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# Assessing the impact of sponsored clinical trials in a university hospital

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ABSTRACT OF THE MASTER´S THESIS

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Clinical trials are the normal path for new drugs to enter the market. They are also a major economic factor both for the healthcare systems in which they are carried out, as well as for the individual hospitals. However, limited study exists on the total effect they have in hospitals.

This thesis studied the costs and benefits of conducting clinical trials in a University hospital. The study combined qualitative analysis through a questionnaire conducted with all staff members related to clinical trials as well as quantitative analysis of the bookkeeping data and drug cost data. All the studies of Helsinki University Hospital's oncology and hematology wards from 2017 and 2018 were analyzed.

The main finding of this study is that clinical trials are highly beneficial, and they carry many benefits in addition to the drug cost avoidance that has been identified in previous literature. Clinical trials enhance the quality of care patients receive, as well as can help heighten work motivation. Drug cost avoidance has been somewhat overestimated in the past, due to many modern drugs being highly expensive and clinical trials being focused on last-line treatments. As most of the patients would no longer receive expensive drugs as part of standard protocol, the savings have been overestimated in previous studies.

Future research should focus on identifying and quantifying in more detail the qualitative benefits clinical trials have on staff performing them, as well as identifying efficient managerial actions that can enhance those benefits.

| Keywords: | Publishing language: |
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AALTO-YLIOPISTO
Perustieteiden korkeakoulu DIPLOMITYÖN
Tuotantotalouden tutkinto-ohjelma TIIVISTELMÄ

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Kliininen lääketutkimus on keskeinen vaihe uusien lääkkeiden matkaa markkinoille. Niillä on myös merkittävä taloudellinen vaikutus niin sairaaloille, jotka niitä tekeävt, kuin myös terveydenhuoltojärjestelmälle yleisemmin. Tästä huolimatta niiden kokonaisvaikutuksia on tutkittu vain vähän kirjallisuudessa.

Tässä tutkimuksessa tutkittiin kliinisten lääketutkimusten kokonaisvaikutusta yliopistosairaalassa. Aineistona olivat kaikki Helsingin Yliopistollisessa Keskussairaalassa vuosina 2017 ja 2018 tehdyt kliiniset tutkimukset. Niiden osalta yhdisteltiin kvalitatiivista tutkimusta, joka tehtiin kyselyllä henkilöstölle, sekä kvantitaviista analyysiä kirjanpidosta.

Tutkimuksessa havaittiin että kliinisellä lääketutkimuksella on kokonaisuutena suuri positiivinen vaikutus. Erityisesti aiemmin kirjallisuudessa havaitun lääkesäästön oheen tunnistettiin useita vaikutuksia, joista on hyötyä sairaalalle. Näihin kuuluvat esimerkiksi työhyvinvoinnin lisääntyminen sekä hoidon laadun paraneminen. Tutkimuksessa havaittiin myös, että aiemmat selvitykset ovat yliarvioineet lääkekustannussäästön suuruutta. Tämä johtuu pitkälti siitä, että nykyisin tutkittavat lääkkeet ovat viimeisen linjan lääkkeitä, ja niitä saavat potilaat eivät saisi normaalihoidon piirissä muuta kuin palliatiivista hoitoa.

Jatkotutkimuksen tulisi keskittyä tunnistamaan ja kavantifioimaan tarkemmin se vaikutus, joka kliinisillä lääketutkimuksilla on, sillä tässä tutkimuksessa ei kyetty erottelemaan näitä vaikutuksia kokonaisuudesta. Toinen jatkotutkimuksen aihe on sellaiset toimenpiteet, joilla yliopistosairaala voisi lisätä kliinisen lääketutkimuksen positiivisia vaikutuksia.



| | |
|---|---|
| Avainsanat:<br>Kliinisen tutkimuksen vaikutukset, kliininen tutkimus, lääketutkimus | Julkaisukieli:<br>Englanti |

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Saara: this is why daddy had to work all summer. Thanks for letting me do it!

Helsinki, 21.10.2019
Kristian Sjölund.

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# 1 Introduction

Over the past two decades vast amounts of new drugs have entered the market, and the types of diseases that are treatable with drugs have increased. There are, for example, many types of cancers which are today treatable with drugs that extend the expected lifespan, that were not treatable at all just 20 years ago. At the same time, immense amounts of money are used for investigational drugs, with U.S. spending increasing by 27% to $121.8 billion between 2013 and 2017 (Research America, 2018). This spending is both vital for future developments in medicine as well as a major economic factor for developed countries, where the research is carried out. This has led to competition between countries on where clinical trials are performed. However, previous research into the total effects that clinical trials have in hospitals is limited. In order to give decisionmakers at both national level and in individual hospitals more knowledge about the total effects of clinical trials to base decisions on, this study was conducted.

## 1.1 Background

The road from an investigational drug to the market is long, with three main phases of clinical trials. The total duration of the process is up to 6 years (FDA, 2019). Phase 1 means, usually but not always, testing the drug on healthy individuals to find unwanted side-effects. Phase 2 means giving the drug to patients with the disease the drug should have an effect on in order to observe if it has the desired effect. Phase 3 is comparing the treatment to standard care in order to find out if the drug is more effective at treating the disease than existing alternatives. (Cancer research UK, 2019).

A large part of this process is clinical trials in university hospitals, as they are a required stepping stone for new drugs to enter the market through phases 2 and 3. These have both direct financial implications for the hospitals carrying out the research as well as indirect effects by, for example, giving earlier access to new, promising drugs (LaFleur et al., 2004). The impact these clinical trials have has been studied before, but often only from the perspective of drug cost avoidance. This study aims to set a context for the cost avoidance received from drugs by analyzing the total impact sponsored clinical trials have on a university hospital.

While the total amount of investigational drugs has increased worldwide, there has been a relatively sharp decline in the amount of sponsored clinical trials in Finland from 268 in 2008 to a low of only 144 trials in 2017 (Fimea, 2018). The decline seems

to have stopped, with 150 trials in 2018 (Fimea, 2019) The reasons for this are unknown, but taking efforts to increase the number of clinical trials back to the level of 2008 might prove to be a profitable investment for Finland and university hospitals in Finland. This study aims to give decisionmakers a tool for evaluating the potential effects of clinical trials in order to make more informed decisions about them in the future.

Finland has also fallen behind in relation to other Nordic countries, with Denmark being a successful example of increasing the number of studies over the past decade (U.S. National Library of Medicine, 2019). Denmark has an active government, that has focused heavily on increasing the amount of scientific research in general, for example waiving fees from phase I clinical trials in order to increase their amount. Thanks to their efforts, Denmark has the highest number of clinical trials per capita in the world in 2017 (U.S. National Library of Medicine, 2019). Thus, there is no fundamental reason related to healthcare system or regulation that prevents Finland from gaining a similar position.

Of the clinical trials carried out in Finland roughly 40% are phase 3, 25% phase 2, 20% phase 4 and 15% phase 1 (Fimea, 2019). Of these this study focuses on phases 2 and 3, as well as those phase 1 trials that are carried out in a similar fashion to phases 2 and 3. In modern drug development the drugs are often ill-suited for traditional phase 1 trials, as they have so sever effects giving them to healthy individuals would be unethical (Cancer research UK, 2019). Thus, phase 1 trials are essentially carried out in a similar manner as phase 2 trials, with differing focus points and goals.

The total costs and benefits of clinical trials are an interesting area due to several factors. Most importantly, the amount of clinical trials performed at a hospital is highly influenced by not only the actions of that hospital, but by the government and how willing they are to encourage clinical trials in a country. Denmark has invested heavily into clinical trials, with much success (Ministry of foreign affairs of Denmark, 2019). In order to persuade decisionmakers in Finland to invest in clinical trials a comprehensive look at the total benefits and costs involved is needed.

One aspect of public discussion often focuses on the quality of studies conducted with a pharmaceutical company. It is a realistic concern: if conducting clinical trials is too beneficial there is a risk of hospitals being too eager to take them and bend the rules. Fraud and misconduct are also widespread in clinical research (Gupta, 2013). However, based on discussions with both pharmaceutical corporation and doctors, there is minimal risk of this on a systemic level as the integrity of everyone involved is at a very high level. Indeed, one could argue that highly monitored,

sponsored clinical trials are less subject to bias than less monitored, purely academic research.

The study was conducted under Helsingin ja Uudenmaan sairaanhoitopiiri HUS, the public health care provider of Helsinki and Uusimaa. It is publicly funded and provides all levels of healthcare. Specifically, the study was conducted in Helsinki University Hospital, which provides tertiary care for citizens of southern Finland. It also has research and teaching duties and conducts large amounts of both sponsored and non-sponsored clinical research.

## 1.2 Clinical trials

Clinical trials are performed at all university hospitals in Finland as one of the core activities (Fimea, 2019). Clinical trials commonly last several years with several phases, and include three main activities for the hospitals involved. First, patient recruitment. Secondly, administering care. Lastly, measuring effects.

Patient recruitment is the act of finding suitable patients for the clinical trial. This is often done in modern settings with the help of electronic patient records, as many new trials are for very specific subsets of patients and finding those is difficult.

