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Clinical Research and Innovation



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Authors

Marte Haavel¹, Arne Abrahamsen² and Olav Flaten³

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¹ Independent research consultant, martehaavel@gmail.com

² Nor PR, Thormøhlensgate 37, 5006 Bergen, abrahamsen@norpr.no

³ Nor PR, Thormøhlensgate 37, 5006 Bergen, abrahamsen@norpr.no



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Author:

Marte Haavel, Arne Abrahamsen and Olav Flaten

Publisher

Nordic Innovation, Stensberggata 25, NO-0170 Oslo, Norway

Phone: (+47) 22 61 44 00. Fax: (+47) 22 55 65 56.

E-mail: info@nordicinnovation.org

www.nordicinnovation.org

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Preface

Clinical trials have had a firm position in the Nordic countries. This has encouraged innovation and has been important for the quality and the improvement of the clinical services offered to patients. Industry-sponsored clinical trials have also been a valuable source for funding of research, and have had a role in developing a well-functioning research infrastructure contributing to the overall research environment at the hospitals.

Clinical trials in the Nordic Region are currently declining and face strong competition. The decline is greatest for industry-sponsored studies that have been reduced by almost 50 per cent since 2005. Also for Small and Medium-sized Enterprises (SMEs) there has been a shift of activity to countries outside the Nordic region. If this trend continues the infrastructure and expertise that are important to research and innovation will suffer and may ultimately disappear.

This study has examined a complex of problems to elucidate the cause for the decline: How is the framework and the environment for performing clinical trials in the Nordic countries? How does the industry and hospitals collaborate? Do the hospitals meet their role as a driving force in the innovation process? Where are the major obstacles and what can be improved to facilitate the process of clinical trials? Are there differences among the various Nordic countries and companies, and what can we possibly learn from each other?

The respondents in the study were invited representatives from Big Pharma and SME's in all the Nordic Countries, who responded to an electronic questionnaire. In depth-interviews were conducted with a smaller, randomly selected group. This broadened the perspective, and gave the possibility to interpret findings and responses from the digital questionnaire. The end result was a broader basis for understanding the current situation and a number of suggestions for improvement and development of the relationship between the hospitals and the industry, in the interest of clinical trials in the Nordic countries.

Oslo, March 20, 2013

Olav Flaten



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Summary

Clinical trials are important both in themselves and through the positive effects they have on the research environment at the institutions where they are performed. They contribute to train the research staff and increase the knowledge about new drugs and procedures. An active research environment in turn contributes to innovation and to a continuous improvement of the clinical services. The observed decline in clinical trials over the past decade may therefore ultimately be detrimental to patient welfare. Hence it is important to find means to improve the situation before the change is irreversible.

This study investigates the current environment for collaboration in clinical trials between hospitals, the pharmaceutical industry (Big Pharma -BP) and small and medium sized enterprises (SME), from the perspective of the industry. The topic has been investigated by a combination of a quantitative analysis using a digital questionnaire, and a qualitative investigation with in-depth interviews. The study has focused on three main aspects in relation to the onset and completion of clinical trials: The functionality of the current regulatory framework, the environment for collaboration in hospitals, and finally the interest for facilitation of extended Nordic collaboration by use of i.e. electronic registries and common Nordic web-sites.

The study was conducted in 2012. Results from the study show that the regulatory framework (national authorities, ethical committees and hospital agreements) need to be predictable and applications processed fast in order for the region to be competitive. The national authorities have succeeded in this over the past years, but regional differences when it comes to hospital agreements and ethics committees still serve as obstacles to the onset of clinical trials.

The cost-level in the Nordic countries was not found to be decisive for the decline in clinical trials in the Nordic countries. Costs are not unimportant, but as long as quality and performance are maintained, the costs are of less importance to the pharmaceutical industry.

Patient safety is an important aspect for the pharmaceutical industry, and is also highly evaluated in all the Nordic countries. However, the Nordic countries can no longer claim

that GCP or quality of research is a competitive edge compared to other regions. Regional differences in research quality were indicated.

The environment for collaboration within hospitals is generally perceived as good. Lack of resources, such as study staff and time dedicated to participate in clinical trials poses a threat to the quality and performance in clinical trials. It is an expressed wish that hospitals change or improve the infrastructure to allow time and space for clinical trials in order to be competitive. Two-thirds of the respondents to in-depth interviews reinforced the importance of hospitals delivering as promised and on time, to maintain a good track record and to maintain the chances to be included in future clinical trials.

The expectations of the pharmaceutical industry are not met, according to the evaluation.

Structural changes in hospitals in order to stimulate and facilitate the participation in clinical trials were suggested. This seems to be one of the main identified areas of improvement.

A diminished quality of research and a loss of functional infrastructure may be further accentuated in case of a continued decline in the number of clinical trials in the region.

There is a positive interest in the facilitation of a common Nordic region with 25 million patients. Companies that have already started a process of performing clinical trials in a joint Nordic region have seen positive results. Such experience may be drawn upon in the continued process of facilitating a joint Nordic region. The use of electronic patient registries is not regarded as a major improvement to facilitate clinical trials.

1. Background

The Nordic Region has been perceived as having specific advantages when it comes to performing clinical trials: high competence, highly qualified personnel, well-functioning infrastructure, comprehensive health records going back generations, Good Clinical Practice (GCP) with informed and conscientious patients who see the value of taking part in a study and a well-functioning regulatory framework. The level of activity in clinical trials has traditionally been high in all the Nordic countries. The positive influence of clinical research both on development of research competence, innovation and patient welfare has been previously discussed elsewhere (Hanning og Rentowl 2006; Hemminki og Kellokumpu-Lehtinen 2006; Mitchell 2006; Watson 2006; EFGCP 2009; Eriksen og Kierulf 2010; Gestrelus 2010). But the past decades have seen a shift in the worldwide dynamics of clinical trials. Nordic and Northern European countries have experienced a declining number of trials, while the activity has increased in large countries in Asia and in Eastern Europe (EFGCP 2009).

Implementation of the EU Clinical trials directive, posing more strain on clinical trials, demanding more resources and a closer audit, has been discussed as a potential reason for the decline (Hemminki og Kellokumpu-Lehtinen 2006), but it has also been seen as market driven (EFGCP 2009). Studies involving common diseases with a large study population are more efficiently performed in areas with a large patient population that allows quick enrolment of patients, reducing inclusion time and costs. One should also bear in mind that clinical trials may be considered both as a research investment and as a marketing tool in emerging markets.

A continued decline of clinical trials in the Nordic countries has been predicted to have potential major consequences for clinical research in the Nordic countries in general, as it will inevitably diminish the development and maintenance of research competence in the Nordic hospitals. It can also be argued how reduction in research competence may lead to loss of innovation through basic research, thus affecting the future growth of medical, biotech, and health tech industry in the region. The increased knowledge base, accrued by active participation in clinical studies, is a key element for the Nordic based industry and SMEs, and in particular the small start-up companies within the biotechnology sector. These are dependent on the competence and experience at the local university

hospitals in order to move innovative ideas from the primary phase of detection to a commercial product that will benefit the patients. Finally, a lack of first-hand knowledge about emerging products among physicians may ultimately reduce therapeutic options to patients and thus patient welfare.

Numerous previous studies and reports have called for improvement in the environment for clinical research (see for example Hemminki og Kellokumpu-Lehtinen 2006; EFGCP 2009; Eriksen og Kierulf 2010; Gestrelus 2010). A suboptimal collaboration between industry and academia has been highlighted as an area of concern and a potential arena for amelioration.

The present study may be seen as a direct continuation of the Nordic Innovation project: A Study of Clinical Trials in a Nordic Arena (Eriksen og Kierulf 2010). The study examines the possibility of cooperation in clinical studies across borders and concludes with a series of recommendations on how this could be done.

Eriksen and Kierulf (2010) is a qualitative study which identifies certain problem areas and discusses a broad range of reasons for the difficulties in industry-hospital collaboration. The present study builds upon the existing knowledge and previous discussions, while it is the first to include a quantitative analysis of responses regarding central success factors in this problem complex.

Aim of the study

The overall aim of the study was to establish a scientifically based knowledge platform to identify and quantify the needs of sponsors and the potential causes for the reduction of clinical trials in the Nordic countries, from the perspective of the BPs and SMEs. It is performed in order to identify efficient means to counteract the observed decline. The study also investigates the importance of clinical trials for the pharmaceutical industry, and what can be done to strengthen the collaboration between hospitals and industry in clinical research to facilitate research, innovation and commercialization of new discoveries. The three main areas for the investigation are:

- The political and regulatory framework, rules and regulations related to the initiation of clinical research in the Nordic countries.
- The current conditions for collaboration among hospitals and sponsors (BPs and SMEs) in sponsor-driven trials and the dominating success factors.
- The perceptions on a joint Nordic region and ideas on how this may be facilitated.

