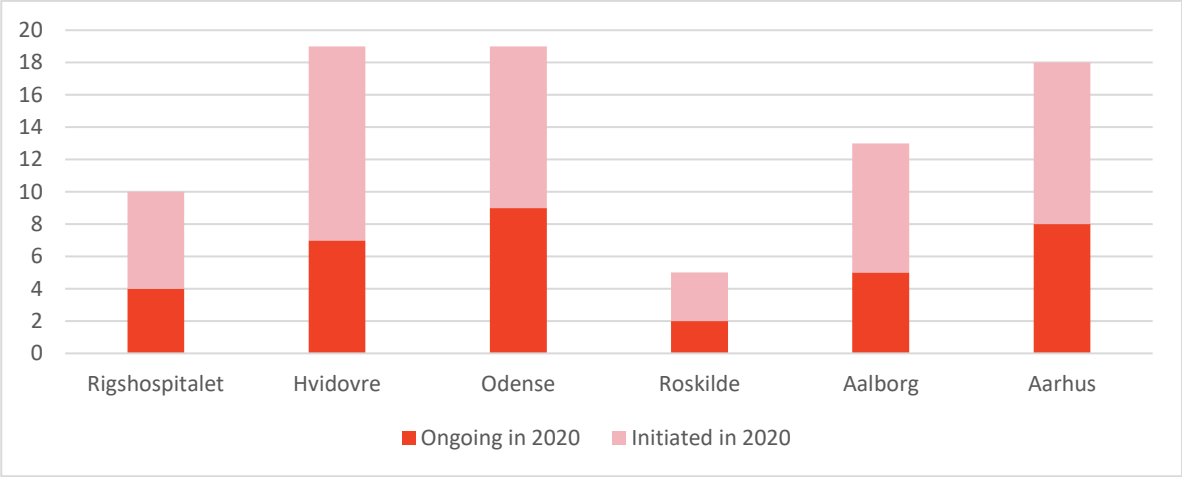



*Figure 10.* Number of clinical trials ongoing and initiated at the sites constituting Trial Nation Center for Infectious Disease and Immune Modulation in 2020

### Recruitment

At least 952 patients were included in clinical trials in 2020, distributed among 563 patients in commercially funded trials and 389 patients in investigator-funded trials. The center has achieved extraordinary recruitment due to the high number of COVID-19 and vaccine trials.

## Center activities

1. The center welcomed the Department of Infectious Diseases at Zealand University Hospital, Roskilde, led by Chief physician Lothar Wiese in January 2020. The site was fully involved in the network from day one.
2. The Center for Infectious Diseases and Immune Modulation, together with IiDK, set up and hosted collaborator meetings with international headquarter participation from a pharma company which had not planned to place clinical trials in this disease in Denmark. This company subsequently placed their first trial in this disease in Denmark.
3. The center, together with IiDK, reached out to approximately 20 relevant companies who were in the development of COVID-19 vaccines to draw attention to the capability and capacity of conducting COVID-19 vaccine trials.
4. In addition, all six sites had updated the center's existing databases on HIV, cystic fibrosis, central nervous system infections and hepatitis.
5. In the autumn of 2020, a virtual meeting for research nurses on infectious disease was arranged to bring learning from the first COVID-19 wave into the second wave.
6. In 2020, the Center for Infectious Diseases and Immune Modulation got tremendously busy due to the COVID-19 pandemic. The huge need for new and better treatments for the COVID-19 infection and the need for developing vaccines against COVID-19 increased the need of quickly being able to handle and conduct many clinical trials.
7. 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.

This project, the COVID19-MITC project, made it possible for the six sites in the Center for Infectious Diseases and Immune Modulation to scale up and conduct many of the important trials in addition to the ongoing and already planned clinical trials.

8. The COVID19-MITC project is planned to run until the end of July 2021. The project is steered by a committee consisting of the Trial Nation responsible medical doctor from each of the participating departments, the feasibility coordinator, and the facilitator from the Trial Nation secretariat. The steering group met every month to follow up on issues such as ongoing and planned trials, to ensure efficient resource utilisation, trial handling and making the most of national capability. 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, coordinate activities and share best practice on COVID-19 trials. These regular meetings have strengthened the collaboration within the Center for Infectious Diseases and Immune Modulation further.
9. One effect of this strengthened, close collaboration is that it has been possible to set up and initiate a huge COVID-19 phase IV vaccine trial (ENFORCE) within two months. The objective is to evaluate four COVID-19 vaccines in all five regions. 10.000 participants will be enrolled and followed for two years. The trial is funded by the Danish Ministry of Health and has started to enroll participants in 2021.

## Cost summary

In 2020, each of the clinical departments in Center for Infectious Disease and Immune Modulation was supported by a grant of DKK210,000. 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.

**Department of Infectious Diseases at Aarhus University Hospital** spent the grant expanding the capability to conduct commercial funded trials, expanding project staff and conducting education, training and network meetings. The Medical Lead participated in and chaired several meetings with the industry from Denmark and abroad to represent the center. There were two virtual center meetings this year. The coordinator worked closely with the facilitator of the center, handling feasibilities, pre-feasibilities and other requests from the pharma industry and taking responsibility for the feasibility and trial log.

**Department of Infectious Diseases at Odense University Hospital** spent the grant handling the increasing numbers of feasibilities and expanding the capacity for conducting clinical trials. They built a local biobank and database for COVID-19 patients and updated the HIV- and the hepatitis databases. They also established new databases for latent and active tuberculosis and infectious spondylitis.

**Department of Infectious Diseases at Copenhagen University Hospital, Rigshospitalet** spent the grant on expanding the clinical trial capacity in new locations, with room for an increased number of trials due to COVID-19. The databases have been updated for HIV, hepatitis, cerebral abscess, and COVID-19 which makes it possible to answer the feasibilities from commercial sponsors quickly.

**Department of Infectious Diseases at Zealand University Hospital, Roskilde** spent the grant on building and expanding the capacity to conduct sponsor-funded clinical trials. They hired a new employee and trained project nurses and project staff. They also performed further training of employees in administrative function to support the feasibility process.

**Department of Infectious Diseases at Aalborg University Hospital** spent part of the grant on a research nurse two days a week for feasibility handling, database updating, educating new employee and medical students, optimising the general trial support and workflow in clinical research department to be able to handle the increased numbers of trials. The rest of the grant (DKK117,133) will be transferred to the 2021 budget.

**Department of Infectious Diseases at Copenhagen University Hospital, Hvidovre** spent the grant on hiring a trial coordinator, who takes care of the trial overview, feasibility handling and communication with Trial Nation and the industry, administrative tasks related to staffing and budgets. Furthermore, the department hired and educated the medical students who are involved in clinical trials, which makes it possible to run an increased number of industry- and investigator-sponsored trials with a high quality.

The COVID19-MITC project provided additional funding to the Center for Infectious Disease and Immune Modulation. The project is funded with 75% by The Innovation Fund Denmark and 25% by the five regions. The total project cost (including self-financing) is DKK6.6M and is distributed equally between the six sites. The project period is May 2020 till end July 2021.