Administering care is the act of following the trial protocol to administer the care. Many trials include many treatment arms, in which patients receive different treatments that are assessed in relation to each other. In some cases the control treatment arm is a standard treatment, but it can also be placebo, especially for last line treatments that are given to terminally ill patients. Whether the care is administered as part of standard care or by specialized research nurses varies between trials.

The measurement of the effects is often done all throughout the trial and revolves around gathering the data. Clinical research nurses are often in a critical role in this part, filling forms of adverse effects and other variables that are monitored. Clinical research nurses are specialized nurses that are trained to perform activities related to clinical trials, and must often fulfill criteria set by the medical company sponsoring the trials.

Clinical trials are somewhat different from most activities in a hospital, as they can be organized in many different manners. There is no set division of labor, and nurses often conduct more activities than in standard care. The dimensions of clinical nurse activities and their definitions are shown below in figure 1.

1.2 Clinical trials

| Dimension | Definition |
|---|---|
| *Clinical Practice* | Provision of nursing care, education, and support, using the nursing process, to participants in clinical research and their families and significant others. Care requirements are determined by the scope of study participation, the clinical condition of the patient, and the requirements and clinical effects of research procedures and data collection |
| *Study Management* | Management of clinical and research support activities in order to assure patient safety, address clinical needs and assure protocol integrity and accurate data collection |
| *Care Coordination and Continuity* | Coordination of research and clinical activities to meet clinical needs, complete study requirements and manage linkage with referring and primary care providers |
| *Human Subjects Protection* | Facilitation of informed participation by diverse participants in clinical research |
| *Contributing to the Science* | Contributions as a research team member to the development of new ideas for study, explorations of innovations arising for clinical research and application of clinical research findings to practice |

*Figure 1 Dimensions of clinical nurse activities (Hastings et al., 2012)*

## 1.3 Research questions

Based on the literature review no comprehensive framework exists to assess the impact clinical trials have in a university hospital. Therefore, the main theoretical contribution of this work is forming a framework for future analysis of the financial impacts of sponsored clinical trials. So far, the view the academic literature has had has been focused on only some aspects of the question, and thus previous literature fails to give a complete answer. The two research questions formulated are shown below.

1. How should the total costs and benefits of sponsored clinical trials be assessed in a university hospital?
2. What are the total costs and benefits of sponsored clinical trials in the oncology and hematology departments of HUS Helsinki University Hospital?

The research questions are deeply intertwined, with research question 2 being essentially an application of the findings of research question 1. The original task and question asked by HUS, the public health care provider of Helsinki and Uusimaa, was research question 2, but due to the lack of literature on the subject this study needed to develop a suitable framework for assessing the total costs and benefits.

In this context total costs and benefits refer to all possible effects that clinical trials have, whether they are direct or indirect. It includes, but is not limited to, drug cost avoidance, clinical expertise, quality of care and employee satisfaction. The aim is to understand the area wholly, and not just through easily quantifiable measurements. Healthcare is a highly personnel-intensive field, and as such factors affecting employees are of high importance.

## 1.4 Scope

This study was carried out in only one university hospital, the Helsinki university hospitals. The factors creating the impact are the same in other hospitals within similar legislations and can be modified to function also in other legislations. However, the contracts university hospitals and sponsors have in other countries might vary, so the results of this study cannot be directly generalized to other countries without analysis of the differences between Finnish healthcare systems and those of that country. However, the results are in line with those calculated in, for example, New Zealand, which to some extent confirms that the impact is similar in differing legislations.

## 1.4 Scope

The exact system of reimbursing drugs has a high impact on the exact cost saving. In the context of this study, any drug that does not need to be paid for is a cost savings. However, in for example an American setting, where insurance companies pay for the majority of drugs, this incentive might not exist in a similar fashion. Nevertheless, studies from the U.S. are usable as the same effect does exist, even if the benefactor is not the hospital directly.

This study analyzed data gathered at the Hospital from 2012 to 2018. However, only 2017 and 2018 were available for the drug cost avoidance savings, and thus the scope was limited to only 2017 and 2018. Where data was available, the analysis was done 2012-2018, with only the results from 2017-2018 being included in the final totals. For example, overhead and laboratory costs were analyzed 2014-2018 as data was available for that period and analyzing a longer time period validated the way of analysis.

This study is focused on phases 2 and 3 and only on sponsored clinical trials, as assessing the impact of non-sponsored clinical trial would require much additional work focused just on them. The studies being carried out by university hospitals without sponsors vary wildly and can last for decades. Thus, they need to be studied separately if some sort of assessment of their financial impact is desired. There have also been prior studies on their total effects, and as such they are not relevant for the scope of this study. While exploring the trials carried out at HUS, it was noted that hematology also carries out phase 1 trials which are in practice identical to phase 2 trials. This is due to the nature of the new drugs being developed, which is ill suited for the traditional phase 1 approach. Thus, those studies were also included. In effect, all clinical trials at oncology and hematology departments of HUS were included, as there were no phase 4 trials in the data.

This study is limited to only include oncology and hematology, the two major departments that treat cancers. These two departments, whose administrations are to an extent shared, generate the majority of all sponsored clinical trials, and an even larger portion of the drug costs due to the very high cost of highly specialized cancer drugs. Cancer drugs were the investigational drug in 45.1% of clinical trials in Finland in 2018 (Fimea, 2019), and for this reason oncology and hematology are the most interesting specialties for clinical trial effect assessment. However, the framework and results of this study are applicable in other specialties, as no part of the framework is specific to specialty. The analysis of indirect effects to employees was done using a questionnaire that also included rheumatology staff. This was done in order to increase the number of answers. Rheumatology was chosen because it conducts clinical trials in

a similar manner to oncology and hematology departments, and thus the answers from staff in these three departments should be similar.

## 1.5 Structure

The study is structured around the original two research questions and discussion on the managerial implications that this study has. First, a literature review is performed, based on which the framework for assessing total costs and benefits is structured. After that, the framework is applied to the data collected in this study and those results are analyzed. Lastly, those findings are analyzed from a managerial point-of-view in order to give suggestions to HUS on areas of improvement in the future that would maximize the benefits of sponsored clinical trials. Additionally, points of improvement from other points-of-view are also considered, such as whether investments into investigational drug services on a national level might be profitable.

# 2 Literature review

This study combines qualitative and quantitative analyses to form a complete picture of the impact sponsored clinical trial have on university hospitals. This requires careful literature review of not only previous studies on clinical trial costs, but also of studies concerning the effects clinical trials have on e.g. the quality of care. Of these, drug cost avoidance is the most researched topic, with high-quality research for benchmarking. However, in general there is only very limited study into the field. In order to widen the scope and understand how this study relates to prior research this literature review also includes studies that did not directly consider sponsored clinical trials. For example, studies about how clinical expertise develops by conducting research at hospitals is reviewed, as those findings are also applicable in a sponsored clinical trial setting.

Due to the nature of clinical trials in the past 2 decades differing from those performed earlier, some articles were omitted. Results from studies published before 2000 were not included, as the financing model of clinical trials has shifted as the drugs being investigated have evolved, and as such earlier results are not necessarily applicable in 2019.

## 2.1 Total cost

The total benefits and costs of sponsored clinical trials have not been extensively studied. However, studies have identified different factors affected by clinical trials, illustrated in table 1. This only includes those studies that directly explored clinical trial effects. Further research that is applicable includes research into the effects of academic research on personnel at hospitals, but due to the variance in their focuses they are analyzed individually later.

2.1 Total cost

| | Drug cost avoidance | Overhead costs | Laboratory and related costs | Patient care quality |
|---|---|---|---|---|
| Murphy, Lyn 2011 | x | | x | x |
| LaFleur et al. 2004 | x | x | | |
| McDonagh et al. 2000 | x | x | | |
| Bredin et al. 2010 | x | | | |
| Braunholtz et al. 2001 | | | | x |

*Table 1 Literature on the impact of clinical trials*

Drug cost avoidance is the most studied area, with oldest studies dating back to the 80s. As such, the issue is not new to academic literature. However, no comprehensive framework for assessing the total cost effect of sponsored clinical trials exists. The study by Murphy (2011) had the most comprehensive framework, but had a very limited scope, and the final results were never published. Thus, there are no reliable results in prior academic literature about the total costs and benefits of sponsored clinical trials that we could use as a reference. Instead, the framework must be collected by analyzing all existing literature and synthetizing the factors identified in them into one comprehensive framework.

### 2.1.1 Overhead costs

Overhead costs in this context refer to the general overhead costs of acquiring clinical research agreements. This includes administrative work for creating budgets and invoicing, as well as lawyers and contract negotiations. These have a notable effect on the total cost, as they are costs that are incurred solely because clinical trials are performed, and they create no value for the patient. These have not been studied extensively, as they are essentially a managerial challenge. However, the cost-effectiveness of clinical trials has been studied and can be used as a proxy: the higher the cost-effectiveness, the lower the overhead costs.

Multi-country clinical trials have very wildly varying cost-effectiveness numbers in clinical trials (Willke et al., 1998). Thus, the overhead costs must vary, as the treatment issued is identical. There can be several explanations for this, but they can be divided into country-specific and hospital-specific factors. In any case, when discussing costs, it is clear that overhead costs must be included in the framework.