2. Material and methods

General

The study is performed from the perspective of the pharmaceutical industry. To narrow the study area and reduce variation, the study area concerns clinical trials where the pharmaceutical industry or SMEs are collaborating with hospitals. The study does not include clinical trials performed in clinics outside hospitals, or investigator initiated studies in hospitals. This discrimination is necessary in order to ensure a homogenous subset of participants and a common background for the questionnaire.

Two separate methods of data-collection were used in order to obtain a broad perspective on the topic. An initial quantitative analysis done as a digital questionnaire, followed by a series of in-depth interviews of a random selection of the candidates invited to the study.

The digital questionnaire provided data to numerically test working hypotheses, and the in-depth interviews provided nuances, new insight and the opportunity to interpret and validate the findings from the questionnaire. In combination the two methods were seen as complimentary in fulfilling the aim of the study and disclosing the success factors and major obstacles for clinical research, thus identifying where efficient corrective measures may be focused.

The quantitative analysis

The quantitative analysis was performed as a questionnaire and distributed using the questionnaire program Questback (Questback version 9.9, March 5, 2012).

The study was initiated and performed with in-kind contributions from representatives of the pharmaceutical industry associations of the Nordic countries. In order to comply with different national rules and regulations concerning mass-distributions to members of the Associations of the Pharmaceutical Industries (LIF- Sweden, LIF- Denmark, PIF- Finland, LMI- Norway, and Vistor in Iceland), each country's representative contacted a

number of companies (BP and SME) and asked permission to send the questionnaire to a representative for the company. A brief introductory letter stated the background for the study (Appendix 1). The questionnaire was sent to 123 recipients in five countries and the aim was to receive answers from approximately ten BP and ten SMEs per country. The recipients were people in charge of clinical trials or with long experience in performing and organizing clinical trials, such as clinical research directors, medical directors, head of clinical research and head/manager of clinical operations, marketing managers (Iceland) and CEOs. The questionnaire was distributed March 1st 2012 and remained open for the respondents for 15 days. Reminders were sent to all the recipients after seven and ten days.

The questionnaire contained 14 questions (Appendix 2). Questions allowed the respondents to evaluate and quantify their opinions and experiences with clinical trials by grading their response on a scale from 1-5, where five was the best score. The option "other" could be selected if the question did not apply to the respondents' experience or type of work. The questionnaire provided easily accessible definitions of terms which aimed to guide the respondents and thus ensure unified interpretations of the questions. The parameters to be prioritized and evaluated concerned certain key elements in the collaboration, such as the hospitals' reliability, quality and efficiency in performing clinical trials, costs and research quality. It also investigated the need for assistance and scientific input by the investigators and the study staff, and how well this assistance was provided. The respondents were also asked to state their opinion on the role of clinical research as a driving force in innovation, education and the exchange of knowledge between the pharmaceutical industry and hospitals, and rate a set of suggestions for improvement. Finally, the respondents had the opportunity to elaborate any point of view in a comment of max 300 words.

A set of preliminary conclusions were drawn based on an initial analysis of the data obtained.

The qualitative analysis

The preliminary conclusions from the digital questionnaire were used as a background for the following qualitative analysis, performed as in-depth interviews of a random selection of candidates. The in depth interviews were guided conversations of 30 minutes to one hour duration, where the respondents were asked to elaborate on topics related to the questionnaire. The interviewer did not exemplify the kind of responses that were expected or guide the answer in a particular direction other than to explain the questions. The candidates were asked directly whether they agreed with certain statements only when the aim was to comment specifically on the findings from the digital survey. An extensive summary was made from each interview, and the answers tabulated for calculations.

Data analysis

After closure of the digital survey the data was collected from Questback and analyzed using SPSS v 20.0 for windows. The data from the questionnaire were anonymous upon data extraction.

The questions with a graded score were scored from one to five (1-5). Questions answered "other" in the graded questions were left blank.

The analysis compared mean scores among geographical or organizational sub-groups. Sub-groups were defined based on country, company size (BP/SME) or previous experience in clinical research during the past five years. "Experienced companies" were defined as having performed more than ten clinical trials the past five years. "Medium experienced companies" had performed 3-10 trials, while "Inexperienced companies" had performed less than two clinical trials during the past five years.

The quantitative data were tested for normality and homogeneity of variance. Mean scores were compared using Parametric tests (One-way ANOVA with Tukey's B post hoc analysis) when the data-distribution allowed. Most often, data had uneven variance or different group sizes, and was analyzed using the non-parametric Kruskal-Wallis test across groups, with Mann-Whitney U test for pairwise comparisons of means. The level of significance was set at $\alpha=0.05$ for all tests.

3. Results

Quantitative analysis

Demographics for the questionnaire

From the 123 invited respondents, 52 responses to the questionnaire were obtained (response rate = 42.3%). The respondents represented all five countries and were distributed as shown in figure 1. Respondents were 55.8% BP and 44.2% SMEs (Fig. 2B). With the majority of answers from Denmark Finland and Iceland coming from BPs (Fig. 1), statistical analyses concerning SMEs are limited. As SMEs are under-represented in Denmark, Finland and Iceland, comparisons of countries may reflect differences among BPs and SMEs, rather than geographical differences.

The analyses and the current report will therefore primarily focus on differences between experienced and inexperienced companies, as defined previously, rather than geographical differences among countries. A larger number of participants may have made it possible to reveal national differences, but the current study indicates that other factors are more important than geographical differences in this study.

The experience with clinical trials is related to the size of the companies, where the majority of BPs are in the category Experienced, while the majority of SMEs are Medium experienced or Inexperienced (Fig. 2). Previous international and national experience also differs. More than a third of the experienced and medium experienced companies perform clinical trials outside the Nordic countries, and all of them perform trials in the Nordic countries. On the contrary, more than a third of the inexperienced companies perform trials only in their own country, and another third does not perform clinical trials in the Nordic countries at all. Only one of the inexperienced companies performs trials in both Nordic countries and abroad. These findings support that the level of experience is a good basis for sub-group comparison.

Among the inexperienced companies (mainly SMEs) several questions were scored "other", which means that a number of answers from inexperienced companies have been omitted from the calculations. Consequently, the overall mean scores cannot be

Figure 1

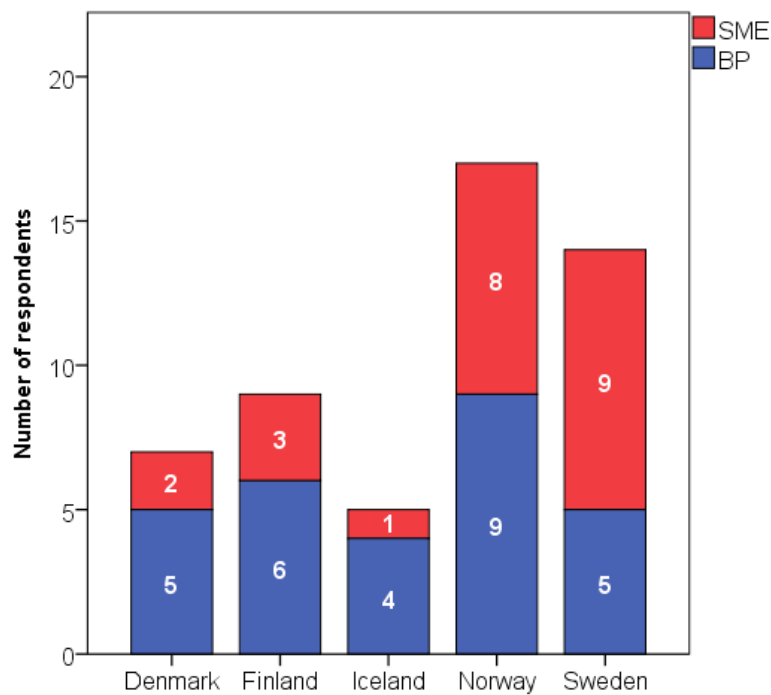


Figure 1: Classification of respondents to the questionnaire as Big Pharma (BP) and Small and Medium Sized Enterprises (SME) per country.

