

Annual Report 2018

Trial Nation
Clinical Trials Denmark

Executive Summary

This annual report is mainly concerning the activities of NEXT Partnership, as the association Trial Nation was founded in December 2018.

As NEXT Bioinformatics is closing, [a separate, final report is available for the center](#).

On March 2nd, 2018, the government announced its Growth Plan for Life Science. NEXT was highlighted as a future governmental investment ensuring a nationally coordinated prioritization of clinical trials in Denmark. This organization should combine and operationalize the assets of both Clinical Trials Office Denmark and NEXT Partnership.

On December 5th, 2018, Trial Nation was founded as the national organization promoting clinical trials. 12 Board members were elected at the founding meeting. The new organization will attract clinical trials to Denmark, generating and anchoring new knowledge about medicines and medtech – for the benefit of society, industry and patients. Trial Nation will carry out this role with an even broader foundation with the inclusion of Ministry of Health and Ministry of Industry, Business and Financial Affairs.

In 2018, NEXT was successfully promoted in several contexts:

- In May, Center for Infectious Diseases was introduced at the Consulate General of Denmark in New York. The center was introduced to the US companies Helocyte, Merck, Novavax, Pfizer, Siga Technologies & ViiV/GSK. The Consul General of Denmark, Anne Dorte Riggelsen, hosted the event.
- In June, NEXT arranged and participated in three debates at the Peoples Political Festival at Bornholm. NEXT also hosted a reception to celebrate being a part of the government's Life Science Growth Plan.
- In September, industry decision makers met with executive clinicians from Trial Nation Center for Respiratory Medicine at an event at Maison du Danemark, Paris.
- In November, NEXT presented at BioEurope together with Invest in Denmark.

It is the intention that the increased marketing activities towards companies in 2018 leads to continued increased volume of clinical trials in 2019.

Our clinical centers made the following structural changes in 2018:

- Center for Oncology and Hematology was split into two centers to increase focus on each specialty and to improve marketing strategy. Professor Niels Abildgaard, Odense University Hospital, is now Medical Lead for Center for Hematology and Kristoffer Staal Rohrberg, Phase 1 Unit of Rigshospitalet, is Medical Lead for Center for Oncology.
- A new disease area was included in NEXT in 2018. We established a network with departments treating dementia; NEXT-Link Dementia with professor Gunhild Waldemar and Peter Johannsen from Rigshospitalet as Medical Leads. Lundbeck joined NEXT as a partner following the establishment of the Dementia network.

Key focus in 2019 is to complete the transition from a project funded by the Danish InnovationFund to an independent association with governmental and regional support that includes both regionally anchored legal, pharma- and medtech advisors and a central secretariat. Furthermore, the association will continue the focus on attracting clinical trials to Denmark. It will strengthen collaboration within the entire ecosystem of clinical trial stakeholders: Clinicians, Industry, Universities, Regulators and Patients.

Key Metrics

In 2018, we have recorded a total of 188 completed feasibility requests, 48 initiated trials and 138 ongoing trials across all centers. The table below breaks down the numbers per center and compares to the previous year. The trial activity has increased significantly from 2017 to 2018. The most obvious reason is inclusion of late phase trials in centers for Dermatology, Infectious Diseases, Respiratory Medicine and Dementia. In addition, four departments were added to the center of Hematology, representing a strong activity. These are the departments of hematology at Copenhagen University Hospital, Herlev Hospital, Little Belt Hospital - Vejle Hospital and Zealand University Hospital.

		NEXT1 Centers		NEXT2 Centers			
		Onco	Hema	Derma	Infection	Resp	Dementia
Feasibilities	2018	83	32	29	18	20	6
	2017	*65	*13	*12	13	16	n/a
Initiated	2018	*16	*8	15	2	5	2
	2017	*11	*3	*6	*3	*4	n/a
Ongoing	2018	*50	*32	40	4	5	7
	2017	*49	*10	*7	*3	*8	n/a

Table 1: * Only Phase I and II trials

Annual Accounts 2018

The NEXT departments of the regions have reported the following spending in 2018:

NEXT1	Adjusted activity	Actual activity	Budget
Region Hovedstaden	12,885	30,345	13,814
Region Midt	2,222	2,484	2,989
Region Nord	1,938	1,980	2,440
Region Syd	3,344	3,984	3,969
Bioneer	4,569	4,569	3,976
Total	24,958	43,364	27,188

Table 2: NEXT1 spending and budget for 2018 in DKK 1,000

NEXT2	Adjusted activity	Actual activity	Budget
Region Hovedstaden	5,056	5,833	5,063
Region Midt	2,014	2,014	2,658
Region Nord	1,564	1,803	1,564
Region Syd	2,070	2,070	2,344
Region Sjælland	661	895	965
Bioneer	9,172	12,583	9,172
OPEN	340	340	890
Total	20,877	25,538	22,656

Table 3: NEXT2 spending and budget for 2018 in DKK 1,000

If the actual reporting of activity in a year exceeds the budget per department, the maximum payed amount is the budget level, according to project guidelines.

The private NEXT partners have reported the following trial portfolio (money spent for the conduct of clinical trials e.g. directly paid money and in-kind expenses in the company that can be accounted for) and hours spent in NEXT activities in steering committee meetings, general NEXT meetings and general activities apart from specific trial related activities in 2018:

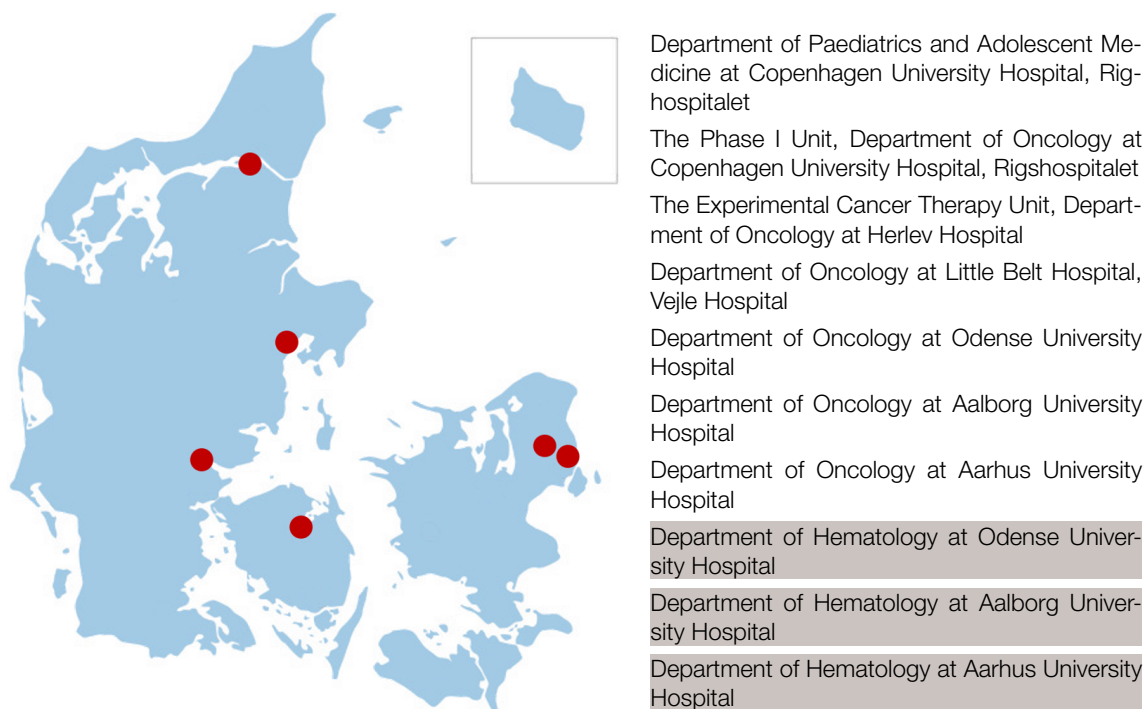
Private NEXT partners	Actual	Investment Agreement
Trial portfolio NEXT1	48,670	14,100
Trial portfolio NEXT2	5,769	32,070
Time spent as partner representative in NEXT1	11,961	6,850
Time spent as partner representative in NEXT2	2,366	8,040

Table 4: Reported and budgeted NEXT Trial portfolio 2018. Based on reporting from 14 partners, and thus not a reflection of the complete activity in the centers.