Overhead costs often have minimal direct financial impact, as they are costs that the sponsors pay. However, minimizing overhead leads to more effective trials, which in turn leads to more trials. This is why overhead costs are important despite not having a direct financial impact on the short run.

Patient recruitment speed and quality is a major factor for the overall cost-effectiveness of the clinical trial. Failing to recruit enough patients can delay the whole trial if conducting a multicenter trial – as most modern trials are – and as such can lead to major costs for the medical company. Studies have found limited difference between nurse and doctor recruitment efficiency in cancer studies, but nurses are more cost-effective due to the lower hourly cost of nurses (Donovan et al., 2003).

### 2.1.2 Laboratory and related costs

Clinical trials often include laboratory tests or imaging, which can sometimes be utilized as part of the care. This creates cost savings, as those laboratory and imaging costs are covered by the sponsor of the clinical trial. Thus, estimating the cost savings achieved here can have a major effect on some research. As an example, a clinical trial that requires constant monitoring of blood values for a patient for whom those markers would be monitored as part of standard care. In this situation the laboratory costs are paid for, at least in part, by the sponsoring medical company, thereby creating cost savings.

The study of Murphy et al. (2011) included this factor in the plans, but the results were never published. Thus, no reference exists as a starting point for the framework. As the total values of laboratory and imaging services at HUS are hard to collect due to being under varying sections in bookkeeping it is also relatively difficult to assess how large this effect could be. However, in relation to drugs and drug administering costs, they are not high and as such we could expect that the effect laboratory and imaging have in clinical trials is relatively small.

### 2.1.3 Patient care

The change in the quality of patient care has been researched extensively. There is evidence of a trial effect, i.e. that participating in a clinical trial benefits the patient (Braunholtz, Edwards, & Lilford, 2001). What causes this is subject to discussion, but in the scope of this study the mere existence of such an effect means we can take it as a given that the effect clinical trials have on patient care is either positive or nonexistent. Thus, our model can ignore this, leaving it for future studies, as it is very difficult to

quantify and is very subjective and dependent on multiple variables such as quality of the physician administering care.

## 2.2 Drug cost avoidance

Drug cost avoidance have been studied somewhat extensively in academic literature. However, the methodology applied varies, with some estimating drug cost avoidance based on the actual drugs used, and some based on estimates of what would have been the cost of standard care. The timespans over which the costs have been analyzed have also often been relatively short, often due to lack of data.

In 1996-1997 McDonagh et al. did the first notable study on the cost savings of investigational drug services, IDS for short. They found that IDS reduced costs by $1 million and $1.6 million in two separate institutions (McDonagh, Miller, & Naden, 2000). However, their study is somewhat outdated, and was solely focused on whether IDS is beneficial to hospitals in general. They do state that there are intangible benefits, such as improved patient safety as well as goodwill and collaboration, but how large these are or whether they are a result of doing clinical trials or of the way a hospital organizes it is left open. It should also be noted that this study is from the U.S., where drug compensation systems differ heavily from those used in Finnish hospitals. Thus, its results are not very applicable beyond the conclusion that investigational drugs have a beneficial effect on the costs of drugs in hospitals.

LaFleur, Tyler & Sharma found in their study that investigational drug services accounted for substantial reductions in drug costs. Their methodology was based on two fiscal years' of data and focused heavily on drug costs. They included drug dispensing costs and estimated contract acquisition costs, but they did not assess other, non-drug related impacts. Their results found that the 107 investigational studies accounted for roughly $2.5 million of drug cost avoidance annualized. However, the actual realized drug cost avoidance varied highly, being under $2 million one year and over $3 million in the last year. (LaFleur, Tyler, & Sharma, 2004)

What is noteworthy in the study of LaFleur et al. is the high variance in cost reductions between specialties. This reflects the fact that the timespan of only 2 years is short for studying cost reductions when singular drugs might cause very high fluctuations in cost savings. On the other hand, this is a natural consequence of the very high cost of modern cancer drugs. As the treatments are highly expensive, singular trials have a major impact on the total value of drug savings even if the number of clinical trials does not very much.

The cost savings found in these studies are in line with each other, and thus we should expect our study to find similar results for the drug cost avoidance. However, as clinical research spending has increased and the drug spending in healthcare has grown, we expect the numbers of 2012-2018 to be somewhat higher than in earlier studies.

However, there is one study with quite differing results. This study only released preliminary results, which only included two trials over a longer time span. Those trials actually had a negative cost saving result for the university hospital (Murphy, n.d.). If a patient has a response to the trial drug, they are given it also after the trial, naturally. However, the drugs are free of cost only for the duration of the study, and continuing treatment with the trial drug after the trial has ended might be more expensive than standard care would have been. What this study highlights are that not all clinical trials are beneficial, and care must be taken that the picture we have of clinical trials is not overly positive. It is indeed possible that a trial has negative results for the cashflows of the hospital as well as for the patient herself. Investigational drugs are investigational because there is limited scientific proof of their effectiveness, and this must be kept in mind when discussing the total costs of investigational drugs. The process put in place for new drugs to enter the market has been developed for a reason.

There have been estimates in HUS and in Finland on the size of drug cost avoidance due to sponsored clinical trials. The most recent and comprehensive is a non-academic study by Karma (2012). Despite not being peer-reviewed, it is well written, and the results are supported by academic research. The study cites drug cost avoidance at a value of €15 million in HUS in 2010 (Karma, 2012). However, this number has two main issues. Firstly, it is outdated as the amount of clinical trials in Finland has declined sharply since 2010 and the types of clinical trials might also have shifted heavily since then. Secondly, it is an estimate from the medical industry in Finland, and the original source is not well available. Based on interviews conducted during this study it is safe to assume that it is purely based on the value of drugs provided free of cost to HUS as part of clinical trials, and as such is somewhat inaccurate.

## 2.3 Factors not directly linked to sponsored clinical trials

Academic literature has considered other impacts of clinical trials, but not in the context of total cost analysis and they have not been analyzed from a monetary perspective. However, when creating the framework in this study these factors were considered, as they have a major impact on the total benefits.

Research in general has been studied previously, often being coupled with teaching in order to calculate how much university hospitals should be compensated

due to their responsibilities including these activities. The total cost of research and teaching in University hospitals in Finland was between €78 million and €104 million in 2002-2006, of which slightly under half consisted of research. The study used a statistical approach to estimate the amounts, as they are practically impossible to calculate otherwise. (Linna, 2006).

This estimate gives a ballpark figure on what the results of this study should be. However, it includes many activities not included in this study, and thus the validation must be done with care. It is very difficult to say which part of this number is related to clinical trials, as only a small portion of those activities are relevant. According to interviews conducted in this study, however, there is some overlap in managing research as both sponsored clinical trials as well as academic research often goes through HUCH.

When discussing benefits, one major factor that cannot be ignored is employee well-being, and through it, employee turnover rate. The cost of replacing a faculty member ranges from $115,554 to $587,125 based on specialty (Schloss et al., 2009), and overall medical staff turnover comprises 3.4-5.8 percent of the total operating budget (Waldman et al., 2004). Although these results are from the U.S., we can safely assume that the costs of turnover are high also in Finland. Although the salaries and income models differ, it is clear that turnover is a major expense. Considering that HUS employs thousands of nurses and doctors, the effect of clinical trials on employee turnover and recruitment should be assessed. As HUS has an operating budget of €2 277 million in 2019, employee turnover comprises between €77.8 million and €132 million. The major driver of this cost is nurse turnover (Waldman et al., 2004).

Indeed, nurses have a relatively high turnover globally, and most member states of the WHO have reported nurse resource difficulties (Kingma, 2001). Job satisfaction is a major factor in nurses' turnover, and job involvement, autonomy, collaboration with medical performance have been found to have a correlation with job satisfaction (H. Lu et al., 2005). Clinical trial involvement could thus increase job satisfaction, leading to cost savings through lower turnover. However, there is not yet enough literature to understand the relative importance of different factors linked to nurse commitment, and thus it is hard to estimate the magnitude clinical trials might have on nurse turnover (Lu, Yang & While, 2005).

A study performed at HUS found a strong link between research and clinical expertise. Käypä hoito -recommendations, a national system of treatment protocols, was heavily influenced by the research performed at HUS, and this effect had a higher effect on clinical practices than the direct findings of research (Karma, 2012). Similarly

it has been found that most nurses report participating in clinical trials as an important factor for improving standards of care (Burnett et al., 2001).

We can assume that this effect exists in clinical trials, and not only academic research, and should be considered in a comprehensive framework. However, this aspect has two challenges in the context of this study. Firstly, it is very difficult to measure in any fashion, as the effect of different factors related to clinical expertise and clinical practices are hard to distinguish from each other. Secondly, the studies either did not focus on nurses or they were performed based on self-assessment. As clinical expertise is a complicated issue, relying on self-assessment is somewhat unreliable and thus care needs to be taken when assuming effects on quality of care.

## 2.4 Clinical trial quality

The quality of clinical trials is the main factor affecting the willingness of medical companies to continue co-operation with a university hospital according to the interviews with a medical company conducted in this study. Therefore, the factors affecting clinical trial quality are of interest for this study despite not having a direct effect on university hospitals.