Figure 2A

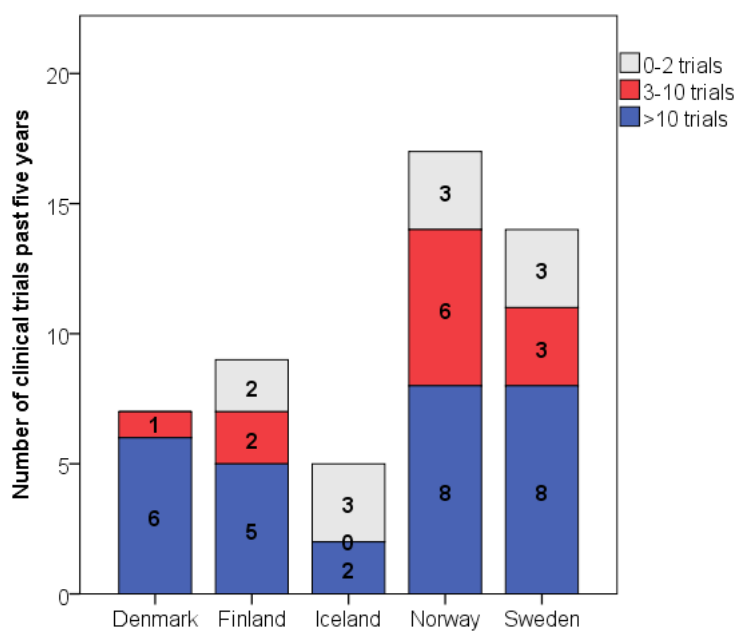


Figure 2B

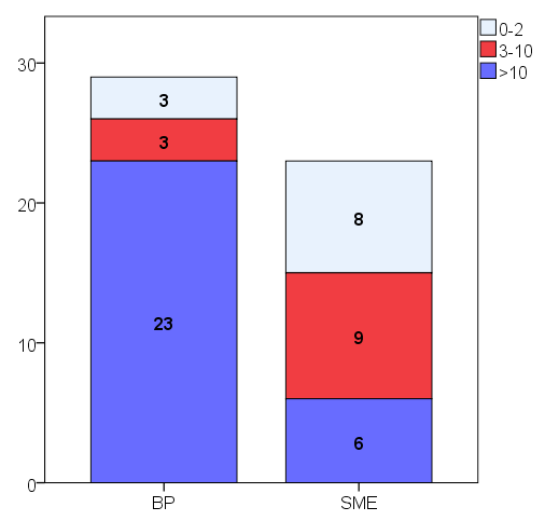


Figure 2 A) Experience in clinical trials per country, and B) experience in clinical trials for BPs and SMEs in all countries taken together

taken as fully representative of the opinion of the inexperienced companies.

Priorities for collaboration

Access to the right patients, patient safety, and research quality are rated as the top three priorities both as a total, and for experienced companies. Efficiency is among the top three for the inexperienced companies (Table 1).

Table 1

Mean standard deviation (SD), lowest and highest score (Min-max) showing priorities for collaboration. The respondents are categorized after number of clinical trials

Priorities for collaboration										
Experience in Clinical trials the past five years		Access to the right patients	Patient safety	Research quality	Predictability	Availability of key personnel	Efficiency	Service and organization	Total costs	Scientific reputation/ Key opinion leader
2 or less	Mean ± SD	4.9 ± 0.3	4.7 ± 0.6	4.4 ± 1.2	4.4 ± 0.8	4.4 ± 0.8	4.6 ± 0.7	4.5 ± 0.8	4.2 ± 1.0	4.2 ± 1.0 *
(n=11)	(min-max)	(4-5)	(3-5)	(2-5)	(3-5)	(3-5)	(3-5)	(3-5)	(2-5)	(2-5)
3 - 10	Mean ± SD	4.8 ± 0.4	4.8 ± 0.4	4.8 ± 0.4	4.7 ± 0.5	4.8 ± 0.5	4.5 ± 0.5	4.6 ± 0.5	3.9 ± 0.7	4.1 ± 0.8
(n=12)	(min-max)	(4-5)	(4-5)	(4-5)	(4-5)	(4-5)	(4-5)	(4-5)	(3-5)	(3-5)
10 or more	Mean ± SD	5.0 ± 0.0	4.9 ± 0.3	4.8 ± 0.4	4.7 ± 0.6	4.6 ± 0.6	4.5 ± 0.6	4.3 ± 0.5	3.7 ± 0.8	3.3 ± 1.1*
(n=28-29)	(min-max)	(5-5)	(4-5)	(4-5)	(3-5)	(3-5)	(3-5)	(3-5)	(3-5)	(1-3)
Total	Mean ± SD	4.9 ± 0.2	4.9 ± 0.4	4.7 ± 0.7	4.6 ± 0.6	4.6 ± 0.6	4.5 ± 0.6	4.4 ± 0.6	3.8 ± 0.8	3.7 ± 1.1
Total n		52.0	51.0	51.0	51.0	52.0	52.0	52.0	52.0	52.0

* = Signifies that the two groups marked * are significantly different (Mann-Whitney U: $p < 0.05$)

performed the past five years, and the priorities have been organized from most to least important (overall mean). n= number of respondents.

The cost of clinical trials has been discussed as a high priority and an important factor in the decline of clinical trials in the Nordic countries. According to this study, total cost is among the lowest priorities when selecting a site for a clinical study. However, the mean score for total cost is in the upper half of the scale for all subgroups, and thus not regarded as unimportant. The importance of the scientific reputation and collaboration with key opinion leaders is rated the lowest (Table 1).

However, the inexperienced companies placed significantly more emphasis on the scientific reputation of their collaborators than the more experienced companies (mean

score 4.2 vs. 3.3, Mann-Whitney U test, $p < 0.05$). No further significant differences among experienced and less experienced companies are observed.

Table 2

Evaluation of collaboration

Mean standard deviation (SD), lowest and highest score (min-max), showing the respondents' evaluation of the collaborators performance. The respondents are

Evaluation of collaboration										
Experience in Clinical trials the past five years		Patient safety	Research quality	Access to the right patients	Scientific reputation/ Key opinion leader	Availability of key personnel	Total costs	Service and organization	Efficiency	Predictability
2 or less	Mean $\pm$ SD	4.6 $\pm$ 0.7	3.5 $\pm$ 1.3	4.2 $\pm$ 1.1	3.8 $\pm$ 0.8	3.9 $\pm$ 1.2	3.8 $\pm$ 1.3	4.0 $\pm$ 1.0*	4.0 $\pm$ 1.2	3.1 $\pm$ 1.5
(n=8-9)	(min-max)	(3-5)	(2-5)	(2-5)	(3-5)	(2-5)	(2-5)	(2-5)	(2-5)	(1-5)
3-10	Mean $\pm$ SD	4.7 $\pm$ 0.5	4.2 $\pm$ 0.8	4.2 $\pm$ 0.6	4.0 $\pm$ 0.6	3.8 $\pm$ 0.9	3.5 $\pm$ 0.8	3.8 $\pm$ 1.0	3.5 $\pm$ 1.0	3.7 $\pm$ 0.9
(n=11)	(min-max)	(4-5)	(3-5)	(3-5)	(3-5)	(3-5)	(2-5)	(2-5)	(2-5)	(2-5)
10 or more	Mean $\pm$ SD	4.6 $\pm$ 0.8	4.0 $\pm$ 0.9	3.9 $\pm$ 0.6	3.8 $\pm$ 0.8	3.4 $\pm$ 0.7	3.3 $\pm$ 1	3.2 $\pm$ 0.9*	3.2 $\pm$ 0.8	3.0 $\pm$ 0.8
(n=28-29)	(min-max)	(2-5)	(2-5)	(3-5)	(2-5)	(2-5)	(1-5)	(2-5)	(2-5)	(1-4)
Total	Mean $\pm$ SD	4.6 $\pm$ 0.7	4.0 $\pm$ 0.9	4.0 $\pm$ 0.7	3.8 $\pm$ 0.8	3.6 $\pm$ 0.8	3.5 $\pm$ 1.0	3.5 $\pm$ 1.0	3.4 $\pm$ 1.0	3.2 $\pm$ 1.0
n		48.0	48.0	49.0	49.0	49.0	48.0	49.0	48.0	47.0

* = Signifies that the two groups marked * are significantly different (Mann-Whitney U: $p < 0.05$)

categorized after number of clinical trials performed the past five years and the evaluations have been organized from high to low (overall mean). n= number of respondents.

Table 2 shows the evaluation of performance in the same aspects as prioritized in Table 1. Patient safety scored the highest, and predictability the lowest (overall mean, Table 2). Efficiency shows a trend to lower score among experienced than inexperienced companies (mean scores: 3.2 and 4.0, Mann-Whitney U test, $p < 0.1$). However, both efficiency and predictability have scores in the upper half of the scale, showing that the general performance is not unacceptable for most respondents.

The evaluation also differs between the subgroups, with experienced companies rating service and organization among their collaborators lower than the inexperienced companies (mean score 3.2 vs. 4.0, $p < 0.05$). Again, both scores are in the top half of the scale.

Unlike the prioritization, the evaluation showed no differences regarding the scientific reputation of collaborators.

Need for support

The results from the questionnaire identify differences in the companies' need for support and ideas for innovation from the collaborating hospitals (Table 3). Regarding development of protocol, the results show that less experienced companies require significantly more help to develop the protocol than the experienced companies (Table 3). This is supported by the evaluation of protocol development, where the less experienced companies evaluate the help they receive with protocols significantly higher than the more experienced (mean score 4.1 vs. 2.5, Mann-Whitney U: $p < 0.01$) (Fig. 3).