NEXT 1

Center for Oncology

Center for Oncology and Hematology consisted of the following departments in the first half of 2018:



The hematologic departments (grey shaded) in the center were split out as of 1st July, when the Center for Oncology was formed. Accordingly, Center for Oncology at the end of 2018 consisted of seven departments.

Medical Lead for the Center for Oncology and Hematology and the Center for Oncology after the split from the hematologic departments was Chief Consultant Morten Mau-Sørensen from The Phase I Unit at Copenhagen University Hospital. However, in December 2018 Morten Mau-Sørensen handed over the Medical Lead role to Chief Consultant Kristoffer Rohrberg from The Phase I Unit at Copenhagen University Hospital.

The seven oncology departments cover the vast majority of the Danish population, treat all oncology diagnoses in pediatric, adolescent and adult patients and cover all phases of clinical trials.

The yearly activities are summarized in Table 5 and described below.

Overall activities of feasibilities, trials and patients

A total of 82 clinical trial feasibilities involving 54 phase I-II feasibilities, 22 phase III-IV feasibilities, and 26 feasibilities of unknown phase involving one or more of the clinical departments were performed in Center of Oncology in 2018 (see Table 5 below). Also,

a biomarker feasibility was performed. 22 of these feasibilities were shared via the secretariat, whereas the secretariat assisted sponsors with the identification of appropriate departments and investigators for an additional 21 feasibilities.

Center for Oncology	2016	2017	2018
Number of feasibilities received	56*	65	83
Number of initiated trials	16*	11	16
Number of trials open in year	51*	49	50

Table 5: Overall activities of feasibilities, trials and patients. * Figures cover both hematology and oncology

Clinical trials

In 2018, Center for Oncology initiated a total of 16 commercial clinical phase I & II trials involving one or more of the clinical trial units. 14 trials are already planned for initiation in 2019. Overall, 50 clinical trials were ongoing in 2018, as 34 trial were ongoing from earlier years. 10 of the ongoing trials were pediatric and four of these were initiated in 2018.

By the end of 2018, all departments were involved in the conduct of between 2 and 27 clinical trials. See Figure 1.

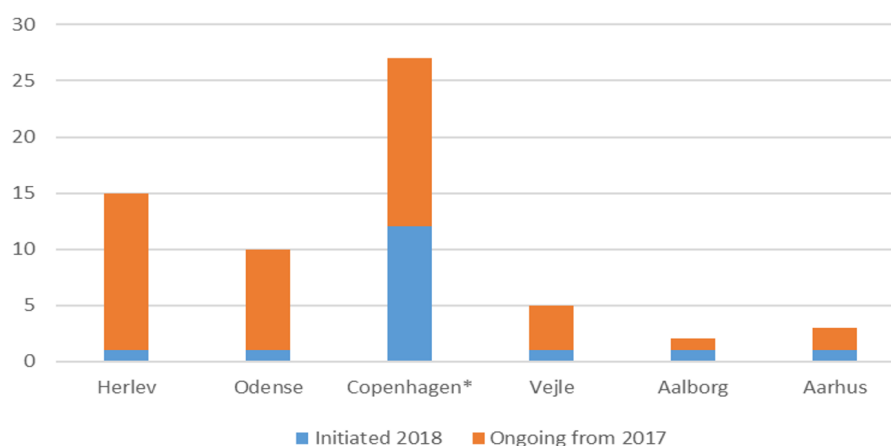


Figure 1. Number of commercial phase I & II clinical trials initiated and ongoing at the departments in Center for Oncology in 2018. *10 trials ongoing and 4 initiated pediatric clinical trials.

Center activities

In 2018, the following joint activities took place in Center for Oncology:

- Sharing of feasibilities
- Face to face center meeting – March 2018
- Dialogue meeting with Danish Medicines Agency and the National Research Ethics Committee (NVK) – March 2018
- Department of Paediatrics and Adolescent Medicine at Copenhagen University Hospital, joined Center for Oncology & Hematology - January 2018
- Center for Oncology & Hematology split in two: Center for Oncology and Center for Hematology – July 2018

- Change of Medical Lead role from Morten Mau-Sørensen to Kristoffer Rohrberg, The Phase 1 Unite, Department of Oncology, Copenhagen University Hospital – December 2018
- Dialogue meeting between patient organizations, sponsor companies, clinical research organizations and hospital departments – September 2018

Further,

- The secretariat held individual meetings with all departments in Center for Oncology (in a few cases jointly with the local hematology department)
- The secretariat organized a political debate in collaboration with the Danish Cancer Association at Denmark's Political Festival on Bornholm on the prioritization of clinical research within the public health care sector – June 2018
- Novartis oncology headquarter representatives visited Copenhagen University Hospital, Herlev Hospital and the secretariat – November 2018
- Increased focus on referral of patients between hospitals for clinical trials
- National tumor board established by Copenhagen University Hospital, Herlev Hospital, Odense University Hospital and Aarhus University Hospital
- Daiichi Sankyo established an office in Copenhagen based on talks with departments from Center for Oncology, Invest in Denmark, Copenhagen Capacity and the secretariat – November 2018

Issues to consider

- Sharing of feasibilities have improved significantly, but can still be improved
- Real-time national database on clinical trials is imperative to support referral of patients for clinical trials
- Improved structures for referral of patients between hospitals for clinical trials within Denmark and within the Nordics are needed
- Improved collaboration between clinical departments and departments for analysis of biomarkers are needed
- Improved collaborations with patient organizations on clinical research are needed
- Political prioritization of clinical research needed e.g. through goals for clinical research

Cost summary

The departments of the center have reported the following in 2018:

Center for Oncology	Reported Spending	Actual Spending	Budget
Department of Pediatrics and Adolescent Medicine, Copenhagen University Hospital	618,600.00	790,712.05	618,600.00
The Phase I Unit, Copenhagen University Hospital	5,837,273.53	21,431,088.52	5,837,274.00
Herlev Hospital	1,759,354.07	2,081,418.34	1,759,354.00
Little Belt Hospital – Vejle Hospital	296,927.34	296,927.34	618,600.00
Odense University Hospital	618,600.00	862,826.89	618,600.00
Aalborg University Hospital	322,565.20	322,565.20	618,600.00
Aarhus University Hospital	214,436.82	214,436.82	618,600.00
Total	9,667,756.97	25,999,975.15	10,689,628.00

Table 6: Center spending and budget in DKK.

In 2018, the Center for Oncology received DKK 9,667,756.97, which was 90% of the total budget for the year. Four departments had their spending capped with respectively DKK 172,112.05; 15,593,814.99; 322,064.26 and 244,226.89 to stay within budget for the year.

At the Department of Pediatric and Adolescent Medicine at Copenhagen University Hospital the primary focus has been to ensure readiness through systematization, development and quality assurance of work procedures and work flow, and the continued development of internal and external agreements, not least with the Phase I Unit at Copenhagen University Hospital, which ensures more open trials with patient cohorts over and under the age of 18.

At the Phase I Unit at Copenhagen University Hospital, the primary focus has been to ensure readiness for phase I clinical trials through upfront genomic analysis of patients, the national tumor board established in 2018, clinical trials with patient cohorts over and under the age of 18 and marketing of the departments and the centers' competences.

At Herlev Hospital, the primary focus has been to ensure readiness for phase I-II clinical trials through upfront genomic analysis of patients, the national tumor board established in 2018.