Quality is a multidimensional concept, which could relate to the design, conduct, and analysis of a trial, its clinical relevance, or quality of reporting (Jüni, Altman & Egger, 2001). However, only some of these aspects are influenced by the hospital conducting the trial. Clinical trial quality can be divided into internal and external validity. Internal validity means minimizing bias in clinical trials, such as selection bias and performance bias. External validity relates to reproducibility of the results, and includes patients, treatment regimens, setting and modalities of outcomes (Jüni, Altman & Egger, 2001).

Of these the hospital has a clear effect on external validity factors. Essentially how well the university hospital delivers on the agreed upon tasks determines the quality of the university hospital for the clinical trial. The treatment regimen and conforming to the trial are of high importance. Internal validity factors are largely dependent on only the sponsor of the clinical trial, and as such they can be ignored from the point of view of the hospital.

# 3 Methodology

In this chapter we develop the framework based on prior research that will be used to assess the costs and benefits of sponsored clinical trials. This framework is based on prior academic literature as well as the questionnaire that was used to assess the qualitative effects clinical trials have on personnel. The framework also incorporates areas that have not been previously considered, such as employee well-being, that have a major impact on the cost effect clinical trials have according to our research.

## 3.1 Performance measurement

In general measuring indirect effects is difficult, as there is no direct indicator of them. For direct costs, the pure monetary value can be analyzed, but indirect costs and benefits require a set of measurements. In order to combine these two types of effects a tool is required. In this study the framework utilizes an approach called Balanced Scorecard, which has four perspectives: Financial, customer, internal business and innovation and learning perspective (Kaplan & Norton, 1992). The total value of clinical trials is the sum of the impact that clinical trials have across all perspectives. In the case of hospitals, the customer perspective becomes the patient perspective, as Finnish healthcare is publicly funded.

## 3.2 Theoretical framework

The framework developed in this study is shown below in table 2. As we can see, a majority of the factors identified in this study are indirect, and relatively difficult to measure. This explains why those factors have been largely ignored in prior research, and simultaneously shows why their assessment is so important in order to understand the whole of the issue.

The factors are divided into benefits and costs as well as into indirect and direct effects. Direct effects are all effects that cannot be directly measured in monetary value. Indirect effects include everything else, ranging from faster access to new treatments to employee well-being.

This framework displays all the aspects that must be considered when assessing the total effect clinical trials have. Each of these factors has several further implications that need to be considered and require a measuring tool to be usable. Below each factor is analyzed in relation to the literature review and interviews carried

out at HUS. The table also displays the perspective of the balanced scorecard that each individual effect relates to.

| | | |
|---|---|---|
| +Benefits | **Direct** | **Perspectives** |
| | Drug cost avoidance | Financial |
| | Laboratory and imaging expenses | Financial |
| | Monetary compensation | Financial |
| | **Indirect** | |
| | Recruitment | Innovation and learning, internal business |
| | Clinical expertise | Innovation and learning, Internal business |
| | Clinical practices | Internal business, patient |
| | Employee well-being | Internal business |
| | Trial effect | Patient |
| | Faster access to new treatments | Patient |
| -Costs | **Direct** | |
| | Overhead expenses | Financial |
| | **Indirect** | |
| | Employee well-being | Internal business |

*Table 2 Framework for analyzing total costs and benefits of sponsored clinical trials*

### 3.2.1 Drug cost avoidance

Drug cost avoidance is the major factor impacting direct financial benefits from sponsored clinical trials. It is mainly affected by two variables. Firstly, the amount of clinical trials carried out. This is largely uncontrollable in the short term for the hospital, but the quality of the research can over the long-term lead to an increase in the amount of research being carried out. Secondly, it is impacted by the cost of care given to patients that are not taking part in clinical trials. As the amount of drug cost avoided is based on the drug the patient would have received had they not participated in the trial there is considerable fluctuation in the exact amount saved. Finally, using theoretical patients is inaccurate as it is very difficult to estimate the exact dosages each individual patient would have received.

Measuring drug cost avoidance has one major decision that must be made: whether the prices used as a reference include discounts that the hospital gets via deals, or if standard prices are used. In order to increase transparency of the results, this study calculates both. As the deals and exact costs of drugs might change annually, using the prices HUS would have in 2018 for drugs received in e.g. 2017 might be inaccurate, and thus both values are needed. In 2017 and 2018 this price difference was roughly 10% of the total cost of drugs received free of charge.

### 3.2.2 Laboratory and imaging expenses

The number of laboratory tests and scans performed due to be a part of clinical trials that can also be utilized as part of standard care. This is a very difficult factor to estimate, as the tests carried out on patients in standard care can vary based on the doctor giving care. One possible method of estimating this factor would be to determine based on the clinical trial protocol the proportion of tests that are relevant for patient care for each clinical trial separately. Whether this is sensible remains open, because this method would cause major overhead. As some level of clinical expertise is required for assessing whether some tests are useful or not, doctors would need to do this to some extent case-by-case. The workload this would cause is major, but whether it is still a viable method is open to exploration.

In any case, this is a factor that is very dependent on the specialty being assessed. In cancer care, it is not a major factor in relation to drugs mainly because drugs are so highly expensive. In other specialties where drug treatment is less expensive, the relative importance of laboratory and imaging expenses might be higher.

### 3.2.3 Overhead expenses

The costs incurred by performing sponsored clinical trials in general. This includes overhead costs from contracts as well as the costs incurred from reporting and related tasks that are mandatory for the clinical trials. These overhead expenses can often be at least partially paid by the sponsors, but they are still a factor that must be considered when assessing the total effect of sponsored clinical trials.

It is often nigh impossible to separate the overhead costs pertaining to clinical trials from those related to other forms of research and teaching at a hospital, as these are often done in tandem. For example, HUS has a research director who oversees both sponsored clinical trials and purely academic research. However, we can analyze the total budgets and distribute overhead costs based on that, if need be.

### 3.2.4 Recruitment

Recruitment of professionals, especially highly skilled ones, is often related to the amount of clinical research performed. Thus, a major indirect benefit of conducting clinical trials is being able to recruit more skilled professionals. This also has a positive feedback loop, as according to our interviews medical companies' value highly skilled individual doctors when choosing the hospital to carry out clinical trials. Thus, actively recruiting doctors who have a good reputation in clinical research might increase the amount of clinical trials being carried out, which in turn makes recruiting those individuals easier.

However, also nurses and other care personnel are often involved and interested in clinical trials. These are not highly experienced individuals and competition for them is far lower, but easier recruitment of nurses is a possible benefit of clinical trials as well. As there are far more nurses than specialists in a Hospital, the different employee groups should all be analyzed in order to assess the impact on recruitment.

### 3.2.5 Clinical expertise

Research in general has been shown to have a major impact on the clinical expertise of personnel (Karma, 2012). This translates to many intangible benefits such as quality of care the patients receive. There are also benefits that reach out to the whole country, as Käypä hoito -recommendations, the Finnish best practices for healthcare, that are used countrywide are also affected by the research done in HUS. Thus, we can assume that also sponsored clinical trials have an impact on the clinical expertise of personnel.

For this study it is important to note that this factor includes both the clinical expertise of nurses as well as the clinical expertise of doctors. These two effects need to be measured and considered separately and might have very varying scales. This is also a factor that is very difficult to measure. It would be possible to do a comparative analysis of nurses involved in clinical trials and those not involved in them and analyze the outcomes of treatments, but due to the process having so many variables it would be very impractical. Thus, it is most likely best measured with self-assessment, despite the inherent issues in self-assessment.

### 3.2.6 Clinical practices

Clinical research performed at HUS has a major impact on the clinical practices at both HUS and a national level (Karma, 2012). These practices are most likely also impacted by sponsored clinical trials, as they keep the organization up to date with the newest advances in medical treatments, thereby enhancing clinical practices. Whether there is also an effect of clinical trial practices enhancing how standard care is administered is considered in the factor “clinical expertise”.

Another aspect of clinical practice is whether conducting clinical trials speeds up new treatment adoption. This was suggested by both nurses and doctors in interviews, with a few possible hypotheses for how the impact works. Firstly, it was hypothesized that in general conducting clinical trials requires and teaches skills required for adopting new treatments. Thus, it would increase the capability of staff to adopt new treatments. Secondly, having given the treatment as part of a clinical trial naturally makes it easier to adopt it into standard care later. Whatever the reason, this study focuses on determining if such an effect exists via the questionnaire.

### 3.2.7 Employee well-being

Performing clinical trials can be a source of employee well-being when organized properly. It can give a sense of meaning and be a way of delivering the absolute newest and best care available in the world, which increases employee motivation. In general personnel expenses are a major factor in all areas of healthcare, and therefore employee well-being is a factor that should be considered when discussing total benefits of clinical trials.

However, clinical trials can also decrease employee well-being if they are not organized effectively. They might increase the workload of employees so much that it

becomes a negative, leading to a decrease in well-being. Thus, it is included in the framework on both sides as the effect might be positive or negative.