## Focus in 2021

1. In 2021, the center will continue attracting new trials and build on and further improve the national collaboration across departments, ensuring effective feasibility handling and follow up, secure sufficient capacity for clinical trials, and predictable deliverables including capture of relevant trial performance data and patient empowerment.
2. The experiences gained through the logistically highly complex and high patient number COVID-19 vaccine trial, ENFORCE, will boost Denmark's readiness for future large-scale vaccine trials.
3. It is expected that the field of vaccine studies will be an important part of the center's activities in the future and the center will specifically focus on attracting vaccine trials.
4. The center also expects COVID-19 treatment trials and trials investigating post-COVID-19 syndrome to be an important part of the 2021 portfolio.
5. The center will investigate the possibilities of building collaboration in the form of a network with other, smaller infectious disease clinics, to be able to further strengthen the collaboration with clinics that are active within the infectious disease area in Denmark.
6. Additionally, the center will further extend collaboration with other specialties, e.g., pediatrics, respiratory, and hematology to widen the range of study possibilities for the center.
7. 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.

## Special Cases to Point Out

During the COVID-19 pandemic, the Trial Nation Center for Infectious Disease and Immune Modulation managed to attract more than double the number of clinical trials than the year before. Notably, these departments have also had the main responsibility for the treatment of some of the patients most affected by COVID-19. This achievement was possible because of a huge dedication shown by the people working in this area and this center, and because of the close collaboration between research departments. This collaboration was already established with the Trial Nation network but expanded further during the pandemic.

The Center for Infectious Disease and Immune Modulation in many cases shared the relevant feasibilities with the Center of Respiratory Medicine. During this very busy year, it was also possible to establish meetings with foreign parent companies in collaboration with IiDK, and it was possible to attract feasibilities and trials to Denmark in areas where Denmark was not on the company's priority list.

# Center for Oncology

Medical Lead for the center was Senior Consultant & Phase I Unit Leader Kristoffer Rohrberg from The Phase I Unit at Copenhagen University Hospital. Research Coordinator Laurine Harsloeff from the Phase I Unit at Copenhagen University Hospital was responsible for national feasibility handling and coordination, while Ask Aabenhus from the Trial Nation secretariat was responsible for center facilitation.

The nine oncology departments treat almost all Danish oncology patients (pediatric, adolescent, or adult) and cover all phases of clinical trials. The few patients not covered by the center are mainly treated at Northern Zealand Hospital or late phase pediatric and adolescent patients treated at Odense University Hospital and Aarhus University Hospital.

*In 2020, the Center for Oncology consisted of the following trial sites:*

Department of Pediatrics and Adolescent Medicine at Copenhagen University Hospital (Rigshospitalet). Senior Consultant & Clinical Research Unit (CRU) Leader Karsten Nysom.

The Phase I Unit, Department of Oncology at Copenhagen University Hospital (Rigshospitalet). Senior Consultant & Phase I Unit Leader Kristoffer Rohrberg.

The Experimental Cancer Therapy Unit, Department of Oncology at Herlev and Gentofte Hospital. Clinical Professor & CRU Leader Dorte Nielsen and Consultant Rikke Eefsen.

Department of Oncology at Herning Hospital (Hospital Unit West). Senior Consultant & CRU Leader Halla Skulladottir.

Department of Oncology at Little Belt Hospital, Vejle Hospital. Senior Consultant Torben Frøstrup Hansen.

Department of Oncology at Odense University Hospital. Senior Consultant & CRU Leader Karin Holmskov and Clinical Professor & Research Leader Per Pfeiffer.

Department of Oncology at Zealand University Hospital. Clinical Professor, Clinical Professor & Research Leader Joern Herrstedt and Senior Consultant & CRU Leader Kell Erik Oesterlind.

Department of Oncology at Aalborg University Hospital. Clinical Professor Ursula Falkmer and Consultant CRU Leader Laurids Oestergaard Poulsen.

Department of Oncology at Aarhus University Hospital. Clinical Professor & Research Leader Signe Borgquist and Senior Consultant & CRU Leader Mads Agersbaek.

The Department of Oncology at Zealand University Hospital and at Herning Hospital (Regional Hospital West) joined the center from January 1st, 2020 to further broaden the geographic reach.

## Overall activities of feasibilities, trials and recruitment

The yearly activities are summarised in Table 5. Overall activities of feasibilities, trials and patients.and described below.

| Center for Oncology | 2018 | 2019 | 2020 |
|---|---|---|---|
| Number of feasibilities received | 83 | 65 | 115 |
| Number of initiated trials (phase I-II/all) | 16/16 | 18/18 | 10/29 |
| Number of trials open in year (phase I-II/all) | 50/50 | 59/59 | 71/134 |

*Table 5. Overall activities of feasibilities, trials and patients.*

## Feasibilities

The center received a total of 115 commercial feasibilities in 2020 via Trial Nation or documented by oncological departments forming part of the Center for Oncology. Even when figures from the new departments at Herning Hospital and Zealand University Hospital are subtracted, this is a substantial increase compared to 2019 where 65 feasibilities were documented. Trial Nation shared 34 feasibilities directly with the departments in the center. See distribution across trial phases in Figure 11. As in previous years, the numbers are subject to considerable uncertainty as most of the feasibilities are shared directly with Investigators leaving the clinical research sites uninformed in several cases and resulting in reporting bias. The numbers are therefore likely to be higher.

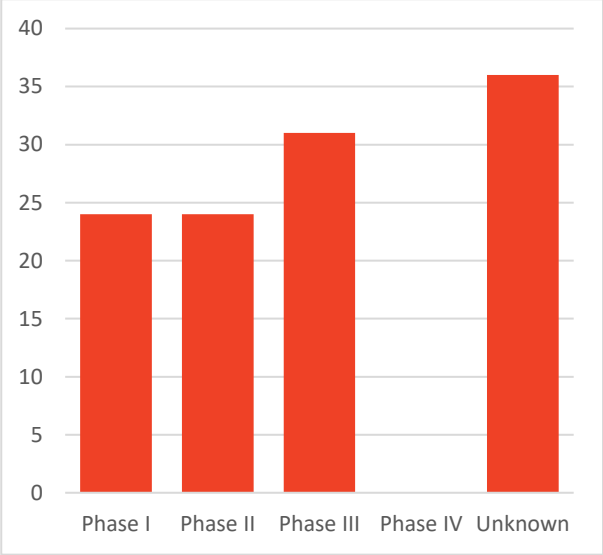



*Figure 11. Feasibilities received in 2020 by Trial Nation Center for Oncology or documented by affiliated departments.*

## Clinical trials

In 2020, 134 commercial clinical phase trials were reported. Of these, 71 were phase I-II trials compared to 59 the year before. Nine of the ongoing trials were pediatric oncology trials. As in previous years, the numbers are subject to uncertainty and are likely to be minimum estimates.

Of the 134 trials, the initiation of 29 commercial clinical trials in involving one or more of the clinical departments were reported, 10 of which being phase I-II. This means that the number of documented commercial clinical trial initiated in phase I-II was reduced by eight compared to 2019. The reduction is most likely due to the many challenges brought on by COVID-19 in 2020. The challenges include temporarily stalled recruitment as well as visit restrictions.

As in the past years, all departments were involved in the conduct of commercial clinical trials. See Figure 12.