All companies score the need for help with data collection highest (Table 3). The experienced companies require less input from the collaborators concerning ideas for innovation and research areas than the inexperienced companies (Table 3). This may imply that the collaborators are functioning as manual labor for the most experienced companies, while the less experienced use the scientific expertise of their collaborators more actively. However, the experienced as well as inexperienced rate the importance of the hospitals' role in communicating findings highly (overall mean score 4.2).

Table 3

Mean standard deviation (SD), lowest and highest score (min-max) showing the

Evaluation of collaboration								
Experience in Clinical trials the past five years		Data collection / protocol	Communicating findings	Training of hospital staff	Application	Data interpretation	Ideas for innovation and potential research areas	Development of protocol
2 or less	Mean ± SD	4.7 ± 0.5	3.9 ± 1.4	4.5 ± 0.9	3.9 ± 1.2	3.6 ± 1.4	3.4 ± 1.0	3.8 ± 1.5*
(n=11)	(min-max)	(4-5)	(1-5)	(2-5)	(1-5)	(1-5)	(2-5)	(1-5)
3 -10	Mean ± SD	4.2 ± 1.0	4.0 ± 0.9	3.9 ± 0.9	3.92 ± 1.0	3.8 ± 0.9	3.3 ± 1.4	3.1 ± 1.2
(n=12)	(min-max)	(2-5)	(2-5)	(2-5)	(2-5)	(2-5)	(1-5)	(1-5)
10+	Mean ± SD	4.6 ± 0.7	4.3 ± 0.8	4.03 ± 0.8	3.6 ± 1.3	3.2 ± 1.3	2.9 ± 1.3	2.2 ± 0.92*
(n=27-29)	(min-max)	(3-5)	(3-5)	(2-5)	(1-5)	(1-5)	(1-5)	(1-4)
Total	Mean ± SD	4.5 ± 0.8	4.2 ± 1.0	4.1 ± 0.9	3.7 ± 1.2	3.5 ± 1.3	3.1 ± 1.3	2.7 ± 1.3
n		52	52	52	50	52	52	52

* = Signifies that the two groups marked * are significantly different (Mann-Whitney U test: $p < 0.05$)

Figure 3

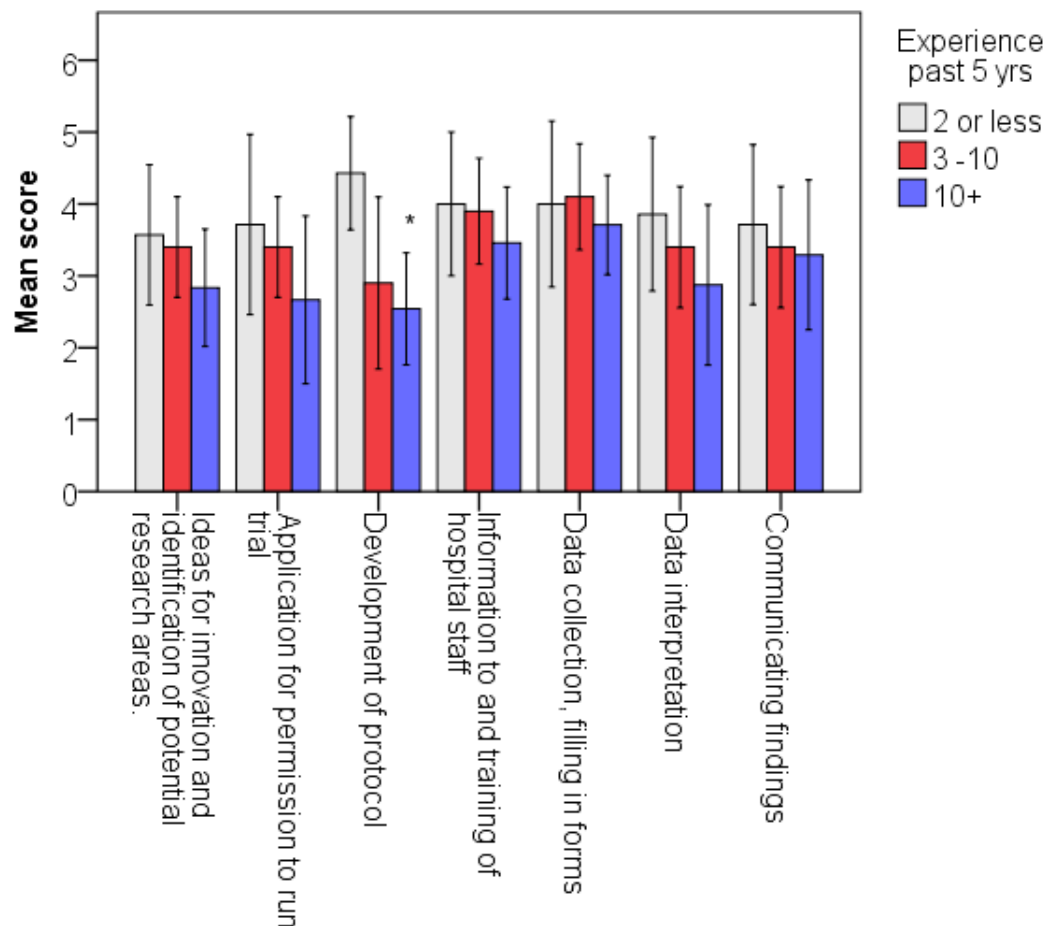


Figure 3: The companies' evaluation of support from collaborating hospitals based on experience in clinical trials over the past five years.

* signifies significant difference from inexperienced companies with <2 trials (Mann-Whitney U test: $p < 0.01$)

respondents' rating of the need for support from their collaborators (total mean). The respondents are categorized after number of clinical trials performed the past five years, and the responses are organized from most to least important. n = number of respondents.

External factors

When investigating potential reasons for the decline in clinical trials in the Nordic countries it is necessary to evaluate both internal and external factors. A list of statements was evaluated by respondents and rated according to level of agreement (Fig. 4).

The highest level of agreement concerned the statement that working in a unity of countries with 25 million patients would increase the desire to perform trials in the

Nordic countries (Statement F).

Concerning the bureaucracy involved with clinical trials (I), the results from the quantitative analysis show that inexperienced companies regard the regulatory framework as a reason for the decline, slightly more than the experienced companies (mean scores 2.8 vs. 1.8 Mann Whitney-U, $p < 0.1$). However, the statement received low scores, indicating that overall, the regulatory framework is not perceived as a major reason for the decline in clinical trials.

Figure 4

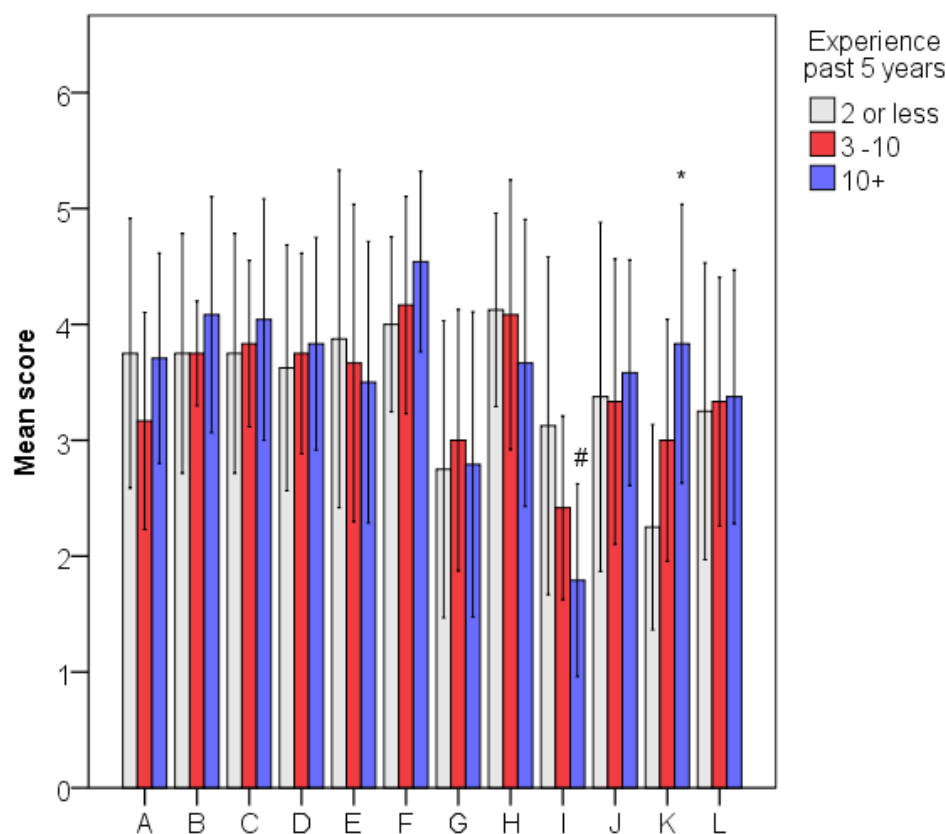


Figure 4: The scores show the companies' agreement with statements concerning the relevance of external factors for the performance of clinical trials in the Nordic countries.