### 3.2.8 Trial effect

Prior research has found evidence for a trial effect, in which individuals partaking in clinical trials seem to benefit from all care more than those not in clinical trials (Braunholtz, Edwards, & Lilford, 2001). This is separate from health benefits related to newer drugs being available earlier, as a trial effect has also been observed in patient groups that receive placebo. Thus, it is included in this framework.

Whether participating in trials enhances quality of care through e.g. patient motivation is open to interpretation. However, for the purposes of this study it is enough to assess that such an effect exists, and not pursue the mechanisms related further as it is not a part of the scope of this study.

## 3.3 Data collection

In order to use the framework described data was gathered from two main sources: accounting systems, and a questionnaire. Some generalized assumptions were also made to approximate aspects that were impractical to measure exactly, such as the amount of laboratory visits and imaging that were useful for the general care. Additionally, data on drug cost avoidance was gathered by creating a data gathering spreadsheet that the departments filled with the relevant information either from their own archives or by consulting the physicians in charge of the studies. All clinical trials between 2012 and 2018 were included, and the following information was gathered: physician in charge of the trial, the phase, internal identifier, starting date, end date, research nurse, number of patients participating, trial arm treatment, control treatment, default treatment if patient was not in a trial and no control treatment exists, the full name of the clinical trial.

Drug cost avoidance used data provided by the hematology and oncology departments about the clinical trials and the control treatments that would have been used if the patients were not in clinical trials. This data was verified to include all relevant trials. This data about clinical trials was then combined with the bookkeeping systems of the HUS-pharmacy in order to get the actual savings numbers. As the data in general is not in one place it had to be compiled from multiple sources. Three methods were used to estimate drug cost avoidance: direct value of drugs received, total value of control treatment drugs, and a combination of these in which expensive

drugs – defined as accounting for more than 5% of the total value of drugs received – were replaced with control treatment drugs.

Lastly, the bookkeeping of Clinical Research Institute HUCH, the institute through which financial transactions concerning clinical trials are performed, was analyzed. The relevant projects were selected from a list of all projects, and their internal bookkeeping was analyzed to gain visibility into the overheads and potential cost savings from laboratory expenses.

### 3.3.1 Questionnaire

Three different questionnaires, shown in the appendices A, B and C, were sent out to nurses, residents and specialists, respectively. These were developed based on preliminary exploratory interviews conducted with employees in the respective groups. The questionnaires were focused on the well-being aspect of individuals and aimed to find differences in how clinical trials are perceived in different employee groups. The questionnaires were sent to the personnel by their forepersons, in an attempt to maximize the response rate.

The questionnaire was sent out to staff of oncology, hematology and rheumatology. Rheumatology was included in the study to increase the number of answers, as especially the number of doctors in oncology and hematology departments is relatively small. This was done for two main reasons. Firstly, to increase the trustworthiness of the questionnaire via increased answer amounts. Secondarily, a higher number of respondents makes it harder to distinguish singular doctors from the small subset, which was seen as important to ensure trust in the study. Rheumatology also conducts sponsored clinical trials, and as such their answers should not diverge heavily from those of oncology and hematology

The questions were in part open and in part on a scale of 1 to 7. As the expected number of answers was relatively low the scale of 1 to 7 was chosen to highlight opinions that might not be visible on a scale of 1 to 5. The questionnaire was also kept as short as possible, only taking some minutes to fill out, in order to increase the amount of answers.

## 3.4 Data analysis

As the data is not necessarily directly usable, some analysis is required to reach conclusions. This chapter discusses modifying the data available to be suitable for use in the framework.

### 3.4.1 Drug cost avoidance

Three different values for drug cost avoidance were eventually reached in order to form a complete picture. Firstly, a theoretical cost savings was calculated, i.e. how much the drug treatments outlined in control treatments would have cost if they had been used. The control treatments were taken from either the trial protocols, if a control arm existed, or from expert opinions from the departments at HUS. Secondly, the total value of drugs received as part of clinical trials was calculated. Lastly, a final estimate was calculated based on this by replacing highly expensive drugs with control drugs where applicable. Thus, the total value of drug cost avoidance is somewhere in between these three numbers. If a control treatment could not be reliably found, the value of the drug saving itself was used, as this was likely a case of missing data in our control treatment data, so the results would have been possibly skewed if those drugs were disregarded.

Of these estimates, the higher estimates where highly expensive drugs are removed from the total value but not every drug has been analyzed, are the best estimate available. In general real processes in hospitals tend to use more expensive treatments than theoretical processes, and thus higher estimates are more likely to reflect reality.

### 3.4.2 Laboratory and imaging expenses

We approximated that half of the laboratory tests and imaging performed in clinical trials is useful for the general care, and thus that is the value of laboratory costs avoided. This is a rough estimate based on discussions with doctors at HUS, and the real value is somewhere between 0% and 100%, with the doctor estimates being between 20%-50%.

This number has high uncertainty, but from the discussions with several doctors it is evident that some part of the laboratory expenses is saved in any case. As the total value of laboratory cost savings is relatively small, the uncertainty here has limited impact on the total cost and can be accepted. The impact of laboratory costs is possibly higher in other specialties, where drug costs are far lower, but laboratory treatments might be used to the same extent. When utilizing this framework to other specialties this should be noted and more careful analysis of laboratory expenses is required.

### 3.4.3 Employee well-being

This is the factor that is most difficult to approximate. The potential cost of turnover across all of HUS is somewhere around €100 million. This is the starting point from which we could approximate the magnitude of potential savings, but at best that would be a guess. Thus, this study does not cite a number for the actual savings achievable through employee well-being, instead, focusing on whether clinical trials could be a major driver of job satisfaction.

# 4 Impact of sponsored clinical trials in HUS

This chapter finds relevant measurements for the aspects of the framework introduced in the previous chapter and uses those measurements to assess the impact of sponsored clinical trials in the oncology and hematology wards of Helsinki university hospital. The impacts are divided into direct and indirect costs and benefits.

## 4.1 Direct costs and benefits

Firstly, direct costs and benefits were analyzed. These are the effects that are directly measurable in monetary value, whether they generate a cashflow or not. It includes drug cost avoidance, laboratory and imaging costs as well as overhead costs.

### 4.1.1 Drug cost avoidance

The total drug cost avoidance calculated in the hematology and oncology departments in 2017-2018 is shown below in figure 2. The results are in line with prior research on the subject, but differ somewhat from the previous approximations used at HUS. This is mainly due to the previous approximations being purely based on how much drugs are given to HUS without cost. Many of the clinical trials conducted are last line treatments, in which the standard of care might not include any drugs. Similarly, often very expensive drugs are given to patients who might otherwise only receive standard chemotherapy. This is the reason for the large discrepancy between the high value of drugs received without cost and the actual drug cost avoidance.

As the figure below shows, there is high uncertainty related to the exact value of drug costs avoided. The figure shows four values related to the value of savings. The two lowest values are the estimates reached in this study, one being a more conservative estimate where the theorical drug treatment cost of patients enrolled in clinical trials that have a control arm of only placebo would have been 0€. This is inaccurate, as doctors often overtreat, and the higher estimate takes this into account. The highest values are the values of all drugs received in the hematology and oncology departments at default wholesale prices. The second highest value is calculated using the prices negotiated by HUS, which are generally slightly lower than list prices.

## 4.1 Direct costs and benefits

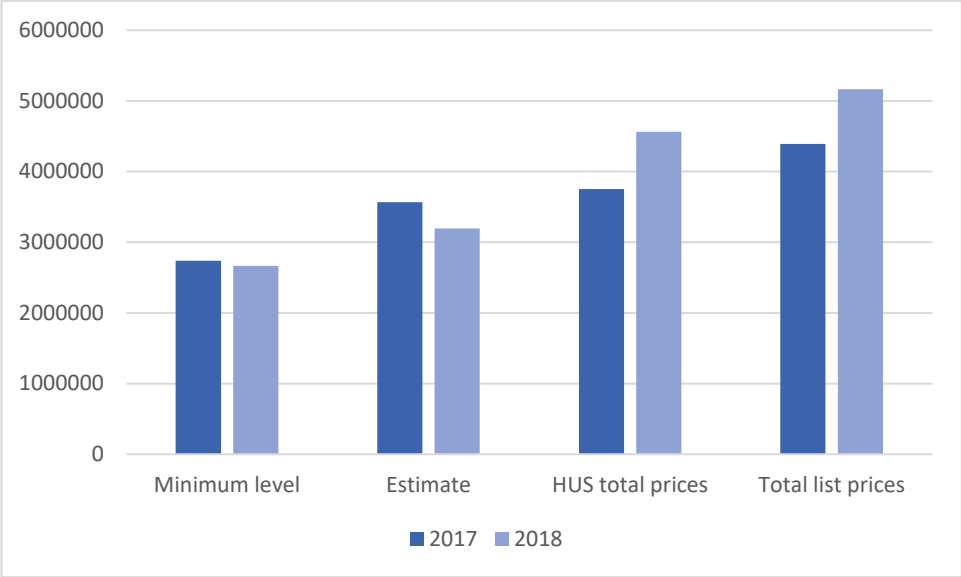


*Figure 2 Values and estimates of drug cost avoidance at HUS in 2017 and 2018*

The direct cost of drugs provided to HUS in 2018 was €5.1 million, using standard prices. The prices negotiated by HUS lower this to €4.5 million due to some drugs being less expensive for HUS than in general. Of these, €4.4 million was the value of drugs received in hematology and oncology departments. I.e. almost all of the drugs, based on value, come to these departments. Same values for 2017 are €4.4 million with stock prices, €3.7million with HUS-prices and €3.6 million euros in the oncology and hematology departments. The estimated value of drug cost savings was €2.66 million in 2018 and €2.74 million in 2017 using a conservative estimate and €3.19 million in 2018 and €3.57 million in 2017 using a balanced estimate.