At Little Belt Hospital, Vejle Hospital, the primary focus has been to ensure readiness for clinical trials, creation and maintenance of databases, training of Clinical Research Unit staff and the general administration associated with the NEXT collaboration.

At Odense University Hospital, the primary focus has been on ensuring readiness for clinical trials, training of Clinical Research Unit staff and improved collaboration with the department of genomic medicine at the University of Southern Denmark.

At Aarhus University Hospital, the primary focus has been on offering experimental or off-label treatment based on genome sequencing and the establishment of a national tumor board.

At Aalborg University Hospital, the primary focus has mainly been to ensure readiness for clinical trials, creation and maintenance of databases, training of Clinical Research Unit staff and administration associated with the NEXT collaboration.

Focus in 2019

In 2019, the center will focus on:

- Attracting new trials
- Increasing the number of shared feasibilities for clinical trials
- Ensuring sufficient capacity for clinical trials
- Improving the national collaboration across departments
- Dialogue with the Danish Medicines Agency and National Ethical Committee on complex clinical trials
- Patient empowerment through collaboration with patient organization on clinical research
- The development of a real-time, national database on clinical trials to support referral of patients for clinical trials and empower patients who seek participation in clinical trials
- Improving structures for referral of patients between hospitals for clinical trials within Denmark and within the Nordics
- Improving collaboration between clinical departments and the departments performing the genomic profiling
- Political prioritization of clinical research needed e.g. through goals for clinical research
- Supporting nationwide trials of personalized medicine involving the national tumor board

Center for Hematology

Center for Oncology and Hematology consisted of the following departments in the first half of 2018:



Department of Paediatrics and Adolescent Medicine at Copenhagen University Hospital, Rigshospitalet

Department of Hematology at Odense University Hospital

Department of Hematology at Aalborg University Hospital

Department of Hematology at Aarhus University Hospital

Department of Hematology at Copenhagen University Hospital, Rigshospitalet

Department of Hematology at Herlev Hospital

Department of Hematology at Little Belt Hospital, Vejle Hospital

Department of Hematology at Zealand University Hospital

The Phase I Unit, Department of the Oncology at Copenhagen University Hospital, Rigshospitalet

The Experimental Cancer Therapy Unit, Department of Oncology at Herlev Hospital

Department of Oncology at Little Belt Hospital, Vejle Hospital

Department of Oncology at Odense University Hospital

Department of Oncology at Aalborg University Hospital

Department of Oncology at Aarhus University Hospital

The oncologic departments (grey shaded) in the center were split out as of 1st July, when the Center for Hematology was formed and the departments of hematology at Copenhagen University Hospital, Herlev Hospital, Little Belt Hospital - Vejle Hospital and Zealand University Hospital joined the center. Accordingly, Center for Hematology at the end of 2018 consisted of eight departments.

Center for Oncology and Hematology had Morten Mau-Sørensen from The Phase I Unit at Copenhagen University Hospital as Medical Lead. Niels Abildgaard from the Department of Hematology at Odense University Hospital was appointed Medical Lead of Center for Hematology.

The eight departments cover the vast majority of the Danish population and treat all hematologic diagnoses in pediatric, adolescent and adult patients and cover all phases of clinical trials.

The yearly activities are summarized in Table 7 and described below.

Overall activities of feasibilities, trials and patients

A total of 32 clinical trial feasibilities involving 14 phase I-II feasibilities, 10 phase III-IV feasibilities and 8 feasibilities of unknown phase involving one or more of the clinical departments were received in Center of Hematology in 2018 (see Table 7 below). Seven of these feasibilities were shared via the secretariat, whereas the secretariat assisted sponsors with the identification of appropriate departments and investigators for an additional four feasibilities.

Center for Hematology	2016	2017	2018
Number of feasibilities received	56*	13	32
Number of initiated trials	16*	3	8
Number of trials open in year	51*	10	32

Table 7: Overall activities of feasibilities, trials and patients. * Figures cover both hematology and oncology

Clinical trials

In 2018, the Center for Hematology initiated a total of eight commercial clinical trials involving one or more of the clinical trial units. Overall, 32 clinical trials were ongoing in 2018. Of these six clinical trials were ongoing in pediatrics and of these three were initiated in 2018. The significant increase in the number of clinical trials performed in 2018 compared to 2017 is largely attributed to the inclusion of the four hematologic departments in the center.

By the end of 2018, seven of eight departments were involved in the conduct of between 0 and 18 clinical trials of the 32 ongoing clinical trials in the center.

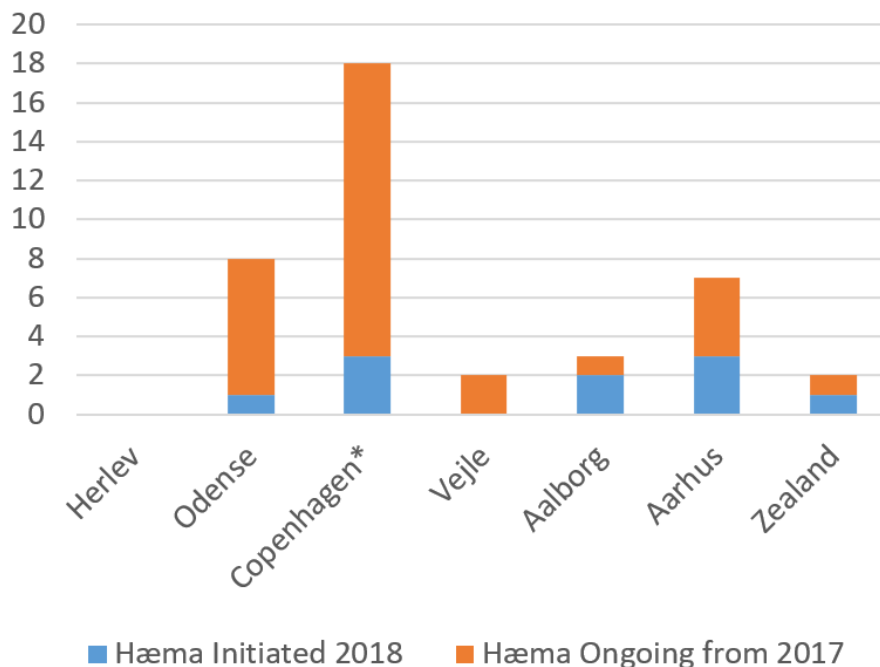


Figure 2: Number of commercial phase I & II clinical trials ongoing and initiated in Center for Hematology in 2018. I.e. eight ongoing clinical trials at Odense University Hospital, of which one was initiated in 2018. *6 trials ongoing and 3 initiated on pediatric patients

Center activities

In 2018, the following joint activities took place in Center for Hematology:

- Sharing of feasibilities
- Face to face center meeting – March 2018
- Dialogue meeting with Danish Medicines Agency and the National Research Ethics Committee (NVK) – March 2018
- Department of Pediatrics and Adolescent Medicine at Copenhagen University Hospital was allocated financial support starting from January 2018
- The departments of Hematology at Copenhagen University Hospital, Herlev Hospital, Little Belt Hospital (Vejle Hospital) and Zealand University Hospital was allocated financial support starting from July 2018
- Center for Oncology & Hematology split in two: Center for Oncology and Center for Hematology – July 2018
- Local hematological center secretariat established at Department of Hematology, Odense University Hospital – July 2018
- Change of Medical Lead role from Morten Mau-Sørensen, The Phase 1 Unit, Department of Oncology, Copenhagen University Hospital to Niels Abildgaard, Department of Hematology as a result of the split of the center – July 2018
- Dialogue meeting between patient organizations, sponsor companies, clinical research organizations and hospital departments – September 2018