Statements are represented by letters A-L:

A) My company prefers working with large university hospitals.

B) The electronic registry of social security number and patient data in the Nordic countries is a benefit to research.

C) Nordic hospitals are not aware of the need for marketing to attract clinical research collaboration.

D) The general health care standard in Nordic countries is an advantage for clinical trials.

E) The number of patients with the relevant diagnosis is too low to perform a clinical trial within a single Nordic country.

F) The ability to work within the Nordic countries as a unity with 25 million patients would increase the desire to perform trials in the Nordic countries.

G) The current regulatory environment is an obstacle for clinical research in the Scandinavian countries.

H) A common application-procedure within several Nordic countries would increase the likelihood that my company would chose to perform i.e. a multicenter clinical trial in the Nordic countries.

I) The regulatory framework is the main reason why the number of clinical trials in the Nordic countries decline.

J) My company prefers doing research in countries where there is an established large market.

K) My company prefers doing research in countries there is an emerging market.

L) My company prefers doing research in countries where there is easy market access.

The results also show that experienced companies put significantly more emphasis on working where there is an emerging market than the inexperienced companies (mean scores 3.8 vs. 2.1, Mann-Whitney U, $p < 0.05$).

The companies do not differ in questions concerning suggestions for improvement in order to attract more clinical trials to the Nordic region (Table 4). The results indicate prioritized areas for improvement, and the areas that work well as it is today. The scores range from one to five, although the mean scores for both experienced and inexperienced companies are similar. A higher willingness to collaborate and more service from the collaborators received the highest score. At the bottom of the list is the suggestion to improve research quality.

Table 4

Suggestions for improvement									
Experience in Clinical trials the past five years		Service. Culture and willingness for collaboration	Nordic, electronic patient registries	Single website with relevant information and application forms	Harmonized Nordic rules and regulations	Closer co-operation between Nordic research institutions.	One stop shop	Common application form valid for clinical trials in all the Nordic countries	Higher quality of research
2 or less	Mean $\pm$ SD	3.8 $\pm$ 1.3	3.5 $\pm$ 1.3	3.5 $\pm$ 1.3	3.5 $\pm$ 1.4	3.5 $\pm$ 1.3	3.4 $\pm$ 1.3	3.5 $\pm$ 1.4	3.3 $\pm$ 1.4
n=11	(min-max)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)
3-10	Mean $\pm$ SD	4.2 $\pm$ 0.7	3.9 $\pm$ 1.2	4.0 $\pm$ 1.1	4.0 $\pm$ 1.1	3.6 $\pm$ 1.0	3.8 $\pm$ 1.3	4.1 $\pm$ 1.2	3.0 $\pm$ 0.9
n=12	(min-max)	(3-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(2-4)
10+	Mean $\pm$ SD	4.1 $\pm$ 0.9	4.0 $\pm$ 1.2	3.8 $\pm$ 1.1	3.4 $\pm$ 1.2	3.7 $\pm$ 1.2	3.7 $\pm$ 1.1	3.3 $\pm$ 1.3	2.7 $\pm$ 0.9
n=28-29	(min-max)	(2-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-5)	(1-4)
Total n=51-52	Mean $\pm$ SD	4.1 $\pm$ 0.9	3.9 $\pm$ 1.2	3.8 $\pm$ 1.1	3.6 $\pm$ 1.2	3.6 $\pm$ 1.2	3.6 $\pm$ 1.2	3.5 $\pm$ 1.3	2.9 $\pm$ 1.0

Mean standard deviation (SD), the lowest and highest scores (min-max), regarding the respondents' ratings of suggestions for improvement. The respondents are categorized by number of clinical trials performed the past five years, and the suggestions are organized from most to least favored suggestion. n = number of respondents.

Qualitative analysis

An extract of the in depth interviews is presented in the following section, representing a summary of independent expressions. Quotations in the text represent actual

statements that were given during interviews. The in-depth interviews provided a comprehensive understanding for the common opinions and the differences. Where alternative interpretations of the digital questionnaire were found, this helped validate and interpret the conclusions from the digital questionnaire.

Demographics for interviews

The extract is based on 18 interviews of candidates from five Nordic countries. The candidates represent Denmark, Sweden, Finland, Norway and Iceland, among 11 BPs, 6 SMEs and one umbrella organization.

78% of the interviewed respondents had participated in the digital survey, 61% of the responding companies had experience with Nordic collaboration, and 72% had performed 10-50 studies during the past 5 years. This means that again the respondents represent largely the experienced companies, although both groups were contacted for interviews.

Priorities and concerns

78% of the interviewed companies had experienced a decline in number of clinical trials the past few years, while 22% had experienced no decline, or even an increase in the number of trials. The decline in the number of clinical trials is an expressed concern and a reality for the pharmaceutical industry in all the Nordic countries. It was repeated from all the countries and participants that if nothing changes the sponsor driven trials will disappear from the Nordic countries.

The main consequence of a continued decline in clinical trials was predicted in 78% of the interviews to be a loss of experience and competence in clinical research, both in pharmaceutical companies and among hospital staff. A reduction in patient welfare caused by loss of expertise and knowledge concerning new drugs was also listed in 50% of the interviews. Loss of clinical trials as an important marketing tool was listed as a consequence by 28%, while reductions in the medical units and loss of competent personnel in the pharmaceutical companies were predicted (and experienced) by 17%.

"This is a dying industry"

One aim of the in-depth interviews was to validate the findings from the digital questionnaire, presented in the previous section.

In support of the digital survey, 72% of the interviews supported the finding that costs were not of the highest importance for selection of study site. The in-depth interviews, however, gave a more nuanced picture of the situation. Many respondents stated that the costs in the Nordic countries were not higher than in many other countries, but

22% of the respondents also said that costs were of a very high importance and could be a reason to exclude certain Nordic countries. Also those who held cost as a moderate impact on choice of site commented that costs could not increase further and that the hospitals were sometimes informed that they were out of line. The main finding from the interviews was that costs are secondary to quality.

Hospital collaboration

In support of the digital questionnaire, the interviews supported the impression that SMEs make more use of the clinical experience of their collaborators than the experienced companies, both in preparation of the protocol and in interpretation of results and presentation of the findings. The level of engagement from principal investigators (PIs) is believed to increase with a hands-on approach and a feeling of ownership for the study, and among incentives for physicians to be involved in clinical trials, 81% mentioned they believed it was a heartfelt scientific interest. 60% mentioned the economical motivation for the clinic, for example as an opportunity to raise funds for the hospital's own research.

Evaluation of performance by hospital collaborators in the quantitative survey was rated high for essential issues such as patient safety and access to the right patients. Efficiency, service, organization and predictability were rated lowest during interviews. As opposed to the finding in the digital survey, the majority of the interviews rated the collaborators as mainly excellent and with a top ethical level. However, the interviews confirmed that there is room for improvement, as 67% of the respondents reinforced the importance of hospitals delivering as promised and on time, and complained that many do not deliver the number of patients promised. This leaves the sponsors with a bad track record which reduces the chances to be included in future clinical trials.

"How do we get the hospitals to be realistic about what they can achieve in terms of number of patients?"

Regulatory framework

With national authorities, ethical committees and hospital administrations involved before the start of a trial, the paper-work will be extensive in order to run joint clinical trials in the Nordic region. This potential major obstacle was investigated both in the digital questionnaire and the in-depth interview.

In support of the digital questionnaire, the interviews confirmed that 76% of the respondents with experience in applications were satisfied with the application process to national authorities, and that improvements over the past years has made this a less time consuming and more predictable procedure. The hospitals' ethical committees were on the other hand often perceived as regionally highly variable, their demands

unpredictable, not related to ethical concerns, and the process too time consuming. However, 43 % of the respondents were mainly satisfied with this process. Suggestions were to create better guidelines for ethical committees in order to ensure more uniform interpretation of ethical rules, and a uniform system to be followed by all ethics committees.

According to the respondents there was room for improvement with respect to the hospital agreements. Only 31% were mainly satisfied with the process of making hospital agreements. However, it was commented by the experienced companies that the reason for their ease at the process was experience and network, which makes it harder for the inexperienced companies to gain access. 69% of the respondents, both among experienced and inexperienced companies saw the hospital administration as a big hurdle to the start of a clinical trial. It was specifically mentioned that processes concerning Intellectual Property Rights (IPR) could sometimes delay the process for six months to a year, and severely impede the performance in competition with countries with much shorter processing times. At this point there were clear regional and national differences that became apparent during in-depth interviews.