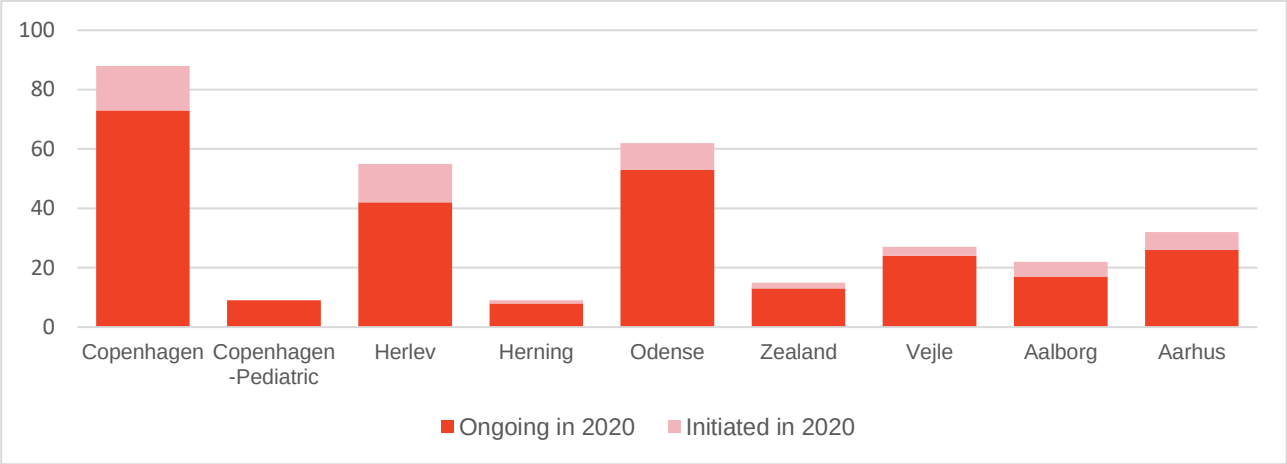



*Figure 12. Number of clinical trials ongoing and initiated in Trial Nation Center for Oncology in 2020.*

## Recruitment

In total, 591 patients were referred to the Phase I Unit at Copenhagen University Hospital for phase I treatment compared to 615 the year before. Of these patients, 89 received experimental treatment via a clinical trial, which is seven less than the year before.

Likewise, a total of 156 patients were referred to the Experimental Cancer Unit at Herlev and Gentofte Hospital for phase I treatment, of which 80 patients had a first visit at the clinic. These numbers, compared to 192 and 190 the year before, are marking a substantial decrease. However, numbers cannot be compared directly, as the procedure at the hospital was changed: Genomic profiling is now largely performed in the disease specific team in the department rather than at the Experimental Cancer Unit. This means that patients are only seen at the Experimental Cancer Unit if specific treatment can be offered.

Approximately 200 patients are discussed on the national tumor board yearly.

In conclusion: Despite the corona pandemic a substantial number of patients were referred to, and treated at, the Phase I Unit and the Experimental Cancer Unit.

Based on the available data (and data capture tools), further elaboration on recruitment figures is not possible.

## Center activities

Due to the COVID-19 pandemic, 2020 was a truly special year for the Danish oncology sites. Although oncology trials in Denmark may have been less impacted compared to many other European countries, recruitment in Denmark was definitely impacted by the pandemic. At most clinical sites, recruitment was paused for a short period during the spring, and for some sites in part again in December. Furthermore, some meeting activity was converted to web-meetings, but planned large physical meetings and conferences were postponed, and other activities were paused. Nonetheless, the following joint activities took place in Trial Nation Center for Oncology:

1. National sharing and handling of feasibilities.

    a. The national feasibility handling was returned to Department of Oncology at Copenhagen University Hospital from January 1, 2020
2. Referral of patients for clinical trials at other departments in the center
3. Web-center center meeting on the direction and organisation of the center
4. Supported the architectural design of a real-time national database on clinical trials.
5. Continued improvement of the collaboration with relevant patient organisations on clinical research
6. Round-table meeting in Boston for US medicinal companies showcasing Trial Nation Center for Oncology in collaboration with IiDK. The meeting lead to discussions with several companies about trials in Denmark and the start of several trials.
7. Company specific web-meetings with subsidiary and headquarter representatives.
8. Supported the Trial Nation CRO Network meetings

Issues to consider

1. National sharing of feasibilities is challenged by use of electronic feasibility platforms and electronic clinical management platforms. The challenges include but is not limited to the number of platforms to be supported, suboptimal user-friendliness, use of legal language (e.g. confidential disclosure) not approved by the hospitals legal counsel. This has been highlighted to the commercial sponsors, however in many cases it is outside the immediate control of local subsidiaries. In other cases, companies prefer to conduct the feasibility process on their own and seeks Trial Nations advise as to which departments and consultants to contact.
2. Precision medicine protocols effectively reduce the potential patient pool due to narrow selection criteria. Consequently, improved structures for referral of patients for all phases between hospitals for clinical trials within Denmark and within the Nordics are needed. The barriers identified so fare are mainly administrative, however complex of nature.
3. A national database on clinical trials is needed support clinician and patient knowledge of clinical trials open for recruitment in Denmark, which is a prerequisite to improve referral of patients for clinical trials.
4. A seminar on patient involvement in clinical trials was postponed several times during 2020 due to corona.
5. Stronger central and regional health policy and hospital prioritisation of clinical research is needed.

## Cost summary

The departments of the center have reported the following spending in 2020:

In 2020 each department in Center for Oncology were supported by a grant of DKK350,000 by Trial Nation to ensure preparedness for clinical trials. Copenhagen University Hospital was further supported with an additional DKK50,000 and DKK175,000 in support of the department's roles as Medical Lead and national

Feasibility Coordinator. A few departments did not use the full grant and have transferred the reminder for their 2021 budget.

**Copenhagen University Hospital, Department of Pediatrics and Adolescent Medicine** spent the grant responding to pre-feasibilities and feasibilities, consolidating its position, and participating in weekly conference calls on experimental treatment for children in the Nordic countries and adding an extra project nurse to the team including training.

**Copenhagen University Hospital, the Phase I Unit** spent the grant on national as well as local handling and coordination of pre-feasibilities and feasibilities and additional resources in the form of research nurses. Due to the pandemic physical participation in ASCO, AACR and ESMO was impossible. Still the Medical Lead has actively marketed Center for Oncology at individual company meetings and a round table meeting in Boston in February together with a representative from the Trial Nation secretariat and through other meetings in collaboration with the Trial Nation facilitator

**Herlev & Gentofte Hospital** spent the grant responding to pre-feasibilities and feasibilities, a 25% increase in phase I activity, updates of CVs, a 15% increase in commercial clinical trials, optimised processes for genetic-profiling, GMO handling and GCP-standards for para-clinical departments.

**Herning Hospital** spent the grant responding to pre-feasibilities and feasibilities, introduction of new staff to the Clinical Trial Unit and training of new staff, Shared Investigator Platform (SIP) completion, post-ESMO webinars, updating of DCCCs protocol overview, Trial Nation collaboration and budget developments.

**Odense University Hospital** spent the grant responding to pre-feasibilities and feasibilities, genetic-profiling, clinic for precision medicine, and supporting the use of the Shared Investigator Platform (SIP).

**Zealand University Hospital** spent the grant responding to pre-feasibilities and feasibilities and the employment of a medical leader for the clinical research site and project nurse and to free up time for investigators participating in commercial clinical trials.