Further,

- The secretariat held individual meetings with all departments in Center for Hematology (in a few cases jointly with the local oncology department)
- The secretariat organized a political debate in collaboration with the Danish Cancer Association at Denmark's Political Festival on Bornholm on the prioritization of clinical research within the public health care sector – June 2018
- Increased focus on referral of patients between hospitals for clinical trials
- Increased collaboration between clinical departments and laboratories for analysis and validation of biomarkers in clinical trials

Issues to consider

- Sharing of feasibilities have improved significantly, but can still be improved
- Real-time national database on clinical trials is imperative to support referral of patients for clinical trials
- Improved structures for referral of patients between hospitals for clinical trials within Denmark
- Establishment of tumor boards for hematology
- Improved collaborations with patient organizations on clinical research are needed
- Political prioritization of clinical research is needed e.g. by defining goals

Cost summary

The departments of the center have reported the following spending in 2018:

	Reported Spending	Actual Spending	Budget
Center for Oncology			
Copenhagen University Hospital	232,330.82	232,330.82	309,300.00
Herlev Hospital	0.00	0.00	309,300.00
Little Belt Hospital – Vejle Hospital	277,026.81	277,026.81	309,300.00
Odense University Hospital	618,600.00	758,374.85	618,600.00
Zealand University Hospital	309,300.00	935,638.20	309,300.00
Aalborg University Hospital	412,016.99	412,016.99	618,600.00
Aarhus University Hospital	618,600.00	743,237.25	618,600.00
Total	2,457,564.63	3,358,624.92	3,093,000.00

Table 8: Center spending and budget.

In 2018, the Center for Hematology received DKK 2.457.564,63, which was 79% of the total budget for the year. Three departments had their spending capped with DKK 150,084.85; 626,338.20 and 124,637.25 to stay within budget for the year.

At the Department of Pediatric and Adolescent Medicine, Copenhagen University Hospital, the primary focus has been to ensure readiness through systematization, development and quality assurance of work procedures and work flow and the continued development of internal and external agreements, not least with the Phase I Unit at Copenhagen University Hospital, which ensures more open trials with patient cohorts over and under the age of 18.

At the Department of Hematology at Copenhagen University Hospital, the focus has primarily been to develop tools for existing and future protocols, and to create and maintain homepages that promote open protocols, feasibilities and preparedness for clinical trials.

At Herlev Hospital, the primary focus has been to ensure readiness for clinical trials through change of the work flow in the Clinical Research Unit and development of Standard Operating Procedures, so as to reduce the waste time and improve recruitment of patients for clinical trials. The inclusion rate has improved 46% from 2017 to 2018.

At Little Belt Hospital, Vejle Hospital, the focus has been to ensure readiness for clinical trials through databases on myelomatose patients' treatment and response and the development (Standard Operation Procedures).

At Odense University Hospital, activities and funds has been spend on qualifying and strengthening the local infrastructure to support early phase trials, including lab facilities. Extension and qualification of SOPs and training of clinical staff to handle clinical trials, in particular early phase trials. In connection with the establishment of Center for Hematology in July 2018, a national hematologic secretariat was placed at Odense University Hospital. The secretariat was established and is being developed to strengthen the infrastructure of Center for Hematology.

At Zealand University Hospital, the activities have mainly been the development of a Clinical Trial Handbook, SOP development and optimizing oversight and processes like the start-up phase to ensure readiness for clinical trials through change of the work flow in the Clinical Research Unit and in the Zealand Region.

At Aarhus University Hospital, the primary focus has been on NEXT meetings, development and revision of Standard Operating Procedures, collaboration meeting with para-clinical departments at Aarhus University Hospital to improve work flow, continued development of PROPER and development and execution of NEXT Project Nurse courses.

At Aalborg University Hospital, the funds have been used for travel and meeting activities, oversight and screening of hematologic patients referred to the Phase I Unit at Copenhagen University Hospital. In the first six months in the Clinical Implementation Unit, and in the last six months in the Clinical Research Unit.

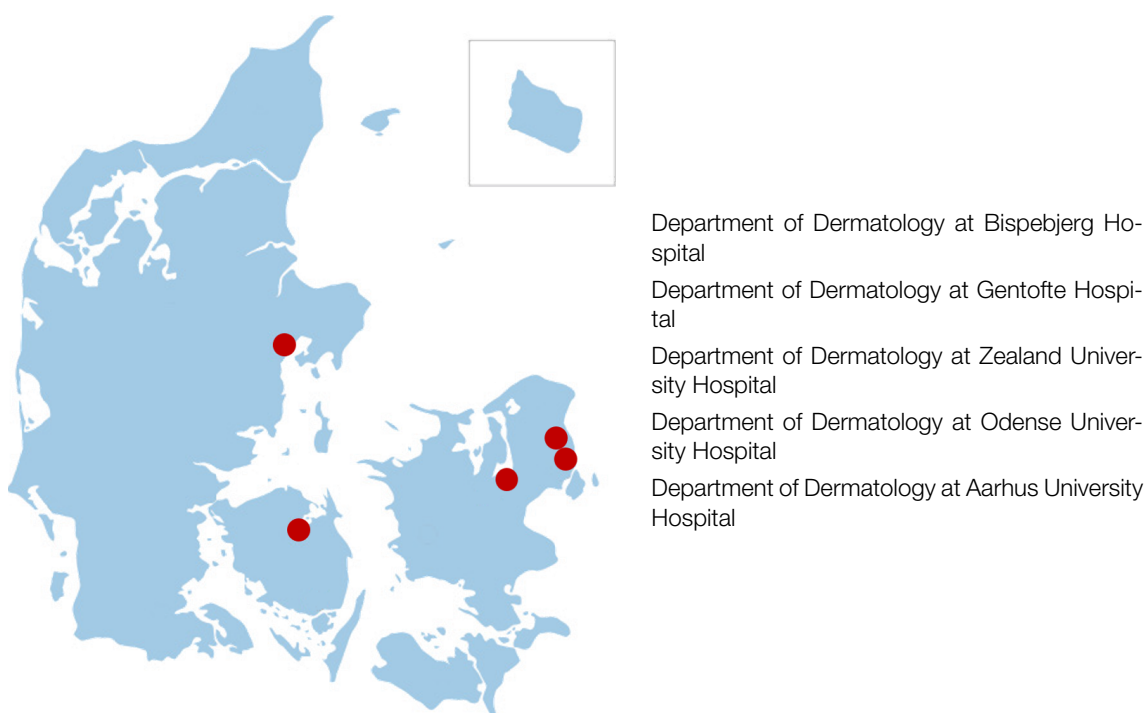
Focus in 2019

In 2019, the center will focus on:

- Attracting new trials
- Increasing the number of shared feasibilities for clinical trials
- Ensuring sufficient capacity for clinical trials
- Improving the national collaboration across departments
- Establishing a national hematologic secretariat at Department of Hematology, Odense University Hospital, aiming to support the national collaboration across departments
- Dialogue with the Danish Medicines Agency and National Ethical Committee on complex clinical trials
- Patient empowerment through collaboration with patient organization on clinical research
- The development of a real-time national database on clinical trials to support referral of patients for clinical trials and empower patients who seek participation in clinical trials
- Improving structures for referral of patients between hospitals for clinical trials within Denmark and within the Nordics
- Improving collaboration between clinical departments and laboratories performing genomic analyses
- Political prioritization of clinical research is needed e.g. by defining goals for clinical research

Center for Dermatology

The Center for Dermatology was established in 2015 and consists of the dermatological departments at Bispebjerg Hospital, Gentofte Hospital, Zealand University Hospital, Odense University Hospital and Aarhus University Hospital, and is coordinated by Professor Simon Francis Thomsen from Bispebjerg Hospital. The five dermatological departments treat all dermatological and venerological diseases as well as chronic wounds in children and adults.



The yearly activities are summarized in Table 9 and described in further detail below. In 2018, it was decided to include all phases of trials in the recording of activities.