“There is a seeming lack of urgency in the hospitals. They need to be aware of the high demands by the Pharma-industry, and the criteria for success in clinical trials. Hospitals must deliver according to the industry's demands in order to be considered as a site for future trials”

Priorities for improvement

The respondents were asked directly to validate the priorities for improvement from the digital questionnaire. The in depth interviews contradicted the digital survey with respect to suggestion for a higher willingness for cooperation in the hospitals. Interviews rated the service- mindedness in hospitals as generally good, but 67% of the respondent spontaneously addressed that investigators and hospital staff did not have time to engage in, or perform clinical trials of high quality. 50% of the respondents stated that that dedicated study staff was desirable or essential in order for hospitals to deliver as promised during a trial. This supports the evaluation from the quantitative survey that availability of key personnel receives a low score (Table 2). Allocating time for staff to be involved in clinical trials was also the most common suggestion for hospitals to perform according to agreement.

The interviews highlighted a difference among countries in the perception of research quality that was not as noticeable from the quantitative analysis. The majority of respondents from Iceland spoke highly of the research quality in Iceland and the level of education and engagement of the clinicians. It was commented that the requirement for Icelandic clinicians to study abroad resulted in highly interested and skilled investigators

that were eager to perform clinical trials. In Norway, on the other hand, the respondents indicated that the research quality these days was easily matched by Eastern European countries. The high quality of research and education that once was a competitive edge for the Nordic countries was now far from exceptional by international standards, and Nordic hospitals were advised to be aware of this before they lose more ground.

“We have become nonchalant in the Nordic countries. Eastern Europe is in many ways better than us.”

Although the interest in electronic patient registries seemed high based on the digital survey, the interviews did not confirm the faith in the use of electronic registries to facilitate clinical trials. It was confirmed as a welcomed hypothetical way to perform feasibility studies more efficiently, but the belief that such patient registries could identify patients for inclusion into trials was low, and varied depending on therapeutic area. In general the interviews did not confirm the belief that electronic registries would have such a decisive role in facilitating clinical trials.

“We have electronic registries already, but nobody can use them”

Facilitation by change of infrastructure

The respondents had many suggestions to change the infrastructure for clinical trials in hospitals to facilitate better performance in clinical trials from the industry's point of view. A general strategy concerning allocation of time for research also stood out as a main suggestion. Reimbursement of time spent on clinical trials or making research a mandatory part of the hospital work was also suggested. Variations including participation in clinical trials as meriting for higher positions for clinicians, intermittent years of clinical research and clinical practice, and more focus on clinical trials during the medical training and education. The result would in all cases be higher degree of competence and involvement in clinical research, leading to a better understanding of the requirements for clinical trials.

Another suggestion for structural improvements was to disintegrate clinical trials from the general clinical practice, and allow clinical trials to be performed outside the clinical work at the wards.

4. Discussion

To our knowledge the study is the first to elucidate the challenges for the pharmaceutical industry using a quantitative approach. The study has investigated the regulatory framework and the current conditions for sponsor driven clinical trials in Nordic hospitals. Our aim has been to quantify the reasons for the decline of clinical trials in the Nordic countries in order to establish operative knowledge that may help prioritize areas for improvement. The random selection of candidates for interviews is a benefit to the study, and ensures that not only the most engaged candidates or candidates sharing the same perspective were heard.

The combined results of the quantitative analysis and in-depth interviews highlight the most important challenges for the majority of the companies and emphasize prioritized suggestions for improvement of conditions for clinical trials in hospitals.

Demographics of the respondents

A larger study-material for both groups would be desirable to distinguish better between the needs of SMEs and BPs, and among countries. Obtaining answers from at least 10 BPs or 10 SMEs from each country should be possible in a larger-scale study if the limitations of sending digital questionnaires to members of umbrella organizations were not present. The dataset for this study was limited by the fact that umbrella organizations of certain Nordic countries are not permitted to send invitations to participate in studies to all their members.

The respondents represent companies of all sizes, with BPs representing the majority of the experienced companies, and SMEs representing the majority of the less experienced. Different requirements in these groups may stem from their previous experience as well as the size of the departments dedicated to perform clinical trials. The overrepresentation of BPs compared to SMEs in this study indicates that the results must be interpreted as valid mainly for BPs.

The invitations to the digital questionnaire and in-depth interviews were issued to both BPs and SME, but largely BPs responded. The reasons for the low response rate

among SMEs may be divided: The questions in the digital survey may have been mostly relevant for BPs that perform large-scale studies in hospitals and /or have the opportunity to run a study in multiple countries. The questions were based on the assumption that companies had applied for and run at least one clinical trial, which may not be the case for all SMEs. Representatives from SMEs may therefore have closed the survey half way instead of submitting incomplete questionnaires. The impressions from the interviews were the same, that SMEs were reluctant to give their opinion on challenges, unless they had experience from clinical trials in hospitals. This study thus pinpointed that a separate study is warranted to disclose the needs and challenges of the less experienced companies (often SMEs), in order to facilitate the continued innovation in these companies.

The present findings, within these limitations, may still serve as a useful tool for a continued dialogue among the pharmaceutical industry, hospitals and the political decision makers. One may presume that once the smaller SMEs become more mature and experienced, they will face the same reality as the BPs, hence the challenges will be comparable.

Quantitative versus qualitative results

Occasional results from the interviews do not fully agree with the digital questionnaire, as was the case regarding “service and willingness for collaboration” in the hospitals. It is possible that the discrepancy was due to a lack of discrimination between hospital staff and the hospital administration in the digital questionnaire. Comments from the in-depth interviews gave a more nuanced picture and indicated that the seeming lack of willingness to cooperate was not attributed to the attitude of the hospital staff, but may reflect problems within hospital administration - e.g. the fundamental conditions and the incentives for conducting studies in a hectic clinical setting.

The digital survey has limitations in nuancing the diversity of opinions, and the interviews are therefore important in order to see the full picture. On the other hand, the interview situation may function as a valve to release frustration, and cause the respondents to focus on the difficulties in the collaboration, rather than opportunities and positive aspects. In most cases though, there is correspondence between the two types of analysis, which supports the conclusions.

Expectations and performance

It is highly noticeable how the lack of time and resources in hospitals affects the ability and desire to get involved in clinical trials. A lack of dedicated study staff in turn affects the quality of research.

It is also noteworthy that the evaluation of performance is generally lower than the expectations and needs of the sponsors. The track record in clinical trials is one of the main predictors for being granted participation in future studies. Thus, a well-functioning collaboration and emphasis on communication of needs and expectations between the industry and the hospitals is vital for the survival of this research activity.

Changes in infrastructure.

More knowledge is needed to ensure that desired changes in infrastructure to accommodate clinical trials will benefit both parts of the collaboration. A close dialogue and further studies should be undertaken in order to spend time and resources wisely and ensure that the desired effects on performance of clinical trials are obtained.

Regional differences

Although limited data made geographical comparisons difficult, in most cases the countries within the Nordic region were of similar opinions. In general the differences based on geography were less significant than those based on other factors. This may be interpreted as an argument in favor of closer cooperation between the Nordic countries. However, the evaluation of research quality showed clear geographical differences, with Iceland claiming a high quality, and Norway a low quality of research. Although the data is limited, this may be a symptom of an unfortunate trend. As quality of research has traditionally been seen as one of the advantages of the Nordic countries, this is comparable to a loss of territory. The difference among countries in this respect may be due to differences in experience in clinical trials, but may also indicate that there is a real need to improve the quality of clinical research in Norwegian hospitals in particular.

Facilitation of Nordic collaboration

For the BPs, with capability to perform large multicenter trials, the idea of a Nordic collaboration with a patient basis of 25 million patients is highly appealing, as this is competitive with many large countries with comparable infrastructure and health care systems, i.e. France and the UK. During interviews it became obvious that many of the BPs have already implemented models that in fact encompass the whole Nordic population. Moreover, such studies are success stories that improve the track record and help the companies secure their position in the competition for European clinical trials. The paperwork connected to the trials has been handled by each country involved, which naturally requires a certain degree of administration that may exclude the smaller companies. However, even the smaller companies have examples of Nordic collaboration where patients are flown into a country in order to participate in clinical trials.

“We have attempted Nordic collaboration before, but this time we really had to make it work, and we did”

Therapeutic areas that do not require large patient populations may provide niches where the Nordic region could be able to compete on equal terms. Considering the high level of specialization required to find and treat certain rare diseases, the Western European countries may still hold a competitive edge to the developing countries and some of the large markets. The potential to find niches where the Nordic countries could excel may be explored more actively to ensure continued participation in clinical trials and clinical research. In addition, regulatory measures may be taken to facilitate the Nordic countries ability to compete for such studies and thus maintain the research competence in the Nordic countries.

The idea of Nordic, regional uniformity

The study shows that the application process is not a major obstacle on a national level. Regionally, however, the process is said to be more unpredictable, and may already have caused regional differences in selection or exclusion of sites. A uniform and well-functioning system has been accomplished among the national authorities over the past years, and a similar system for hospital agreements and ethical committees should be within reach. This will undoubtedly facilitate common Nordic trials. In the next step, a common Nordic application procedure would further increase the likelihood for joint Nordic trials.