**Aalborg University Hospital** spent the grant responding to pre-feasibilities and feasibilities, COVID-19 changes to timelines and protocol etc., the employment of an addition two project nurses, training activities and the Shared Investigator Platform (SIP).

**Aarhus University Hospital** spent the grant responding to pre-feasibilities and feasibilities, established a unit for precision medicine in collaboration with the Department for Molecular Medicine and for the development of a database to support the new site.

## Focus in 2021

In 2021, 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 (web-based), marketing the competences in the center and at the departments to the industry. The activities will be conducted in collaboration with IiDK 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. Supporting the development of a national database on clinical trials. This will improve referral of patients for clinical trials and provide patients with an opportunity to seek participation in clinical trials.
7. Raising awareness on the importance of prioritisation of clinical research with regional and national decision makers.

## Center for Respiratory Medicine

In 2020, Center for Respiratory Medicine consisted of the following research units and their Trial Nation responsible medical doctors:

*In 2020, the Center for Respiratory Medicine consisted of the following trial sites:*

Respiratory Research Unit, Dept. of Respiratory Medicine, Copenhagen University Hospital-Hvidovre. Professor, Senior Consultant Charlotte Suppli Ulrik.

Respiratory Research Unit, Dept. of Respiratory Medicine, Copenhagen University Hospital-Bispebjerg. Professor, Senior Consultant Celeste Porsbjerg.

Respiratory Research Unit, Dept of Respiratory Medicine, Næstved University Hospital, Professor. Senior Consultant Uffe Bødtger.

Respiratory Research Unit, Dept. of Respiratory Medicine, Odense University Hospital. Senior Consultant Ingrid Louise Titlestad.

Respiratory Research Unit, Dept. of Respiratory Medicine, Aalborg University Hospital, Senior Consultant Ulla Møller Weinreich.

Respiratory Research Unit, Dept. of Respiratory Diseases and Allergy, Aarhus University Hospital (Professor, Senior Consultant Elisabeth Bendstrup)

The Center for Respiratory Medicine was established in 2016 and is being led by Professor Charlotte Suppli Ulrik from Copenhagen University Hospital Hvidovre. Within the Center for Respiratory Medicine, the capital region is represented by two sites, and the four remaining regions by one site. The Trial Nation Center for Respiratory Medicine is also part of the larger Respiratory Medicine Research Network, which consists of all sites in Denmark taking part in pharma-sponsored clinical trials within the respiratory field. All feasibilities were circulated to all relevant sites within Center for Respiratory Medicine (and the Respiratory Medicine Research network). This open handling of feasibilities within the network did not interfere with the sponsors' right to select their preferred sites.

Mikkel Lindskov Sachs and (since late 2020) Annette Buusman from the Trial Nation secretariat were facilitators of the center.

## Overall activities of feasibilities, trials and recruitment

A total of 22 clinical trial feasibilities involving four phase I-II feasibilities, nine phase III-IV feasibilities and nine feasibilities of undisclosed phase involving one or more of the clinical departments were performed in Center for Respiratory Medicine in 2020 (see Table 6 below).

| Center for Respiratory Medicine | 2018 | 2019 | 2020 |
|---|---|---|---|
| Number of feasibilities received | 18 | 24 | 22 |
| Number of initiated trials | 2 | 13 | 10 |
| Number of trials open in year | 4 | 19 | 31 |
| Number of patients enrolled in trials | 38 | 124 | N/A |

*Table 6. Overall activities of feasibilities, enrollment, and trials. The number of recruited patients is not available for 2020.*

### Feasibilities

A total of 22 commercially funded feasibilities were received and shared in the Center for Respiratory Medicine in 2020 (see distribution across trial phases in Figure 13 below).

Of the 22 feasibilities received, 11 resulted in one or more center departments participating in a clinical trial. Three were declined, and six feasibilities are currently circulating in the departments in the Respiratory Network. For two feasibilities, there are no data yet on the outcome.

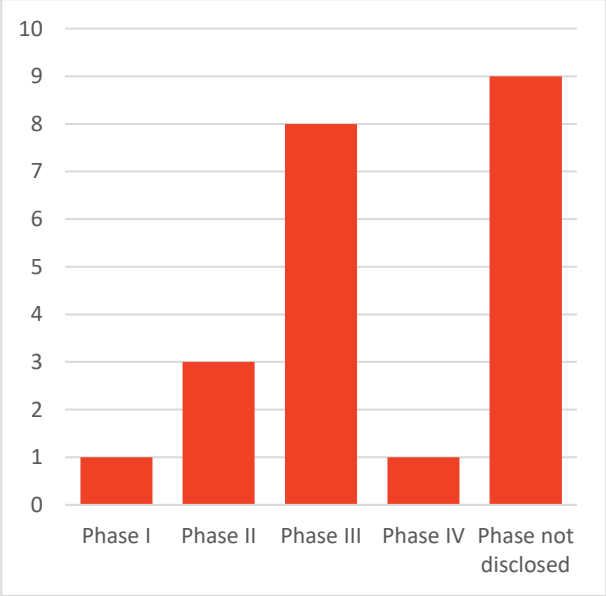



*Figure 13. Number of feasibilities received in Center for Respiratory Medicine in 2020.*

It is noteworthy that in spite of the many setbacks suffered in the research community as a consequence of the COVID-19 pandemic, the number of feasibilities resulting in clinical trial participation has more than doubled (from five in 2019 to 11 in 2020). This achievement is put into perspective by recent reports that in many other European countries, clinical trial activities have been put almost entirely on hold. It is therefore a strong indication of an increased capability and preparedness for clinical trial participation at the departments in the center.

## Clinical trials

In 2020, the Center for Respiratory Medicine initiated a total of 10 commercial clinical trials involving one or more of the clinical trial sites. Nine trials are already planned for initiation in 2021. Overall, 31 clinical trials were ongoing in 2020, as 21 trial initiated in 2019 was still open in the first half of 2020 (See Figure 14 below). This is a substantial increase in clinical trial activity compared to the 19 trials ongoing in 2019.

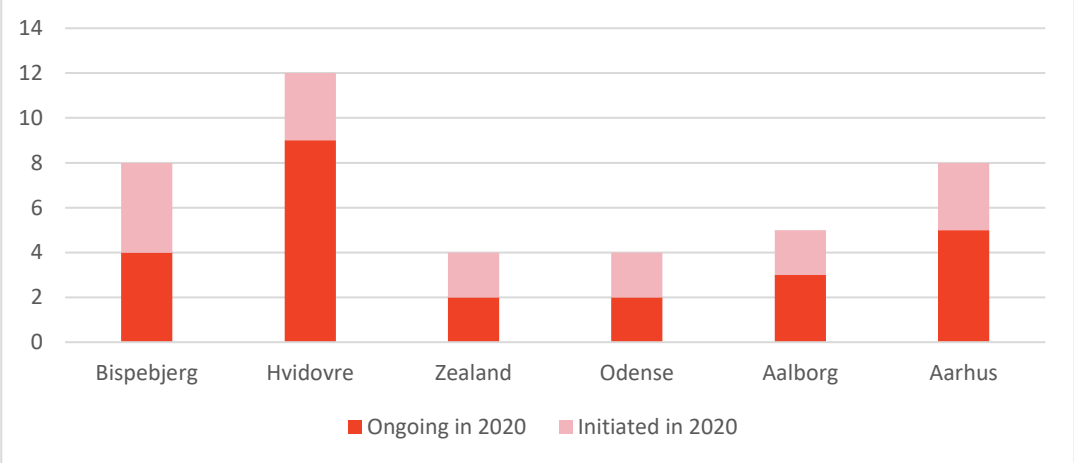



*Figure 14. Number of clinical trials ongoing and initiated in Center for Respiratory Medicine in 2020.*

By the end of 2020, all departments were involved in the conduct of between four and 12 clinical trials, and 31 ongoing trials were performed with all six sites involved. For an overview of distribution of clinical trials by phase, see Figure 15.