Overall activities of feasibilities, trials and patients

Center for Dermatology	2016	2017	2018
Number of feasibilities received	12	12	29
Number of initiated trials	2	6	15*
Number of trials open in year	4	7	40**
Number of patients enrolled in trials	37	30	62***

Table 9: Overall activities of feasibilities, trials and patients.

* 5 phase I-II, 5 phase III-IV and 5 other types of studies (meddev, observational etc.)

** 13 I-II phase, 15 III-IV phase and 12 other types of studies

*** 19 patients I-II phase, 43 III-IV phase and other types of studies

Feasibilities

A total of 29 clinical trial feasibilities involving one or more of the clinical departments were coordinated in Center of Dermatology in 2018. 8 feasibilities related to phase I-II studies, 13 related to phase III-IV studies, 2 to observational studies, 1 to a medical

device study and 5 feasibilities of unknown phase. The three major indications are psoriasis (10 feasibilities), atopic dermatitis (7 feasibilities) and hidradenitis suppurativa (5 feasibilities).

As seen in Figure 3, the sharing of feasibilities is not implemented throughout the center. We continue to urge sponsors as well as clinicians to direct all feasibility requests to the coordinator.

Companies and CROs increasingly use proprietary online feasibility request processes. When used it is not possible for the center feasibility coordinator to intercept the feasibility request. This is the reason why a rather large part of feasibilities is lost to follow-up, as seen in Figure 4. Sponsors are primarily big pharma companies and two thirds of the requests are coordinated by CROs.

Sharing of Feasibilities

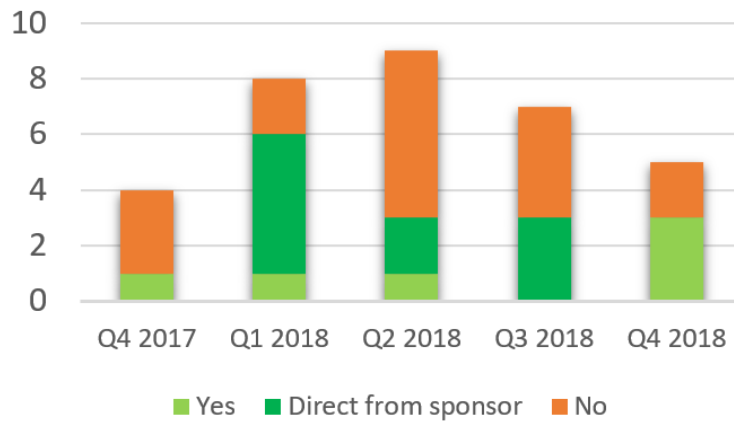


Figure 3: Shared feasibilities received in Center for Dermatology, per quarter, in 2018.

Status of Feasibilities

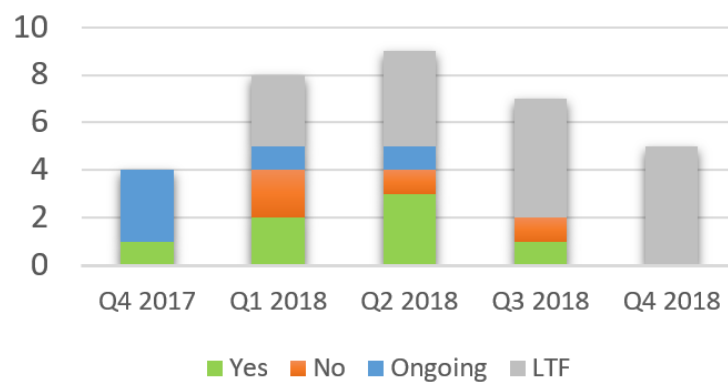


Figure 4: Quarterly status for feasibilities received in Center for Dermatology in 2018 (LTF: Lost to follow-up).

Clinical trials

In 2018, the Center for Dermatology initiated a total of 15 commercial clinical trials involving one or more of the clinical trial units. Furthermore, 11 trials are already planned for initiation in 2019. Overall, 40 clinical trials were ongoing in 2018, as 25 trials initiated in the years prior to 2018 were still open.

This year has been challenging as several studies have been stopped prior to or just after initiation or discontinued before end of study.

Departments involved

By the end of 2018, all departments were involved in the conduct of between 5 and 17 clinical trials, as seen in Figure 5 below.

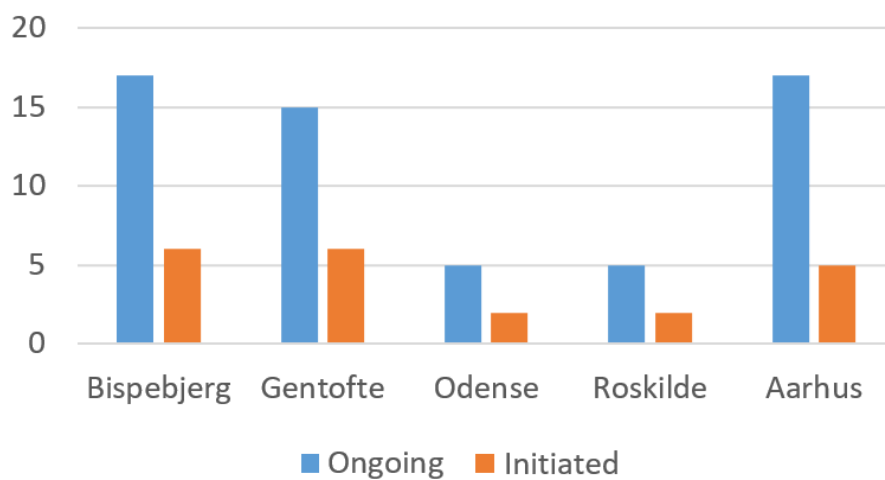


Figure 5: Trial activity in the five dermatological departments.

Number of patients included

The recording shows that 62 dermatology patients were included in the clinical trials in 2018, of which 19 patients were involved in early phase trials. This number should be compared to prior years with caution as difference in methods appears.

Center activities

In 2018, the Center for Dermatology had five virtual meetings with focus on the following themes: Yearly reporting of activities, temporary halt and finally closing of a study open in all units, feasibility process, the legal structure of the patient database, patient organizations as patient partners to the center, application for extra resources to the center to increase capacity and patient recruitment and the re-organization of NEXT to Trial Nation.

In 2018, the Department of Dermatology at Bispebjerg Hospital initiated a patient-directed pre-screening strategy in the out-patient clinic where doctors and nurses actively, and based on inclusion criteria, identify possible study participants. Further, local databases for atopic dermatitis, chronic wounds, hidradenitis suppurativa and chronic

urticaria are being used more actively for recruitment. This has led to identification of a larger pool of eligible study participants, which in one study of hidradenitis suppurativa yielded a 133% recruitment rate compared with the projected.

The department of Dermatology at Odense University Hospital has established a database with 300 patient entries until now suffering from hyperhidrosis, and a study in hyperhidrosis therapy is expected to be initiated in 2019. Furthermore, the department has a database and biobank with 563 genodermatosis patients. From this database, patients suffering from hereditary angioedema and Gorlin-Goltz syndrome are recruited for clinical studies. A database of patients with cutaneous lupus is also existing and patients will be contacted and asked to join a clinical study of treatment of discoid lupus planned for 2019.

In 2018, Department of Dermatology, AUH established access to Trialfinder to all nurses and doctors working in the clinic in order to keep everyone informed about the different protocols running in the clinic. Furthermore, permission from all relevant authorities was obtained to access referrals sent via Refhost from general practitioners (GPs) to office based dermatologist. If a potential patient is identified, we now have permission to send a letter informing about possible trials in the department at AUH. This initiative is expected to enhance recruitment to the different trials in 2019 and onward.