Figure 3 shows the pharmaceutical costs related to clinical trials in 2014-2018. A portion of these costs are related to the clinical trial itself, but a substantial portion are related to different types of drug handling that is required always, such as preparing IV-infusions, which generate cost savings for HUS. The total effect these have is relatively small, and because they are so difficult to estimate this study ignores them for the cost savings calculations.

## 4.1 Direct costs and benefits

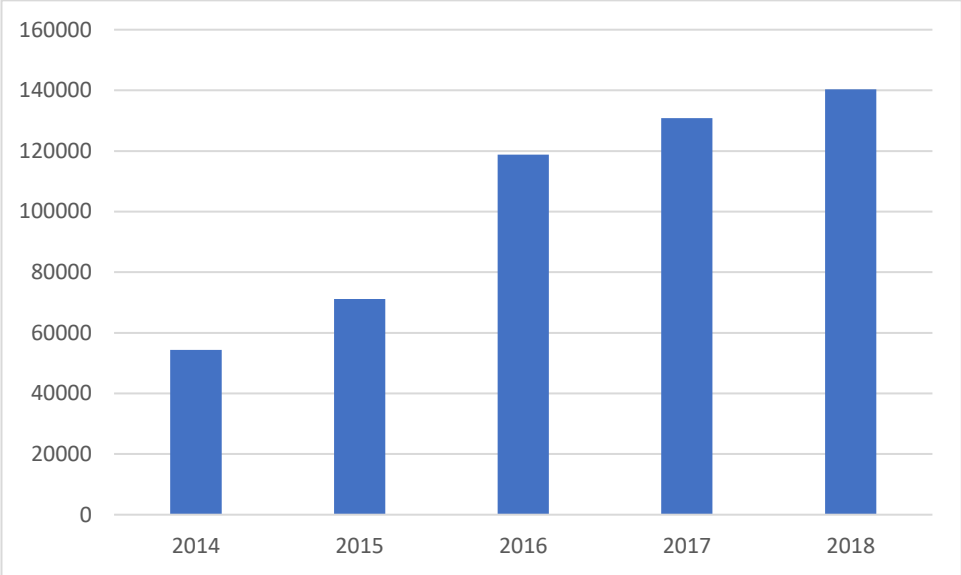


*Figure 3 Pharmaceutical costs related to clinical trials at HUS 2014-2018*

Our data also displays the variance in drug costs, which includes 50 drugs. Of these 50 drugs, the four most expensive comprise 50.4% in 2018. Similar results are visible in other years, with a small minority of highly expensive drugs being the major contributor to the upper bound being so high. Figures 4 and 5 show the distribution of all drug cost savings in 2018 and 2017 respectively. They illustrate the 8 most expensive drugs comprise slightly over 70% of savings, with the remaining 42 drugs each having a small impact in 2018. This effect is even more pronounced in 2017, which also showcases the relatively high variance from year to year. The variance outside the most expensive drugs is relatively low.

*Figure 4 Distribution of drug values in clinical trials by drug in 2018*

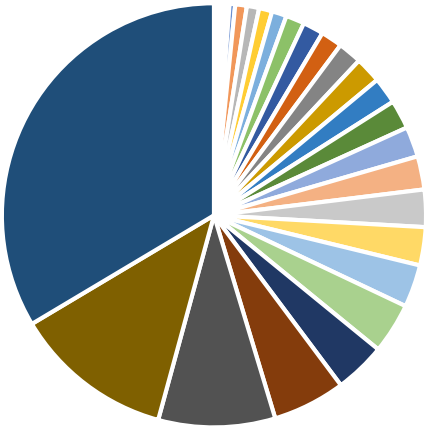

*Figure 5 Distribution of drug values in clinical trials by drug in 2017*

### 4.1.2 Laboratory and imaging expenses

Laboratory and imaging expenses include both blood tests and similar samples as well as imaging such as MRIs. These are often performed on cancer patients, and as such their role in the total cost of treatment is not insignificant. The prices used for laboratory expenses in this study are the standard prices used by HUS when invoicing member municipalities, which reflect the actual costs and do not include excess markup. The value of laboratory testing related to clinical trials in HUS was 235 000€ in 2018 and 198 00€ in 2017 shown in figure 6 below. Based on this, the estimated cost savings were 117 500€ and 99 000€ respectively.

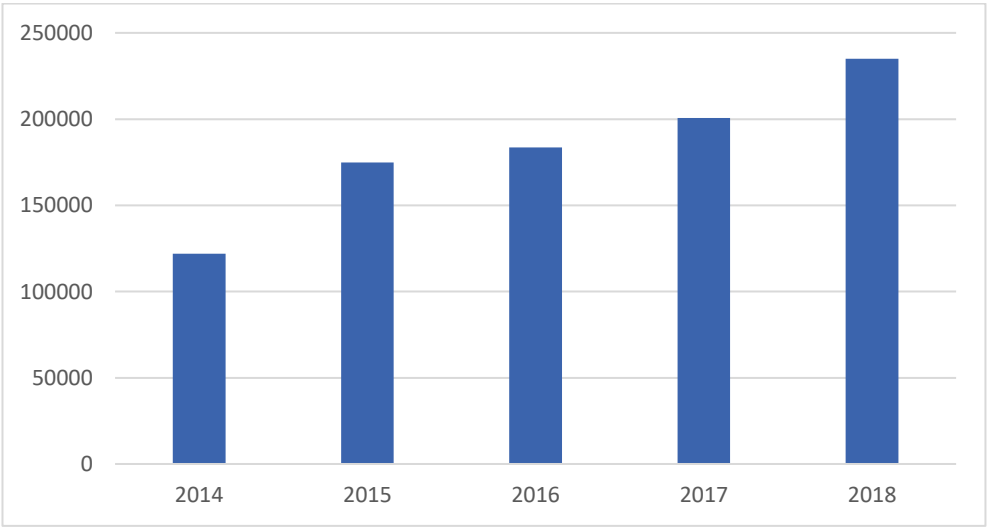


*Figure 6 Laboratory expenses related to clinical trials at HUS 2014-2018*

### 4.1.3 Overhead expenses

For the overhead costs our data is limited, as Helsinki university hospital changed their way of reporting in 2014. Thus, our analysis only covers fiscal years 2014-2018, as the data before that is not comparable. Figure 7 below shows the distribution of costs at HUCH 2014-2018. As was to be expected, personnel expenses are the majority of all costs, varying between 63% and 68% of all costs. No data is available on the distribution of these costs beyond these high-level categories.

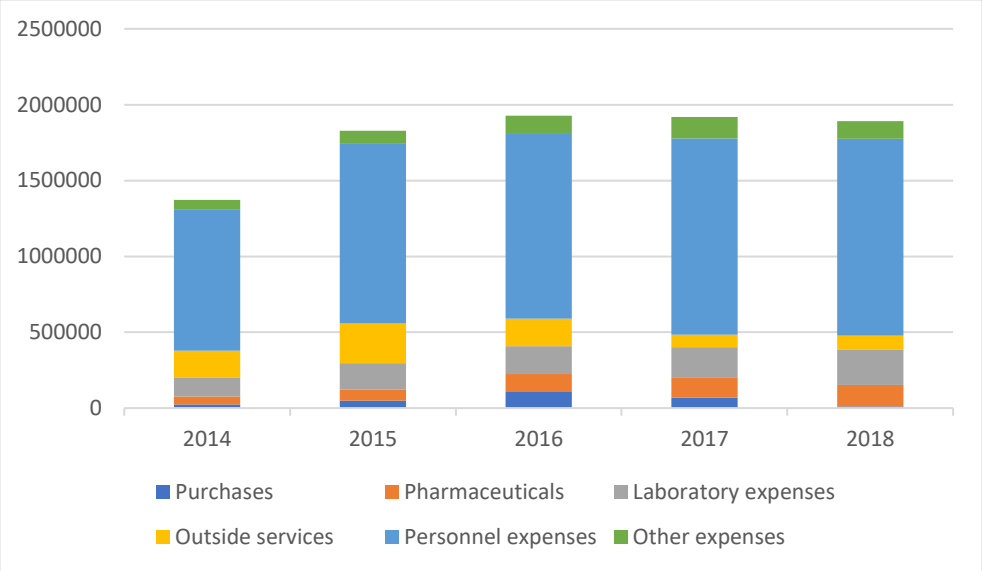


*Figure 7 Development of expenses of clinical trials at oncology and hematology departments in Euros 2014-2018*

During 2014-2018 the annual income from sponsored clinical trials has been 5.9% of the revenue. This is the actual net cashflow from performing sponsored clinical trials. The average net cashflow annualized 2014-2018 was €106 000.