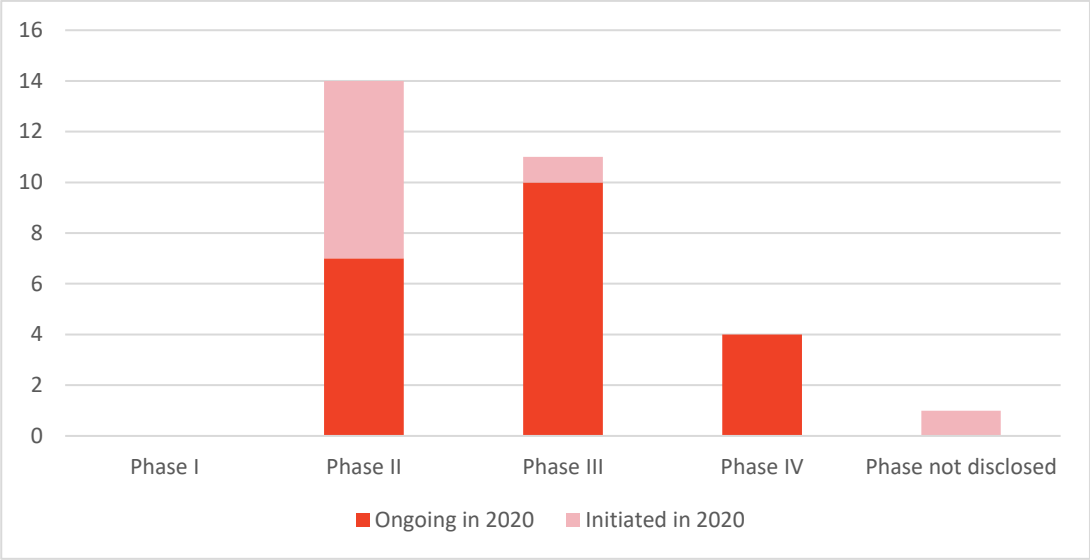



*Figure 15. Number of ongoing and initiated clinical trials in Center for Respiratory Medicine in 2020, distributed across trial phase.*

### Recruitment

Patient recruitment was particularly challenging in 2020 because of the COVID-19 pandemic, as described below. The number of recruited patients is not available for 2020.

## Center activities

1. All departments have strived to perform according to the goals set for 2020, despite the huge setback suffered because of the COVID-19 pandemic. All aspects of running clinical trials presented challenges, with patient recruitment and staff resources being particularly difficult to maintain. Despite these obstacles, the center departments managed to run an impressive number of trials and quickly adapt to circumstances by developing new ways of working and treat patients in an increasingly virtual setting.
2. General activities included national sharing and handling of feasibilities, meetings with sponsor companies on study related topics, and collaborating closely with Trial Nation and other relevant stakeholders.
3. In November, Trial Nation and the Danish Lung Association signed a partnership agreement, with the overall purpose of increasing access to clinical trial participation for Danish patients with respiratory diseases. The infrastructure for clinical trials established in the Trial Nation Center for respiratory medicine will be a great asset for this work. Other collaborative initiatives will include the development of information material about clinical trials, as well as increasing the awareness about ongoing clinical trials of relevance for this group of patients.
4. In December, the Danish Respiratory Medicines network held its annual meeting, which of course this year was executed as a fully virtual event. Participants included clinicians, Trial Nation staff from all over Denmark, as well as representatives from the pharma industry and the Danish Lung

Association. The overall theme of the meeting was to share best practice concerning the challenges of running clinical trials in a time of a pandemic.

5. In addition to the activities in the Center for Respiratory Medicine, it should be noted that departments in the Respiratory Medicine Research Network were involved in nine clinical trials in 2020. Feasibility inquiries from the Trial Nation coordinator are distributed to all departments in Denmark specialised in respiratory medicine, thus generating a considerable amount of research activity also at sites not supported by a grant from Trial Nation. This positive synergy will continue to play an important role in the endeavors to attract clinical trial activity to Danish sites in the respiratory therapeutic area.
6. A donation from the pharmaceutical company Novartis Healthcare A/S was another example of collaboration between departments not only in the center, but in the entire Network. The grant was intended to support clinical research specifically related to COVID-19, and funds were distributed to members of the Network with ongoing clinical trials in this indication, helping to increase the general capacity for clinical research in respiratory medicine in Denmark.

## Cost summary

In 2020, each of the clinical departments in Center for Respiratory Medicine was supported by a grant of DKK210,000 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, and the network coordinator in Region Zealand received DKK175,000 in total to support the national feasibility handling and coordination of network activities.

At **Respiratory Research Unit, Department of Respiratory Medicine at Copenhagen University Hospital-Hvidovre**, the focus was to maintain study activities to the extent possible, despite the challenging situation caused by the pandemic. The site participated in many COVID-19-related studies, and in one of them, a global pharma-sponsored study, the medical lead as national coordinating PI, managed to globally recruit the first patients in the trial. After the first wave of the pandemic, the team has initiated a large number of clinical trials and implemented ways of working which will make the site more resilient towards future waves and consequences of the pandemic.

Furthermore, in 2020 members of the research team co-authored more than 30 papers accepted for publication in peer-reviewed scientific journals.

At **Respiratory Research Unit, Dept. of Respiratory Medicine, Copenhagen University Hospital-Bispebjerg**, the primary focus has been to increase efficiency in patient recruitment. The unit succeeded in establishing a patient database and initiated targeted recruitment activities on social media. Furthermore, many resources were spent on training activities, as a consequence of staff turnover among study nurses and laboratory staff.

At **Respiratory Research Unit, Dept of Respiratory Medicine, Næstved University Hospital**, the grant form Trial nation was spent on expanding the research team, which enabled the site to participate in more complicated studies, and in larger numbers, than the previous years. Many resources were spent mitigating

the effect of COVID-19 on patient visits, such as swabs prior to visits, changes to the CRF and challenges in recruiting. Furthermore, the clinic has been instrumental in knowledge-sharing around clinical pharma-studies with other clinical departments at the hospital.

At **Respiratory Research Unit, Department of Respiratory Medicine, Odense University Hospital**, the primary focus has been on activities in connection with answering feasibilities, preparing for clinical trials, and budgeting. Furthermore, the site was involved in several COVID-19-related trials, some of them in collaboration with specialists in infectious diseases. Plans for the coming year include establishing new recruitment databases and continued collaboration with colleagues across therapeutic areas.