Nordic collaboration, which in effect increases the regional patient population to approximately 25 million, has proven very successful in attracting clinical trials to the Nordic arena, according to some of the larger companies. Facilitation of such collaboration may thus be one prioritized area for improvement.

Web-based services and electronic registries may be a future solution to speed up administration of common Nordic trials. There are already a number of electronic registries, although they may not function as intended. This may have led to the expressed doubt in electronic registries during the interviews. Many respondents had no opinion on the subject, meaning that this is not the area where there is an immediate need for improvement. Still there may be interest in future common Nordic electronic registries in case of an improved functionality compared to current systems.

5. Conclusion

The present study has investigated and elucidated the major challenges and obstacles for participation and performance in clinical trials in the Nordic countries, using a digital questionnaire and in-depth interviews. Although the aspects that emerge are not new to the pharmaceutical industry, this is the first study to quantify the importance of the findings from the perspective of the sponsors of clinical trials.

The current concern with the decline in the number of clinical trials is a reality for the majority of the pharmaceutical industry in the Nordic countries. It has been repeated from all the countries and most of the participants that if nothing changes the sponsor driven trials may to a large extent disappear from the Nordic countries in the near future. The global companies may have the option to perform trials in other countries, but a continued decline will have a regional impact on the smaller companies, and on the research competence in the Nordic countries. This is not easily amended; rather, the loss of competence and ability to perform well in clinical trials represents a self-reinforcing process that will eventually cause a further decline in the number of trials, and will ultimately lead to a loss of patient welfare.

The current study supports the division of sub-groups based on experience rather than nationality, as no significant national differences have been revealed.

Against popular belief, the cost-level in the Nordic countries is not the major reason to exclude the Nordic countries from participation in trials, although the limit for costs has been reached.

The lack of resources and available personnel in hospitals is probably the most prominent issue that has been discussed in both digital survey-comments and interviews, in short: a better infrastructure for clinical trials in Nordic hospitals is highly desirable. The hospital staffs need to be allowed time and incentives in order to participate in clinical trials, in order for the process to run efficiently and the research to be of high quality. . The environment for collaboration between hospitals and the pharmaceutical industry is generally very good, and when time is allocated the will to participate and the quality of work in the Nordic countries is high. Uniformity in the application process to ethical committees and production of hospital

agreements is an important measure to reduce obstacles and to facilitate common Nordic trials. A combination of the Nordic countries with a patient population of approximately 25 million has been successful for some of the larger companies who have managed to overcome the administrative burden of common Nordic trials. Based on these findings one may argue for a joint approach from the Nordic region in order to increase the number of trials.

Common Nordic, digital patient registries have also been shown some positive interest, although the belief in this as a stand-alone tool for inclusion of patients is low.

A well-functioning collaboration and communication between the industry and the hospitals that increases the ability to perform well in clinical trials is vital for the survival of this research industry. Clinical trials will always be a key element of the innovation process.

6. Future perspectives

A future study might attempt to clarify to what extent clinical trials contribute to local innovation. This study failed to fully elucidate the needs and challenges of the small and medium sized enterprises (SMEs) as they, although invited, were underrepresented among the respondents to the study.

The study focuses only on clinical trials in hospitals, purposely leaving out clinical trials performed in GP practices and specialist clinics outside hospitals. However, these arenas for clinical research may also be investigated in the future, as both challenges and incentives may differ from clinical trials in hospitals.

The hospitals' views are not represented in this study. Future studies should also include the hospitals' point of view in the collaboration with the pharmaceutical industry, to provide a broader perspective on the potential for improvement. It is noticeable that in particular among experienced companies, little emphasis is placed on the scientific reputation of the collaborators, and that the collaborators are not important in the protocol development or for innovative ideas. Considering that one of the major incentives for physicians to participate in clinical trials is their scientific interest and "love of science", this may be noteworthy. One must consider that if the current organization of clinical trials reduces the level of involvement of physicians to a degree where participation is less scientifically stimulating, it may prove successful to find ways to counteract this, in order to increase the interest and performance in clinical trials.

Organization and funding

The study was initiated by the Nordic Health Research and Innovation Networks (NRI-Networks) and funded by Nordic Innovation. The board of the NRI-Networks had the overall responsibility for the project.

The board appointed a reference group with representatives from the different stakeholders, hospitals and the industry. The reference group had representatives from the following institutions:

The Associations of the Pharmaceutical Industry in Norway (LMI -Monica Kjeklen), Denmark (LIF - Jakob Bjerg-Larsen), Finland (PIF - Mia Bengtstrøm), Sweden (LIF - Karin Eriksson) and Iceland (Vistor - Gunnur Helgadóttir), Haukeland University Hospital, The University of Turku, Innovest AS, Norway.

Olav Flaten, Medical Director at GlaxoSmithKline AS in Norway has been project leader. In this connection Olav Flaten represents LMI.

Acknowledgements

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Appendix 1: Letter of invitation

Hi,

Many Nordic countries have lately experienced a severe reduction in industry sponsored clinical studies. We are concerned and want to explore what can be done both nationally and on a Nordic level in order to change this trend.

As part of this effort NRC-Network, which is a Nordic network of hospital administrators, researchers and the pharmaceutical industry, are doing a study of the interaction between pharmaceutical companies, SMEs and hospitals involved in clinical trials.

“National Pharmaceutical Industry Association” are cooperating on the study together with their counterparts in the other Nordic countries.

The study has been initiated and is partly funded by the Nordic Council of Ministers through Nordic Innovation Centre (NICE). The objective of the study is to strengthen clinical research and innovation in the Nordic region, contribute to maintain or increase the volume of clinical trials in the Nordic countries and facilitate the cooperation between hospitals, SMBs and big pharma.

The first part of the study is a web based questionnaire with 10 questions which will be sent to 10 representatives from “Big Pharma” and an equal number from SMBs in each country.

Based on the results from this, we will do a series of in depth interviews with a smaller number of participants.

The questionnaire will be sent to you “date”. It takes about 15 minutes to complete, so please help us.

The results will be presented in a report which will be distributed both to the industry and to hospitals involved in clinical research. Your answers will provide valuable data and updated insight to help key decision makers prepare the ground for future clinical trials in the Nordic countries to ensure a continued and healthy research environment and innovation within the health care sector.

I will be happy to answer any questions you may have, or you may contact directly:

Arne Abrahamsen
Project coordinator
NRC - Network
Mobile:
E-mail:

Yours,
National project representative

Appendix 2: Questionnaire

Clinical Research and Innovation

Dear Respondent

You have been especially selected as a candidate to represent your company because of your involvement with clinical research. We ask you to please spend ten minutes to answer our questions concerning clinical trials and innovation in the Nordic Countries.

The study has been initiated and is partly funded by the Nordic Council of Ministers through Nordic Innovation Centre (NICE). NICE funds Nordic projects that boost innovation and competitiveness in the Nordic business sector and lead to commercial and sustainable development. Your answers will provide valuable data and updated insight to help key decision makers prepare the ground for future clinical trials in the Nordic countries to ensure a continued and healthy research environment and innovation within the health care sector.

Traditionally, clinical research has had a firm position in the Nordic countries. Clinical research stimulates innovation and development of knowledge and expertise, new methods and products in the interest of patients and medical institutions. Clinical trials have also played an important part in financing the infrastructure for research, developing a well-functioning research environment.

However, over the past decade changing global dynamics and increased competition has reduced the number of clinical trials in the Nordic countries. If this decline is allowed to continue, the result may be reduced infrastructure for research, loss of local expertise and research competence, and less innovation.

This study aims to understand the driving forces behind these observed changes and the dynamics between pharmaceutical companies, Small and Medium Enterprises (SMEs) and collaborating hospitals.

Thank you for your time.

Best Regards

Olav Flaten
Project leader
NRC-Network

Follow this link to participate:

Clinical Research and Innovation

Your identity will be hidden.

Read more about confidentiality and hidden identity [here](#). (Opens in a new window.)

Definitions of terms used

Please refer to these definitions when answering the questions.

"The company" (your company): refers to the national branch of the company where you work.

Large Pharmaceutical Company: What is normally called "Big Pharma" whether you are the main office or a national branch.

SME: A small or middle sized company which is not a part of Big Pharma.

Clinical trial: The term will be used in the questionnaire and will encompass many forms of clinical research, i.e.

-Study/approval of new medicines (Phase I-III)
-Studies of existing drugs, phase IV studies, comparative studies, new indications, intervention studies, non-intervention studies and register studies. The list is not exclusive.

Collaborating partner/ Primary Collaborating partner: We are interested in your evaluation of Nordic hospitals as such. Please consider your current partner (hospital) or what you would consider a typical partner for your clinical trials in the Nordic countries.