## 4.2 Indirect costs and benefits

Indirect costs and benefits include all effects that are not easily measurable in short-term monetary values. This includes recruitment, clinical expertise, clinical practices, employee well-being as well as trial effect. These results are based on the questionnaires conducted as well as the literature review. Only those questions where answers converged are analyzed here, as the conclusion for some questions was clearly divergent and thus inconclusive.

## 4.2 Indirect costs and benefits

Overall, 56 responses from nurses, 6 from resident doctors and 18 from specialists were received. This translates to response rates of 19%, 7.5% and 15% respectively. The number of answers was higher than anticipated and is high enough to do conclusions from the data. The differences in responses received are largely equal to the differences in general amount of employees, with nurses outnumbering doctors by a factor of 2 to 1. Of the nurses 29% had graduated within the last 5 years, and 71% were more experienced. 41% of the nurses participated in research, and 59% did not. 83% of the specialists had been specialists for more than 5 years. 100% of the specialists participated in clinical research currently or have in the past, with a median time of 5 hours per week being used for clinical research.

### 4.2.1 Recruitment

62% of nurses reported that clinical trials do not have an effect on their choice of workplace. As there have been no prior studies that would indicate otherwise, we can assume that what effect clinical trials might have on recruitment happens through other means than direct influence, e.g. by enhancing the employer brand. There might be potential to leverage cutting-edge treatments available through clinical trials as a recruitment tool, but currently this effect is largely insignificant. The effect clinical trials have on workplace brand should also be noted, as even if there is no direct effect the employer brand might be affected and there might be an effect through it.

50% of specialists reported that clinical research has an impact on their choice of workplace, with a further 28% answering neither yes or no. 66% of resident doctors reported that clinical trials have an impact on their choice of workplace. As specialists are the most expensive employees to recruit, the actual financial impact that this has on recruitment might be relatively high, despite them being a small subgroup of employees. Based on the answers this study finds that clinical trials have a limited positive effect on recruitment.

### 4.2.2 Clinical expertise

5% of nurses, 0% of specialists and 0% of resident doctors reported that clinical trials have a negative impact on the quality of care given at HUS. 22% of nurses, 5% of specialists and 16% of resident doctors reported neither negative nor positive effect. 73% of nurses, 95% of specialists and 84% of resident doctors perceived that clinical trials have a positive effect on the quality of care given at HUS. All personnel groups also reported positive effects for the speed at which new treatments are taken into use as well as in the quality of care they themselves give.

Thus, the questionnaire supports the hypothesis that clinical trials increase the clinical expertise of nurses. As the answers were so clear, it could be hypothesized that the effect is rather substantial, but as the questionnaire did not focus on it more research should be conducted before determining the exact effect. However, the data heavily suggests that the clinical expertise of nurses is enhanced by conducting clinical trials.

Similarly, the results from doctors and especially specialists converged heavily for both the quality of care they themselves give as well as the quality of care given by their wards. They also agreed heavily that clinical trials increase the speed at which new treatments become a routine part of treatment at HUS. Whether this is due to clinical expertise or clinical practices is unclear, but the strong convergence of answers suggests a major effect.

All personnel groups wanted more information about clinical trials conducted across their specialty in HUS. 75% of specialists, 94% of nurses and 50% of resident doctors wanted more enough information about clinical trials being conducted in HUS. The answers reflect a positive approach to clinical trials, and they are largely seen as a tool of learning and enhancing care.

### 4.2.3 Clinical practices

No data about the effect of clinical trials on clinical practices was available for this study, and an in-depth analysis was out of the scope of this study. Thus, this factor was not evaluated. Further research should be conducted if this effect is to be measured. However, we can say that this is a positive factor based on the answers received to questions related to clinical expertise in our questionnaire, only the size of the effect is unknown. The answers for both personal quality of care as well as for the ward quality of care, described in the previous chapter, suggest that the effect exists.

### 4.2.4 Employee well-being

According to our questionnaire 55% of nurses nurses felt that cutting-edge treatments are an integral part of their jobs at HUS. Simultaneously, only 8% of nurses reported unnecessary work due to clinical trials. Combining these with the fact that most nurses wanted more information on research at HUS and were willing to participate in clinical trials more than currently, it seems likely that clinical trials are a major potential source of employee well-being that is already beneficial for HUS but has potential for even more.

These answers are in stark contrast with those reported by specialist doctors. 39% of specialists reported that clinical trials cause unnecessary work. Simultaneously, 78% of specialists agreed strongly or very strongly that they do not have enough time for clinical research in their workdays, and 72% of specialists wished to conduct more clinical trials despite this. They reported in open questions problems with excess workload and a general lack of time was also cited as the main reason for limiting the amount of research that doctors conducted. One respondent stated that clinical trials do not become a part of the normal work routine at HUS well enough, being a separate entity that is done on top of normal clinical work. Simultaneously doctors reported that clinical trials cause unnecessary work for them. This may be indicative of the general stress that doctors are under, where anything not directly related to clinical work is perceived as unnecessary as the normal workload is already very high.

### 4.2.5 Trial effect

We can assume that clinical trials have a beneficial effect for two main reasons. Firstly, it has been shown that patients participating in clinical trials receive better care than those not in clinical trials (Braunholtz, Edwards & Lilford, 2001). The exact reasons are unknown in academic literature, but the phenomenon has been identified. Secondly, clinical trials offer care for those patients who might have no choices any more in standard care. This can be seen as having a positive effect on the total care given. However, this must be analyzed carefully as deciding that clinical trials are beneficial due to health reasons quickly leads to questions about the clinical trial process in general. Nevertheless, these two effects combined clearly have a positive impact on the quality of care given at HUS.

## 4.3 Total effects

Table 3 below outlines all the different aspects considered at HUS, the measurement tools used to assess them as well as the estimates reached. Direct and indirect costs are separated as the indirect costs are very difficult to conclusively assess in euros. Therefore, they are separated and must be interpreted separately.

## 4.3 Total effects

| | Factor | Measure | Finding in HUS oncology and hematology |
|---|---|---|---|
| Direct | Drug cost avoidance | Bookkeeping and control treatments | 3 to 6 million euros annually |
| | Laboratory and imaging expenses | Bookkeeping and expert assessment of the total proportion | €100 000 annually |
| | Monetary compensation | Bookkeeping | €200 000 - €400 000 annually |
| | Overhead expenses | Bookkeeping | €200 000 annually |
| Indirect | Recruitment | Questionnaire to staff | High individual variance, stronger effect for specialists but a major effect also for nurses |
| | Clinical expertise | Questionnaire to staff | Major effect for both nurses and doctors |
| | Clinical practices | Questionnaire to staff | Effect, but extent unknown |
| | Employee wellbeing | Questionnaire to staff | Positive for nurses, negative to neutral for doctors, major potential |
| | Trial effect | Academic literature | Minor effect on patient quality of care |
| | Faster access to new treatments | Not measured | |

*Table 3 Total effects of sponsored clinical trials at HUS*

### 4.3 Total effects

In order to set a context for the savings received through indirect effects we assess the impact of employee retention. As stated earlier, the total employee turnover cost in HUS is roughly €100 million. Based on this, we can approximate that employee turnover in hematology and oncology departments could value anywhere from €100 000 to up to €1 million. Adding to this the employee satisfaction increase, recruitment effects as well as clinical expertise, this study concludes that the indirect effects are roughly equal to the direct effects in the case of oncology and hematology departments of HUS. This is especially noteworthy because these are the departments where drug cost avoidance is highest. In other specialties indirect effects are thereby far larger than the direct effects clinical trials have, according to the findings of this study.

# 5 Discussion and conclusions

The main theoretical contribution of this study was to develop a framework that can be used to assess all different aspects related to clinical trials. As chapter 4 shows, the financial impact of clinical trials is positive for both direct and indirect costs, i.e. it both generates a positive cashflow and has a large number of positive effects on the organization in general. This chapter discusses both how future research and use should refine the framework, as well as the implications that the framework has for HUS.

## 5.1 Analysis

Due to the limited amount of previous literature related to comprehensive clinical trial assessment, this study had to develop new measures and some assumptions had to be made. This allowed for the creation of the first comprehensive framework that can be used to analyze the total impact of clinical trials. Simultaneously, it makes verification of the results somewhat more difficult, as there are no previous results to compare to.

However, for the factors that have been studied before, the findings of this study are in line with those reported in previous literature. The major differences are in drug cost avoidance calculations. Some previous studies have used a more optimistic assessment of the benefit gained from cost-free drugs, using higher values for them than this study used. This is especially true for the numbers cited for HUS from 2010. However, there are previous studies that used a standard-care -approach and still had somewhat differing results. The study by LaFleur et al. (2004) had very similar values with a similar methodology, which gives credibility to the findings here. This suggests that the differences stem from different countries or hospitals, and not from faults in applying the methodology or in the methodology itself.

Having only a singular point of data, in this case one hospital, might skew the results based on the types of clinical trials they carry out. As HUS carries out only tens of clinical trials annually, variance is high and a hospital that carries out different types of trials might have different numbers. Additionally, it is possible that cancer drug costs have changed substantially over the last decade, as the previous studies are from around 2010. As the majority of costs come from single, highly expensive drugs, this most likely has an impact.