In 2018, Department of Dermatology and Allergy at Gentofte Hospital has hired more staff, particularly an extra dermatologist, to be able to carry out the clinical trials. Patients are therefore more actively recruited from the outpatient clinic.

Cost summary

The departments of the center have reported the following in 2018:

	Reported Spending	Actual Spending	Budget
Center for Dermatology			
Bispebjerg	1,260,820	1,472,427	1,260,728
Gentofte	858,745	858,745	970,227
Odense	760,925	760,935	1,021,980
Roskilde	398,831	398,831	485,114
Aarhus	970,227	1,107,475	970,227
Total	4,249,458	4,598,405	4,708,277

Table 10: Center spending and budget in DKK.

In 2018, the Center for Dermatology received DKK 4,249,458, which was 90% of the total budget for the year. Two departments had their spending capped with a total of DKK 348,947 to stay within budget for the year.

Focus in 2019

In 2019, the center will focus on attracting new trials and improving the national collaboration across departments, ensuring effective feasibility handling, sufficient capacity for clinical trials, predictable deliverables, herein capture of relevant trial performance data and patient empow-

ement. Marketing of the competences in the center towards industry will still be in focus.

The following specific activities will be in focus:

- Finalizing the legal framework for the patient database and launch amended version allowing patients to sign up
- Pilot the patient partner concept with Psoriasisforeningen and consider if other patient organizations should become partners

NEXT 2

Center for Infectious Diseases and Immune Modulation

In 2018, The Center for Infectious Diseases and Immune Modulation consisted of five departments:



Department of Infectious Diseases at Copenhagen University Hospital, Rigshospitalet

Department of Infectious Diseases at Copenhagen University Hospital, Hvidovre Hospital

Department of Infectious Diseases at Odense University Hospital

Department of Infectious Diseases at Aalborg University Hospital

Department of Infectious Diseases at Aarhus University Hospital

The Center for Infectious Diseases and Immune Modulation was established in 2016 and is coordinated by Medical Lead, Prof. Lars Østergaard from Aarhus University Hospital. The five infectious disease departments cover the entire Danish population and treat all infectious diseases. The yearly Trial Nation activities are summarized in Table 11 and described in detail below.

Overall activities of feasibilities and trials

A total of 18 clinical trial feasibilities were evaluated and completed by the clinical departments in the center in 2018. The feasibilities were involving 5 phase I-II feasibilities, 12 phase III-IV feasibilities and 1 feasibility of unknown phase (see Table 11 below).

Center for Infectious Diseases	2016	2017	2018
Number of feasibilities received	16	13	18
Number of initiated trials	2	3	2
Number of trials open in year	2	3	4
Number of patients enrolled in trials	n/a	260	38

Table 11: Overall activities of feasibilities, trials and patients.

Feasibilities

Feasibilities were received equally from pharma companies and CROs and all inquiries were shared between center sites. The inquiries have reflected a broad spectrum within infectious diseases with HIV and vaccine trials (influenza and pneumonia) being most frequent followed by various bacterial infections, fungal infections as well as Hepatitis C. All departments in the center had, in addition to new incoming trials, between three and seven ongoing trials from previous years.

Clinical trials

In 2018, the Center for Infectious Diseases initiated new clinical trials, both industry sponsored and investigator initiated. The clinical trials were studies investigating *S. aureus* infection and cystic fibrosis, respectively. The former study was including all five departments in the Center for Infectious Diseases and Immune Modulation.

Overall, the sites had between three to seven ongoing clinical trials in 2018, and several of the trials initiated in 2017 were still open during 2018. The reason for the decrease in patients included in 2018 when compared to the number for 2017, is based on a large multicenter and multinational trial in HIV which was initiated in 2017. In this study, the Danish study sites included more than 200 subjects within a relatively short inclusion period. In 2018, 38 subjects were included in clinical trials at the center, of which 23 subjects were included in ongoing trials and 15 subjects were included in trials initiated in 2018.

Center activities 2018 and focus in 2019

In 2018, The Center for Infectious Diseases and Immune Modulation has proactively worked towards cultivating scientific discussions and establishment of collaborations with global pharmaceutical companies having a clinical trial pipeline within relevant therapeutic areas.

During the past year, the center has successfully set up and hosted two such collaborator meetings with headquarter participation from international pharmaceutical companies. Exclusive industry partner meetings have thus been hosted for MSD/Merck and for ViiV Healthcare/GSK, respectively. The primary focus of both meetings was to discuss future collaboration on clinical trials and, in particular, the center's expertise in running trials in HIV and vaccines became an important focus for both meetings and the discussions.

Furthermore, enabled by Trial Nation's close collaboration with Invest in Denmark (Ministry of Foreign Affairs) the Center for Infectious Diseases and Immune Modulation was invited to present the national center at a roundtable discussion at the Consulate General of Denmark in New York. The roundtable discussion took place in May and attendees included decision makers from a broad range of US-based pharma and biotech companies. Following the roundtable event, several activities have been initiated to follow-up on contacts, specific requests and questions from the attending companies.

In November 2018, representatives from the Center for Infectious Diseases and Immune Modulation participated in the partnering conference BIO-Europe, with representatives from more than 2,000 European biotechnology companies participating. During the conference, partnering meetings were held with several potential, future collaborators.

With respect to feasibilities received from pharmaceutical companies in 2018, the number has increased by almost 25% compared to the previous two years. This may indicate an increased focus from industry on the infectious disease center set-up. In particular, the number of feasibilities on vaccine trials has increased. Although the number of new industry sponsored trials initiated at the center has not been as high as anticipated during 2018, the increased number of feasibilities completed may hold promise for more trials to be initiated during 2019-2020.

In addition, all sites have been updating the center's existing databases for HIV, influenza, sepsis and HCV. These databases are very important tools in the response to feasibility requests as they can provide sponsors with precise figures for number of patients, relevant subpopulations, treatment etc.

In the coming year, the Center for Infectious Diseases and Immune Modulation will continue its strong focus on promoting center competencies and capabilities internationally. The center will thus continue to work very proactively towards establishing collaborations and partnerships with specialized industry partners. These efforts are undertaken primarily in order to attract new trials addressing infectious disease indications and/or vaccine trials. In addition, the center will continue to focus on maintaining the strong and well-established national collaboration across departments to ensure continued sharing of feasibilities, and to further strengthen the dedicated, scientific collaboration already taking place across the center.

Cost summary

The departments of the center have reported the following in 2018:

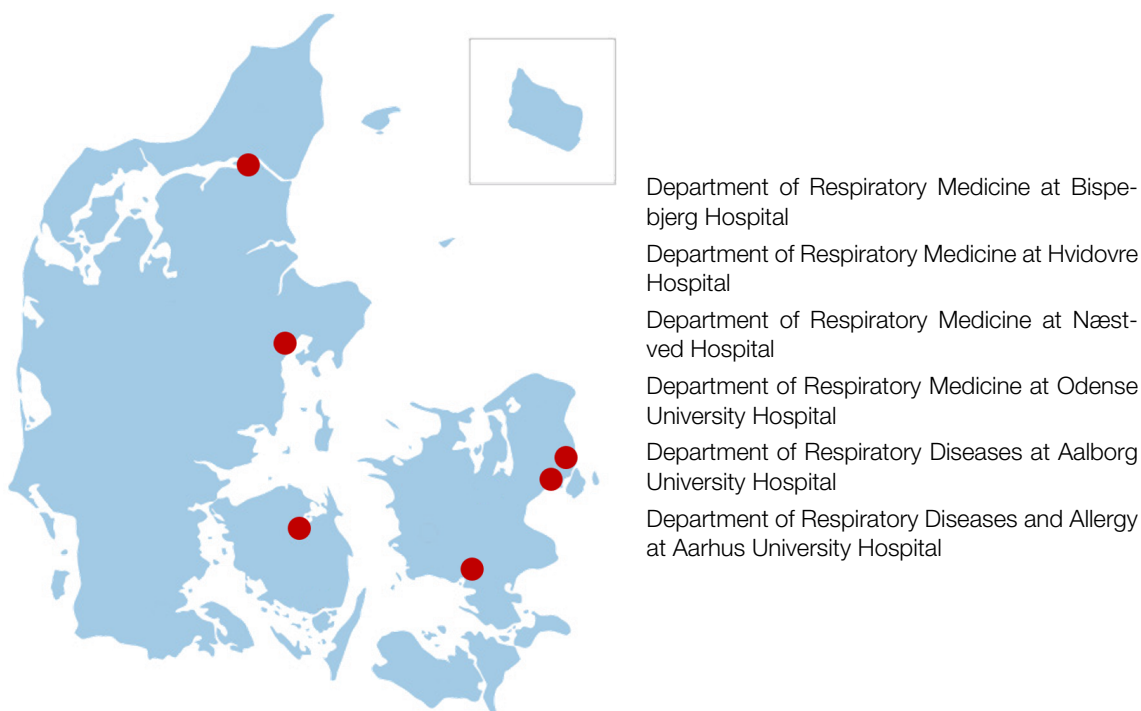
	Reported	Actual	
Center for Infectious Diseases	Spending	Spending	Budget
Aarhus University Hospital	1,100,717	1,100,717	1,399,168
Hvidovre Hospital	816,633	816,633	946,723
Odense University Hospital	954,654	954,654	982,549
Rigshospitalet	946,722	1,061,132	946,722
Aalborg University Hospital	996,494	1,180,174	996,494
Total	4,815,223	5,113,312	5,271,657

Table 12: Center spending and budget in DKK.

In 2018, the Center for Infectious Diseases received DKK 4,815,223, which was 91% of the total budget for the year. Two department had their spending capped by a combined DKK 298,089 to stay within budget for the year.

Center for Respiratory Medicine

In 2018, Center for Respiratory Medicine was represented by research units at six hospital departments:



The Center for Respiratory Medicine was established in 2016 and is led by Professor Vibeke Backer from Bispebjerg Hospital. The six respiratory research units cover the entire Danish population. The yearly activities are summarized in Table 13 and described in detail below.

Overall activities of feasibilities, trials and patients

A total of 20 clinical trial feasibilities involving 8 phase I-II feasibilities, 9 phase III-IV feasibilities and 3 feasibilities of unknown phase involving one or more of the clinical departments were performed in Center of Respiratory Medicine in 2018, see Table 13 below. An increase in feasibilities did not translate into an increase in initiated trials from 2016 to 2017. In 2017 and 2018, however, one in four feasibilities resulted in an initiated trial.

Center for Respiratory Medicine	2016	2017	2018
Number of feasibilities received	9	16	20
Number of initiated trials	5	4	5
Number of trials open in year	no data	8	5
Number of patients enrolled in trials	102	31	27

Table 13: Overall activities of feasibilities, trials and patients.

Feasibilities

We saw two sources for the 20 feasibilities as 13 were received from pharmaceutical

companies and seven were received from CROs, see Table 14 below. All feasibilities were shared in the center.

AstraZeneca	5	IQVIA	4
Novartis	4	PPD	1
Boehringer Ingelheim	2	Syneos	1
Sanofi	2	PRA	1
Total	13	Total	7

Table 14: Feasibilities from Pharma, left and CROs, right.

12 feasibilities were received in the first quarter of 2018. The number of declined feasibilities was correspondingly highest in this quarter. It is not known if sites declined due to issues related to expected capacity or other reasons. Eight feasibilities were received in the remaining part of 2018, see Figure 6 below.

Feasibilities 2018

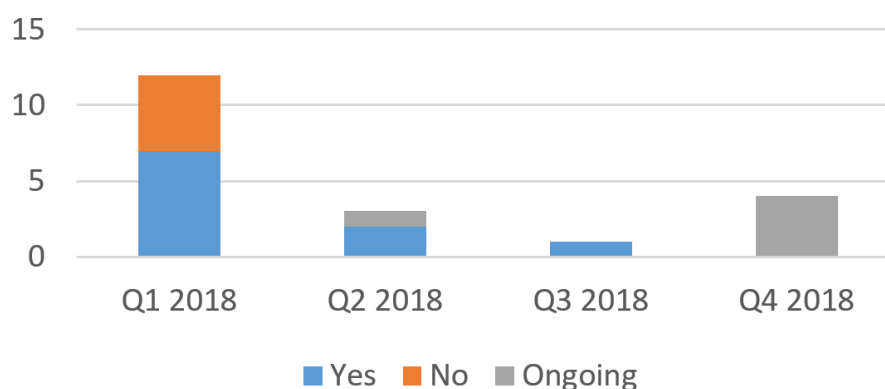


Figure 6: Result of feasibilities. The figure displays number of trial feasibilities with the outcome whether Sponsor decided to conduct the trial in Denmark (based on available data mid-January 2019)

Clinical trials

In 2018, the Center for Respiratory Medicine initiated a total of five commercial clinical trials involving one or more of the clinical trial units. Further, at least six more trials were planned for initiation in 2019. Five clinical trials were ongoing in 2018. Under these five trials, all six sites were active in at least one clinical trial. By the end of 2018, all departments were involved in the conduct of between one and four clinical trials, see Figure 7 below.

Clinical trials 2018

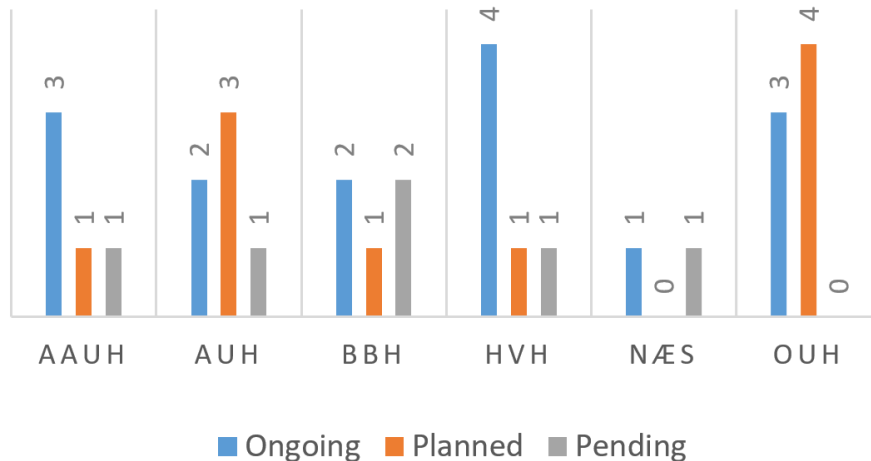


Figure 7: Number of clinical trials ongoing in 2018 and number of trials planned (more certain) and pending (less certain) initiated in Center for Respiratory Medicine end of 2018. AAUH (Aalborg Hospital), AUH (Aarhus University Hospital), BBH (Bispebjerg Hospital), HvH (Hvidovre Hospital), NÆS (Næstved Hospital), OUH (Odense University Hospital)

During 2018, 27 patients were recruited to the trials conducted at the clinical trial units of the Center. At Aarhus University Hospital, five patients were recruited in three trials, Bispebjerg Hospital recruited six patients in one trial, Hvidovre Hospital recruited nine patients in four trials and Odense University Hospital recruited seven patients in three trials. The trials are characterized by highly specific inclusion criteria, and the recruitment of patients for the trials has been demanding in all trials. Therefore, it is decided to increase focus on methods for patient recruitment in 2019.

The center noted the cancellation of three prominent trials and one other trial was postponed from early to late 2018. Together with an expected increase in trial initiations early 2019, these factors are the main reasons for the low number of recruited patients.

It is, however, important to note that the trial units are keeping their commitments to sponsors and that relations among the center stakeholders are strong.