At **Respiratory Research Unit, Dept. of Respiratory Medicine, Aalborg University Hospital**, the primary focus has been to strengthen the recruitment procedures and develop the research site through the pandemic; many patients were previously recruited at the rehabilitation and outpatients' hubs, which were almost completely shut down for most of 2020. The plans to set up a satellite site at another hospital in the region also had to be postponed due to the consequences of the pandemic.

The research lab has been re-designed to optimise processes, and a tool for obtaining electronic informed consent was developed (implemented in Q3). Furthermore, the necessary equipment for virtual meeting activities was purchased and implemented in practice.

At **Respiratory Research Unit, Dept. of Respiratory Diseases and Allergy, Aarhus University Hospital**, the primary focus has been funding an expansion of the clinic with a coordinating study nurse, as well as strengthening the staff resources at the research lab. Furthermore, normal study activities have been maintained. The site had the function of national coordinating investigator (NCI) in seven studies, including contract negotiations with pharma companies and reviewing all study related information for patients and ethics committees. The grant was also spent on new equipment for the research lab and the set-up of a walk tester with e-transfer of the data to the electronic patient journal.

### Focus in 2021

In 2021, the center will focus on attracting new, especially early phase trials and improving the national collaboration across sites, ensuring 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. The following activities will help achieve this goal:

1. Meetings within the respiratory network and across Trial nation centers, where relevant.
2. Following up on feasibilities in each department in a way that allows for deeper understanding and consolidation of data.
3. Continued collaboration with the pharma industry, facilitated by Trial Nation, e.g., at meetings in conjunction with scientific congresses.
4. Optimising key deliverables in clinical trials, including time from site initiation to First Patient First Visit.

# Danish Pediatric Network (DanPedMed)

The network DanPedMed was established in 2016 through a collaboration between the Danish Pediatric Society and the Danish Society of Clinical Pharmacology. Today, DanPedMed is funded by Trial Nation. DanPedMed corresponds to similar networks in the Nordic region, which work together through NordicPedMed.

DanPedMed involves all pediatric departments in Denmark, including direct contact to 150 clinicians working within the field.

## Governance and

The national coordinator was responsible for handling all enquiries regarding industry-sponsored and investigator-initiated clinical trials, including pre-feasibility and feasibility enquiries. It also included knowledge-sharing regarding Pediatric Investigational Plans, PIPs. The national coordinator ensured contact to relevant clinicians at pediatric departments to facilitate participation in relevant research collaborations, including clinical trials.

*In 2020, the Pediatrric Network DanPedMed consisted of the following members:*

*Chair: Lene Hartmann, Advisor at Data and development support, Region Zealand.*

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

Rene Mathiasen, NordicPedMed representative. Consultant at the Department for Pediatric and Adolescent Medicine, Pediatric oncology, Rigshospitalet, University Hospital Copenhagen.

Torben Laursen, NordicPedMed representative. Consultant at the Department for Clinical Pharmacology, Aarhus University Hospital.

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

Søren Hagstrøm, Member of the Danish Society of Pediatrics. Consultant at the Department for Department of Pediatric and Adolescent Medicine; and Department of Clinical Medicine. Aalborg University Hospital.

Anne-Cathrine F.Viuff, PhD., Member of the Danish Society of Pediatrics. Consultant at the Department for Department of Pediatric and Adolescent Medicine. Aalborg University Hospital.

## Activities in 2020

The network disseminated knowledge about clinical trials and research collaborations by managing enquiries and by arranging meetings for doctors, project nurses and other project staff.

32 enquiries were received and distributed in the network. The inquiries divide into different types as follows:

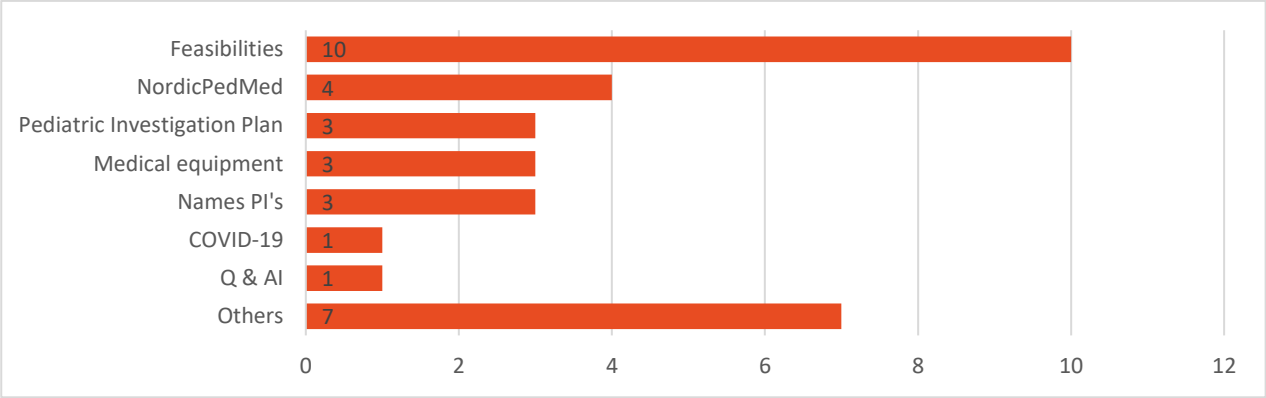



*Figure 16. The enquiries received and distributed in DanPedMed in 2020.*

An annual working meeting was held in Copenhagen in February 2020 with representation of pediatricians, clinical pharmacologists, the steering committee, and a representative from Trial Nation.

Since September 2020, the National Coordinator has worked 30 hour/week to expand the work in DanPedMed and to increase attention clinical trials within the pediatric field.

Trial Nation and DanPedMed is part of the large, pan-European Innovative Medicines Initiative (IMI) project Connect4Children (C4C). IMI has given a grant of up to EUR10,000 annually to cover activities related to C4C, making it possible for DanPedMed to be a part of the pan-European network for sites with interest in clinical trials in children. DanPedMed contributes to three specific tasks in the C4C project description. A 3rd party agreement is established with Haukeland Hospital in Bergen, which is the national hub of Norway, and this is the first step towards making DanPedMed a national Danish hub in C4C. The Department of Neonatology, Rigshospitalet, Denmark is included as a site in one of four investigator-initiated clinical trials running under C4C. Today, DanPedMed has an updated site description for four upcoming feasibilities related to industry-sponsored clinical trials under the C4C.

DanPedMed is also an active partner in NordicPedMed, with Pernille Skovby (in the role of secretary) arranging monthly meetings.

DanPedMed as a network has increased its activities, including raising awareness of the benefits of performing sponsor-initiated clinical trials. Today, more departments at pediatric and adolescent hospitals run industry-sponsored trial clinical trials for children and adolescents, with several enquiries referred from DanPedMed. It is possible to get advice and help to get started with clinical trial as DanPedMed offers advice to Departments of Pediatric and Adolescent Medicine in Denmark. In addition, DanPedMed has achieved a stronger connection to C4C by actively taking part in meetings and working groups.

## Cost summary

DanPedMed has during 2020 received a Trial Nation grant of DKK180,000 to finance the role of national coordinator.

### Focus in 2021

1. In 2021, DanPedMed will continue strengthening national collaboration on medicines for children and be an attractive member of the C4C network. This will be achieved through participating in international meetings related to C4C.
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. DanPedMed willl be hiring three study nurses eight hours/week with the grant from Trial Nation. These three study nurses will work across the country in close cooperation with the steering committee and the National Coordinator to strengthen the sites' readiness to conduct industry-sponsored clinical trials.