INFORMATION ABOUT THE RESPONDENTS

Mandatory information about the participants

2) * 1) Please classify your company as one of the following:

- ☐ Large Pharmaceutical Company (Big Pharma)
- ☐ SMEs

3) * 2) How many employees does your company have in your country in total?

- ☐ 1-25
- ☐ 25-100
- ☐ 100+

4) * 3) What kind of clinical trials do you perform?

- ☐ Clinical studies phase I-III
 - ☐ Phase IV studies
 - ☐ Other
-

5) * 4) Where are you located?

- ☐ Norway
- ☐ Denmark
- ☐ Sweden
- ☐ Iceland
- ☐ Finland



ACTIVITY IN CLINICAL RESEARCH

6) * 5) How many clinical trials have your company performed during the last 5 years?

- ☐ 2 or less
- ☐ 3 -10
- ☐ 10+

7) * 6) For hospital based studies – which hospital (s) have been used?

- ☐ Hospital (s) in my country only
- ☐ Hospitals in my country, I do not know the situation in other countries
- ☐ Nordic hospital (s) outside of my own country
- ☐ Nordic hospitals and hospitals in other countries
- ☐ We do not run clinical trials in hospitals in the Nordic region



REQUIREMENTS OR NEEDS FOR COLLABORATION IN CLINICAL RESEARCH

Range your answers from 1 to 5, where 1 is unimportant and 5 is very important.

Definitions and explanations:

Service and organization: Willingness and ability to collaborate with the pharmaceutical industry.

Efficiency: Efficiency in enrolling enough patients, meeting deadlines, handing in data/forms.

Predictability: Ability to perform and deliver according to contract/agreement.

Patient safety: Ensuring the safety and well being of patients, maintaining patient rights, ensuring informed consent from all patients, adequately reporting adverse events.

8) * 7) Please think of an ideal research partner (hospital). When initially looking for a collaborating partner, which elements do you primarily consider?

	1	2	3	4	5	I don't know
Access to the right patients.	☐	☐	☐	☐	☐	☐
Scientific reputation/Key opinion leader.	☐	☐	☐	☐	☐	☐
Service and organization.	☐	☐	☐	☐	☐	☐
Availability of key personnel.	☐	☐	☐	☐	☐	☐
Total costs.	☐	☐	☐	☐	☐	☐
Efficiency.	☐	☐	☐	☐	☐	☐
Research quality.	☐	☐	☐	☐	☐	☐
Predictability.	☐	☐	☐	☐	☐	☐
Patient safety.	☐	☐	☐	☐	☐	☐

* Current or typical partner.

9) * 8) Evaluate your primary collaborating partner*(hospital) with these previous ideals in mind:

	1	2	3	4	5	I don't know
Access to the right patients.	☐	☐	☐	☐	☐	☐
Scientific reputation/Key opinion leader.	☐	☐	☐	☐	☐	☐
Service and organization.	☐	☐	☐	☐	☐	☐
Availability of key personnel.	☐	☐	☐	☐	☐	☐
Total costs.	☐	☐	☐	☐	☐	☐
Efficiency.	☐	☐	☐	☐	☐	☐
Research quality.	☐	☐	☐	☐	☐	☐
Predictability.	☐	☐	☐	☐	☐	☐
Patient safety.	☐	☐	☐	☐	☐	☐



Range your answers from 1 to 5, where 1 is unimportant and 5 is very important.

10) * 9) What are your requirements for support and involvement from an ideal research partner?

	1	2	3	4	5	I don't know
Ideas for innovation and identification of potential research areas.	☐	☐	☐	☐	☐	☐
Application for permission to run trial.	☐	☐	☐	☐	☐	☐
Development of protocol.	☐	☐	☐	☐	☐	☐
Information to and training of hospital staff.	☐	☐	☐	☐	☐	☐
Data collection, filling in forms.	☐	☐	☐	☐	☐	☐
Data interpretation.	☐	☐	☐	☐	☐	☐
Communicating findings.	☐	☐	☐	☐	☐	☐

* Current or typical partner.

11) * 10) Evaluate the performance of your primary collaborating partner* (hospital) with these previous ideals in mind:

	1	2	3	4	5	I don't know
Ideas for innovation and identification of potential research areas.	☐	☐	☐	☐	☐	☐
Application for permission to run trial.	☐	☐	☐	☐	☐	☐
Development of protocol.	☐	☐	☐	☐	☐	☐
Information to and training of hospital staff.	☐	☐	☐	☐	☐	☐
Data collection, filling in forms.	☐	☐	☐	☐	☐	☐
Data interpretation.	☐	☐	☐	☐	☐	☐
Communicating findings.	☐	☐	☐	☐	☐	☐



IDENTIFICATION OF PROBLEM AREAS FOR CLINICAL RESEARCH IN THE NORDIC COUNTRIES

Range your answers from 1 to 5, where 1 is disagree completely and 5 is agree completely.

12) * 11) To what extent do the following statements describe the current situation for clinical research in the Nordic countries:

[illegible]

○ ○ ○ ○ ○ ○

● ● ● ● ● ●

○ ○ ○ ○ ○ ○



1 2 3 4 5 I don't know

● ● ● ● ● ●

○ ○ ○ ○ ○ ○

○ ○ ○ ○ ○ ○

○ ○ ○ ○ ○ ○

○ ○ ○ ○ ○ ○

○ ○ ○ ○ ○ ○

If there was a single entry point for information and access to hospitals covering the whole Nordic region. (One stop shop).

☐ ☐ ☐ ☐ ☐ ☐

If there was a single website where all relevant information and all application forms concerning clinical trials in the Nordic countries could be accessed.

☐ ☐ ☐ ☐ ☐ ☐

14) * Your overall policy:

I
don't
know
True False

My company has not considered performing trials in the Nordic countries.

☐ ☐ ☐

15) * 13) A well-functioning research hospital is an important arena for development of knowledge, products and procedures, as well as being a venue for hosting clinical trials. Please evaluate the following statements with this in mind:

I
don't
know
1 2 3 4 5

The research climate with our primary collaborating partner (hospital) contributes to innovation and development of new ideas and/or products and/or procedures in my company.

☐ ☐ ☐ ☐ ☐ ☐

The research climate at our primary collaborating partner (hospital) contributes positively to the two-way exchange of knowledge between us.

☐ ☐ ☐ ☐ ☐ ☐

The collaboration increases the level of competence in my company.

☐ ☐ ☐ ☐ ☐ ☐

I believe that an active research climate in hospitals is necessary for the continuous development of the pharmaceutical industry in the Nordic Countries.

☐ ☐ ☐ ☐ ☐ ☐

I believe that the pharmaceutical industry promotes an active research climate.

☐ ☐ ☐ ☐ ☐ ☐

I believe that the pharmaceutical industry improves the quality of health care in the institutions.



16) 14) What do you think it would take for your company to change the location of clinical trials to the Nordic countries or increase the amount of research performed in the Nordic countries? Please explain considering both internal factors (like your ability to influence the key decision makers at you company's headquarter) and external factors (like market access, research quality, framework and legislation).

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Clinical Research and Innovation

Clinical trials are important both in themselves and through the positive effects they have on the research environment at the institutions where they are performed. They contribute to train the research staff and increase the knowledge about new drugs and procedures. An active research environment in turn contributes to innovation and to a continuous improvement of the clinical services. The observed decline in clinical trials over the past decade may therefore ultimately be detrimental to patient welfare. Hence it is important to find means to improve the situation before the change is irreversible.

This study investigates the current environment for collaboration in clinical trials between hospitals, the pharmaceutical industry (Big Pharma -BP) and small and medium sized enterprises (SME), from the perspective of the industry. The topic has been investigated by a combination of a quantitative analysis using a digital questionnaire, and a qualitative investigation with in-depth interviews. The study has focused on three main aspects in relation to the onset and completion of clinical trials: The functionality of the current regulatory framework, the environment for collaboration in hospitals, and finally the interest for facilitation of extended Nordic collaboration by use of i.e. electronic registries and common Nordic web-sites.

The study was conducted in 2012. Results from the study show that the regulatory framework (national authorities, ethical committees and hospital agreements) need to be predictable and applications processed fast in order for the region to be competitive. The national authorities have succeeded in this over the past years, but regional differences when it comes to hospital agreements and ethics committees still serve as obstacles to the onset of clinical trials.

Nordic Innovation is an institution under Nordic Council of Ministers that facilitates sustainable growth in the Nordic region. Our mission is to orchestrate increased value creation through international cooperation.

We stimulate innovation, remove barriers and build relations through Nordic cooperation

NORDIC INNOVATION, Stensberggata 25, NO-0170 Oslo, Norway // Phone (+47) 47 61 44 00 // Fax (+47) 22 56 55 65
info@nordicinnovation.org // www.nordicinnovation.org // Twitter: @nordicinno // [Facebook.com/nordicinnovation.org](https://www.facebook.com/nordicinnovation.org)