Center activities

In 2018, the Center for Respiratory Medicine organized the annual meeting in Danish Network for Respiratory Medicine, where all Danish research units within the field are represented. In addition, relevant industry partners were invited. The meeting serves as a common platform for all parties involved in clinical respiratory research in Denmark. In recognition of the central role of the patients, the network will invite relevant patient organizations to participate in the next annual meeting.

In relation to the annual conference held by the European Respiratory Society, a meeting between industry decision makers and the professors and chief medical officers of the research units of the center was organized. Participants from AstraZeneca, Boehringer Ingelheim, Novartis, Sanofi, Chiesi, Teva and Pfizer together with center clinicians con-

firmed that the meeting was successful since it provided a platform for showcasing the Danish clinical setup and its opportunities. An elaborated meeting will be held in relation to ERS 2019 in Madrid.

Testimonies from the clinics

Respiratory Medical Lead, Prof. Vibeke Backer is proud of the past year for the Center for Respiratory Medicine of Trial Nation.

“We provided our patients with innovative treatments, we made impressive results for sponsors and CROs and we increasingly consolidated ourselves as a center.”

At Bispebjerg and Hvidovre Hospital, the primary focus has been to prepare staff and patients for the initiation of specific trials. The output is tangible as both research units has presented solid recruitment stats. The respiratory research unit at Hvidovre headed by prof. Charlotte Suppli Ulrik accomplished to have First patient in the World among 30 sites worldwide. A direct result of preparation and teamwork. Bispebjerg has also focused on developing an array of services that potentially can save time and money for sponsors and CROs while generating income for the research units in the network.

At Næstved Hospital, Dr. Uffe Bødtger has accomplished his remarkably goal for 2018: To strengthen and consolidate his relatively young clinical organization while allocating resources on his increasingly ambitious recruitment commitments.

At Aarhus University Hospital, Dr. Anders Løkke Ottesen has focused on establishing collaborations with surrounding hospitals to strengthen recruitment and auxiliary services for the future. The clinic has given priority to less mainstream studies within alpha-1-antitrypsin deficiency and bronchiectasis. Also an investment in possible future studies, says Dr. Ottesen.

At Aalborg University Hospital, the new head Dr. Ulla Møller Weinreich had two goals for 2018: Strengthen the economic foundation for the research unit and increase the number of clinical trials. She solved one with help from the other: Trial activity was increased from one to five active trials and the economy followed. Dr. Weinreich is piloting innovative recruitment strategies which draws from decentral clinical partners. The effect of the initiative has already yielded a 200% recruitment increase in one trial. Full impact expected in 2019 and forward.

Cost summary

The departments of the center have reported the following in 2018:

	Reported	Actual	
Center for Respiratory Medicine	Spending	Spending	Budget
Bispebjerg Hospital	1,797,835	2,015,777	1,797,874
Hvidovre Hospital	630,789	1,199,015	753,691
Næstved Sygehus	655,665	889,062	656,000
Odense Universitetshospital	943,724	943,724	950,000
Aalborg Universitetshospital	567,505	623,575	567,554
Aarhus Universitetshospital	765,123	765,123	950,000
Total	5,483,498	6,436,278	5,675,119

Table 15: Center spending and budget in DKK.

In 2018, the Center for Respiratory Medicine was allocated DKK 5,483,498, which was 97% of the total budget for the year. Four departments had their spending capped with a total of DKK 957,134 to stay within budget for the year.

Focus in 2019

In 2019, the center will focus on attracting new trials and improving the national collaboration across departments, ensuring effective feasibility handling, sufficient capacity for clinical trials, predictable deliverables, capture of relevant trial performance data and patient empowerment. The center is expected to affiliate with one or two patient organizations during 2019. Marketing of the competences in the center towards industry will further be intensified.

Center for Dementia

The Center for Dementia was established in 2018 and launched in June 2018 with the name NEXT-Link DEMENTIA. It has now been changed to Trial Nation Center for Dementia.

The center consists of the memory clinics at Rigshospitalet, Zealand University Hospital in Roskilde, Odense University Hospital, Odense University Hospital Svendborg, Aarhus University Hospital and Aalborg University Hospital. The center is coordinated by Professor Gunhild Waldemar and Peter Johannsen from the national Danish Dementia Research Center. Lundbeck A/S joined NEXT Partnership as partners when the center was established.



Danish Dementia Research Centre, Dept. of Neurology at Rigshospitalet
Regional Dementia Research Centre, Dept. of Neurology at Zealand University Hospital
Dementia Clinic, Dept. of Neurology at Odense University Hospital
Department of Geriatrics, Odense University Hospital, Svendborg Hospital
Dementia Clinic, Dept. of Neurology at Aarhus University Hospital
Memory Clinic, Dept. of Neurology at Aalborg University Hospital

An introduction to the center [is available here](#).

The activity in 2018 is summarized in Table 16 and described in further detail below.

Overall activities of feasibilities, trials and patients

Center for Dementia	2018
Number of feasibilities received	6
Number of initiated trials	2
Number of trials open in year	7
Number of patients enrolled in trials	unknown

Table 16: Overall activities of feasibilities, trials and patients.

Feasibilities

A total of six clinical trial feasibilities involving one or more of the clinical departments were coordinated in Center for Dementia in 2018. Five studies in patients with mild cog-

nitive impairment or mild Alzheimer’s disease and one study in patients with agitation. Four feasibilities relate to phase II trials, one relates to a phase II/III trial and one relates to a phase III trial. Two feasibilities arise from sponsor directly and four requests are co-ordinated by CROs. Unfortunately, none of the studies were assigned to Denmark. One trial was stopped before initiation due to need for protocol re-design. Five departments participated in site initiation visits and several departments expected to participate.

Three departments in the center treat patients suffering from Huntington’s disease and participate in the Enroll registry. Two studies in Huntington patients have been assigned to Denmark and will be initiated in 2019.

Clinical trials

In 2018, the Center for Dementia initiated two commercial clinical trials involving the clinical trial units at Rigshospitalet, Odense University Hospital and Aarhus University Hospital. Overall, seven clinical trials were ongoing in 2018, primarily at the units at Rigshospitalet and Aarhus. The unit at Odense University Hospital initiated one study in 2018.

Three department do not participate in clinical trials currently, but have past experience with clinical trials, and are capable of executing trials; one of the department was selected for the study that was discontinued.

Center activities

In 2018, the Center for Dementia had a full day meeting in May 2018 with focus on clinical research, both investigator and sponsor initiated. This was also the kicking off the NEXT partnership collaboration. Furthermore, a steering committee meeting was held in October 2018. In September 2018 a dialogue meeting with participation of industry partners with interest in DEMENTIA, the chairs of the center Gunhild Waldemar and Peter Johannsen and NEXT was held.

Cost summary

The departments of the center have reported the following in 2018:

Center for Dementia	Reported Spending	Actual Spending	Budget
Rigshospitalet	618,600	741,412	618,600
Odense	153,140	153,140	206,200
Roskilde	6,017	6,017	309,300
Aarhus	148,638	148,638	309,300
Svendborg	18,731	18,731	206,200
Total	945,127	1,067,939	1,649,600

Table 17: Center spending and budget in DKK.

In 2018, the Center for Dementia received DKK 945,127, which was 57% of the total budget for the year. Two departments had their spending capped with a total of DKK 122,812 to stay within budget for the year.

Focus in 2019

In 2019, the center will focus on attracting new trials, ensuring effective feasibility handling, sufficient capacity for clinical trials and enforce the collaboration across sites. Marketing of the competences in the center towards industry will still be in focus.

This will be accomplished by:

- A meeting for industry in March 2019 on the complexity of clinical trial in dementia
- Improvement of the research infrastructure at the departments enabled by the financial support from Trial Nation

Trial Nation

Clinical Trials Denmark