## DCT – Decentralised Clinical Trials

### Background

Trial Nation is a part of the project Decentralised Clinical Trials (DCT), in partnership with Studies&Me, LEO Pharma, Novo Nordisk, and Bispebjerg Hospital. The project has been granted two-year funding from Innovation Fund Denmark. The project will explore ways of performing clinical trials in which patients and trial staff are not necessarily at the same physical location. A trial can have several decentralised features. These are described briefly below. DCTs are more dynamic, offer easier patient access, better data and potentially lower cost. Although the project mainly has a national scope, it is also a steppingstone for Denmark to take the lead on decentralised clinical trials in the EU, where further experience and regulatory framework for decentralised clinical trials is still required. The DCT project kicked off late 2019, and already in 2020 the project gained great momentum as the first fully decentralised clinical trial in Denmark was initiated. The project was further accelerated due to the COVID-19 pandemic, where clinical trial teams were forced to adapt to decentralised settings and digital technologies.

### Framework activities

Trial Nation facilitated the first large meetings in Denmark with decentralised clinical trials on the agenda, with participation from patient organisations, pharmaceutical companies, authorities, and investigators. There was a substantial interest from all sides and a need for knowledge, experience, and collaboration was expressed. It was commonly agreed that it is important for Denmark to lead the way and be first mover, and to become the preferred country for decentralised clinical trials, thereby ensuring that Danish patients get faster access to even better treatment than today. Input from the dialogues on experiences, aspirations, and especially challenges with decentralised clinical trials were compiled in two papers. The aim was to create awareness of the cornerstones of decentralised clinical trials, and to show how we work on implementing decentralised clinical trials in Denmark. The papers were produced to target all stakeholders inside the clinical ecosystem as well as outside. The papers were distributed through our communication channels, cited in relevant fora, and received great attention.

The Danish Medicines Agency (DKMA) is actively supporting the development in decentralised clinical trials. The Agency has started a project with the aim of ensuring a contemporary and robust regulatory framework for digitalisation and decentralisation of clinical trials. Denmark will, through this commitment, maintain its strong position in clinical research for the benefit of patients. DKMA encourage sponsors to contact them and initiate a dialogue about all decentralised trials. Furthermore, they wish to collaborate on conduction of pilot projects with elements of decentralised clinical trials. To ensure strong interactions between authorities, patients, researchers, and the industry, DKMA and Trial Nation have set up a forum for dialogue on decentralised clinical trials. The forum provides opportunity for discussion of views, barriers, and experiences with DCT and of regulatory processes, which are not framed at present. The first forum was held in August 2020, and future meetings are planned for every third month.

Trial Nation, the Danish Medicines Agency, and the Danish Association of Pharmaceutical Industry established a collaboration with Innovation Center Denmark (ICDK) 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 plans for webinars for knowledge sharing will be discussed in the beginning of 2021.

### Status – Trial Related Activities

Various decentralised elements can be implemented in a clinical trial, as shown in Figure 17. The decentralised elements that were in focus in the studies initiated in the DCT project are indicated with a checkmark. Some of the decentral elements have been executed in Denmark for some time, e.g., recruitment on social media and electronic signature in the consent process. The next generation of clinical trials elements in the DCT project includes remote assessment of pre-screening and eligibility, as well as community engagement. Examples include study information performed at a hospital pharmacy, collection of biological samples at home, and collection of endpoints based on uploaded mobile phone photos taken by the patient.

The studies in the DCT project are fully decentralised studies, meaning that all elements are integrated in an application for the patient to download. Patients in that type of study do not have any site visits, and all data are collected remotely. The first study is a non-interventional study. In 2021 a decentralised clinical trial is planned to be initiated including investigational medicine; there will be site visits but of a lower frequency compared to a traditional trial.

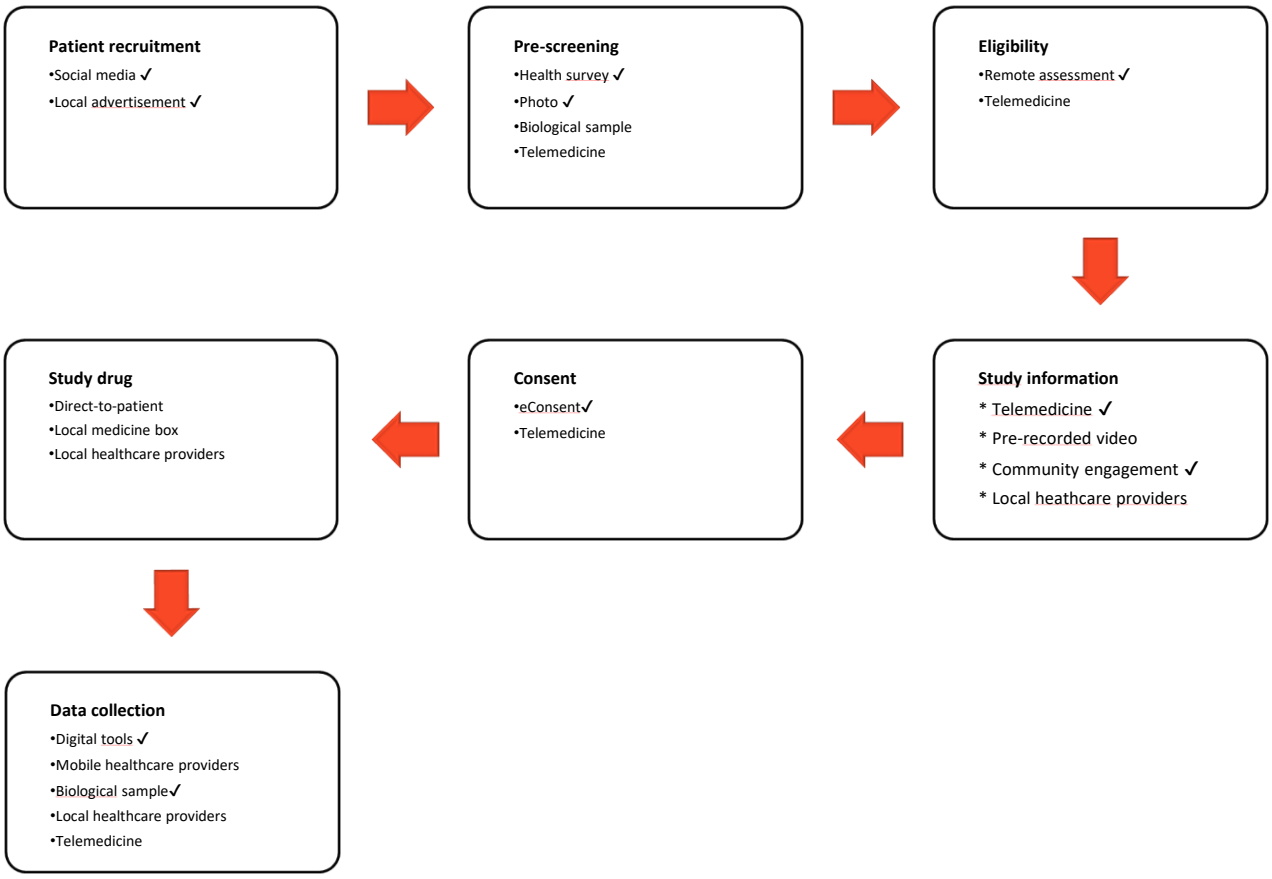



*Figure 17. The boxes reflect the patient-involving elements in a traditional clinical study. The subpoints show a decentralised approach to the elements. The decentralised elements deployed in the DCT project is indicated with a green checkmark.*

### Cost summary

The DCT project is funded for two years by Innovation Fund Denmark with a grant amounting to DKK15M, where the total budget for Trial Nation is DKK2M, including a self-financing rate of 20%. Since December 2019, the Head of Decentralised Clinical Trials Development has worked full-time on the project.

### Focus in 2021

1. Trial Nation will continue to work with the collaboration partners from pharmaceutical companies, hospitals, regulatory authorities, and patient organisations to complete the tasks of the DCT project and to frame a more long-term strategy of DCT.
2. Trial Nation will compile input, experiences, and incentives from relevant stakeholders in a paper to showcase DCT in Denmark.

## Trial Nation MedTech center

The center was started in 2020 and represented by MedTech coordinators from all five regions. Mikkel Lindskov Sachs from Trial Nation Secretariat coordinated center activities.

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

The Center has produced a form to guide interactions with companies and entrepreneurs to streamline the process for contacts. This is available at our website trialnation.dk. In 2020, three contacts from companies were made.

The Center published a call in December 2020 for MedTech projects with artificial intelligence to investigate development and implementation is completed successfully. The call read:

> *How is a clearer path paved for the development and implementation of medical devices that use artificial intelligence?*
>
> *Whether you are affiliated with a knowledge institution, public authority, or private company, and no matter where in the country you are located, Trial Nation will invite you who have insights into developing medical devices with artificial intelligence to contribute to the solution of the points below:*
>
> - *Document the path to clinical trials with artificial intelligence and help identify challenges to success.*
> - *Develop generic knowledge of what it takes for artificial intelligence to be used and implemented in the clinic. What barriers and opportunities exist along the way?*
> - *Create and share knowledge across Denmark about the introduction of medical equipment with artificial intelligence.*

See the entire call here. Trial Nation expect first results late 2021.

## Overall activities of trials

Data extraction was performed using GlobalData, a data analytics database provide data on trial activity, including activity related to testing of medical devices.

Two time periods were chosen, January 1st 2010 to December 31st 2019 and January 1st 2020 to December 31st 2020, to compare the development in selected parameters for clinical trials over time, see Table 7.

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

*Table 7. Ongoing and completed clinical trials on medical devices. Data source: Global Data Feb. 2021. In 2020, slightly fewer trials were recorded than the average for the previous 10 years. Half of the trials were initiated by a single sponsor, multiple sponsors, accordingly, initiated the remaining trials.*

## Data

Cardiovascular Devices, General Surgery and Specialised Sectors were the three markets with most clinical trials in the 2010s. Coronary Artery Disease, Pain, Diabetes Mellitus and Heart Failure were the top three indications that attracted most clinical trials in the 2010s (with Diabetes Mellitus and Heart Failure tied for third place), see Figure 18.

Cardiovascular Diseases, Anesthesia and Respiratory Devices and General Surgery were the three markets with most clinical trials in 2020. COVID-19, Respiratory Failure, and Cardiovascular Diseases were the top three indications that attracted most clinical trials in 2020, see Figure 19.

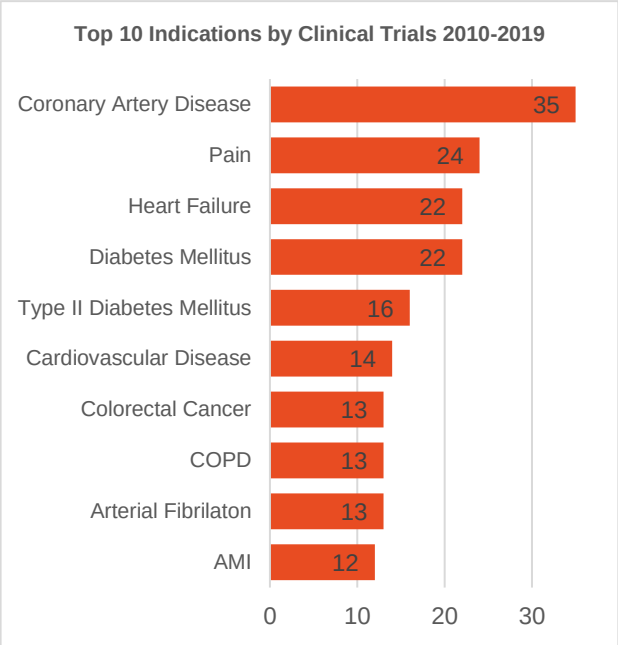



*Figure 18. Top 10 Ongoing and completed clinical trials on medical devices by indication from 2010 to 2019. COPD: Chronic Obstructive Pulmonary Disease. AMI: Acute Myocardial Infarction.*

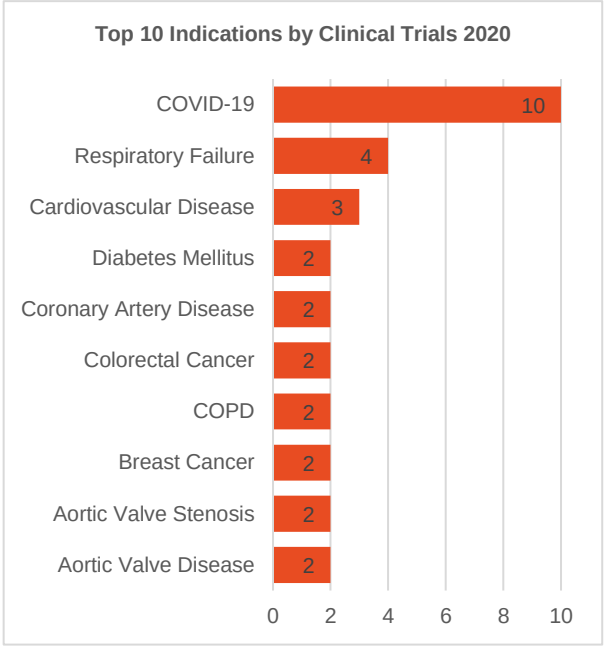



*Figure 19. Top 10 Ongoing and completed clinical trials on medical devices by indication in 2020. Note the prominent shift in indications relevant to the pandemic. COPD: Chronic Obstructive Pulmonary Disease.*

## Cost summary

| Budget approved late 2020 | |
|---|---|
| Artificial Intelligence | DKK 990,000 |
| Road map | DKK 270,000 |
| Infrastructure | DKK 360,000 |
| Innovative procurement | DKK 180,000 |
| Total | DKK 1,800,000 |

## Focus for 2021

In late 2020, the role of Center Coordinator was transferred from Mikkel Lindskov Sachs to Louise Hansen from North Denmark Region. The transfer marks a transition for the center, from a phase of definition and strategy development in 2020 to a phase of execution in 2021. The Center will continue to implement the strategy confirmed by the Board of Directors. This includes

1. Upgrading skills for center advisors
2. Establishing a forum for healthcare professionals working with MedTech trials
3. Continued collaboration with *Invest In Denmark* and *HealthCare Denmark*.