In general, this study brings light to how major the non-quantifiable effects of clinical trials are. This is in line with general findings from other fields, where employee motivation especially for highly skilled and specialized individuals has been seen as a

major contributor to success of a company for decades. Therefore, it is not surprising that clinical trials have major potential for employee well-being and therefore cost savings. Based on the discussions and interviews conducted for this study, it is clear that employee wellbeing is a major issue at HUS due to the high workload and tight budget constraints that specialized healthcare is under. If clinical trials have the potential to alleviate the negatives of high workload by increasing employee motivation and fulfilment even slightly, they should be explored in-depth.

As most of the effects found in this study are hard to quantify, they are also difficult to get funding for. Finnish hospitals are all public, and as such their funding comes from policymakers and their budgets. Therefore, management at hospitals must find ways to convince policymakers that investments into employee well-being are beneficial through non-quantifiable means. On the other hand, the findings of this study clearly show that sponsored clinical trials are a net benefit both indirectly as well as in direct cashflow. Thus, it should be relatively easy to convince policymakers that investing in clinical trials is a smart choice.

### 5.1.1 Direct costs

As noted in the literature review, drug cost avoidance varies very much based on the specialty. Thus, our selected specialties of oncology and hematology have very high drug cost reductions, and they are not representative of other specialties. Indeed, these two specialties comprise more than 90% of the drugs received at HUS without cost as part of sponsored clinical trials.

What is noteworthy is that the total value of drugs received increased from 2017 to 2018, but the value calculated here decreased. This phenomenon is explained by the fact that four extremely expensive drugs were used more in 2018 than in 2017, and the standard care of those patients would have been far less expensive. This illustrates why it is so important to monitor these values closely, as pure value of drugs received is not always reflective of the value of drug cost avoidance.

It should also be noted that this value does not include is the possible savings from pharmaceutical expenses. As from our data it is impossible to distinguish which parts of the pharmaceutical costs are related to dosage and as such would have been incurred without the clinical trial, we cannot determine the exact value of those costs.

Other costs and incomes in the case of Helsinki university hospital are in balance, as the pricing of contracts to the sponsors is done so that they cover the overhead costs. As we can see the total net income from the clinical trials has been roughly 0, as expected. However, we must note that it includes not only overhead costs but also some research that is not sponsored. Thus, in order to have a truthful picture

of what is the impact of sponsored clinical trials we must consider the account other expenses as unrelated. Based on discussions with HUCH, the sponsored clinical trials largely cover all overhead expenses, also those incurred by non-sponsored research. Thus, we estimate that sponsored clinical trials generate a positive cashflow.

One aspect to consider about overhead expenses is the extent to which they can be influenced and the extent to which they are necessary to fulfill the requirements set out by the sponsors of the clinical trials. According to interviews in this study it can be estimated that the overhead costs at HUS are largely at a good level, and there is minimal room for lowering. As the overhead costs are paid by the sponsors, the overhead identified in this study has no effect on the total costs and benefits for HUS. Overall, the pure positive cashflow related to sponsored clinical trials is very small in comparison to the other positive factors, as it should.

### 5.1.2 Indirect costs

Recruitment answers diverged more than in some other areas, and thus they should be analyzed carefully. Answers from different employee groups differed, but there was also divergence in answers within the same personnel group. This is most likely because the recruitment effect is highly individual, and it is to be expected that for some it is an important factor and for some it does not matter at all. Further study on the topic is required to understand the effect fully, and to explore different subsets of personnel and for which types of employees it is important. Thus, recruitment should never focus solely on clinical trials, instead leveraging it where applicable.

There was major divergence in how specialists saw newest treatments at HUS. There is a portion of specialists who do not think that HUS offers the newest treatments available through clinical trials. This should be looked at in more detail: is the reason lack of clinical trials or somewhere else, and indeed what is the reality. A small, divergent set of answers is inconclusive on this issue. It should be explored in more depth whether clinical trials could be used as a recruitment tool to find highly skilled individuals.

When discussing employee well-being doctors and nurses have very different views. Whatever the reason, in the current state clinical trials are not a source of employee well-being for doctors at HUS. However, they could be, as the doctors are highly motivated and willing to do research, as it is a key part of the identity of a university hospital. Indicative of this is that the only reason cited in the question “What are the reasons you have not participated more in clinical trials?”, which was asked if a respondent answered yes to wishing they participated more in clinical trials, was a lack

of time. These are highly motivated, ambitious individuals, and currently it seems they are overburdened and thereby underutilized.

## 5.2 Recommendations for improving the framework

Table 4 below lists recommendations for future research and study in order to improve the framework. These should be explored before utilizing the framework again, e.g. in HUS, as they could have implications that enhance the precision of the framework.

| |
|---|
| Exploring measurement tools for both ease of use and more precision |
| Confirming the findings over longer time periods |
| Patient care quality assessment and monitoring |
| Additional factors currently missing |
| Differences between phases of clinical trials |
| Cost effect of personnel costs in clinical trials |

*Table 4 Recommendations for future studies to improve the framework*

As this is the first holistic framework for assessing the costs and benefits of clinical trials, there is no reference to use to assess if the results are in line with prior results. Drug cost avoidance has been studied extensively in the past, and the process utilized here is largely an industry standard for assessing it. Thus, the framework improvements should focus on finding relevant, easy to use measurement tools for different aspects of the framework.

Future studies should also make sure that the application of the framework gives relevant results that are in line with either expert opinions or previous studies. As this is new ground, there is inherent uncertainty and refinement must be made. Monitoring the results over the timespan of several years and seeing if changes in the workplace and clinical trial conducting methods have effects on the total benefits would give more confirmation that the framework is valid.

The factor this study decided to not incorporate in the framework was patient care quality. However, it is fully possible that studies arise in the next few years that quantify the effect clinical trials have on patient care. If such findings are made, those should be included to the framework. Similarly, some sort of continuous measurement

tools for assessing the patient care quality in clinical trials could be used to incorporate patient care into the framework.

The framework might also miss some factors, and as such it should be freely appended with new aspects. As the idea of the framework is to create a holistic picture that can then be distilled based on the measurements available, all possible aspects should be considered and included in it.

A major area that should be explored in the future is how phase 1 and phase 4 clinical trials differ from the trials studied here. This would help focus on those phases which are most beneficial when taking actions to either increase the amount of clinical trials or to enhance their efficiency. Based on the interviews conducted with experts in this study it would seem that there is not much difference between phases, but further exploration is required to be conclusive.

It should also be explored in more what is the relation between the time spent treating clinical trial patients, i.e. how much time doctors and nurses spend, and the reimbursements paid by sponsors. In this study it was assumed that the sum of these effects is roughly zero. This is based on the assumption that while sponsors reimburse some costs of doctor or nurse visits, often those visits are only needed because the patients are partaking in a clinical trial. For practical reasons it was not possible to explore this issue further in this study, and thus it should be looked at in the future.

## 5.3 Improving the application of the framework at HUS

The application of the framework had several limitations due to being purely retrospective. The suggestions given here should be implemented for the future in order to get more precise numbers more easily in subsequent studies into this topic. The four improvements focus on the following areas:

- Laboratory and imaging cost monitoring
- Drug cost avoidance monitoring for all studies
- Annual surveys to monitor the development of indirect effects
- Widen the scope to include all specialties with clinical trials

The laboratory and imaging cost avoidances could be monitored constantly, for example by including a note in the reservations and invoices related to those the doctor could mark those tests they deem as generally useful, which would make monitoring this factor easy over the long run. It would be essentially similar to how research visits are monitored now, and if done in an intelligent manner this would not

cause more than miniscule amounts of extra work for the doctors. Automating the monitoring of this factor would give more precise data for decisionmakers in coming years at HUS.

Drug cost avoidance, which HUS has already monitored, should be monitored with more precise tools in the future. The main tool for this would be to define a control treatment for each study that is representative of the treatment patients would receive if they did not partake in a clinical trial. This is a small additional step of bureaucracy, but often it is already defined in the research protocols, and doctors need not be too precise of it. Both this number, calculated based on theoretical treatments, and the total value of drugs received should be monitored, as neither of them is precisely correct. Also, a method in which control treatments are only used as a basis for drug cost avoidance calculations if the drug is highly expensive is a viable tool that accounts for the few, highly expensive trials while minimizing bureaucracy related to reporting. This has the benefit of being more precise, as the dosages are real, while being almost as accurate as using theoretical control treatments for all clinical trials.

The qualitative factors are, of course, far more difficult to assess. However, annual surveys and similar tools could be used to assess their impact, and especially to see increases and decreases in them. Implementing factors from this study into general employee well-being questionnaires, if such are used currently, would be an efficient method of following relevant measurements. What is most important in qualitative factors is consistency. I.e. they should be measured for several years, and trends and changes are the important thing, not the absolute values.

Things such as clinical expertise are influenced by multiple variables ranging from individual interests to how the ward an employee works at is led. Thus, it is hard to measure which part of that is the result of clinical trials. This could be countered by trying to separate those participating in clinical trials from those not participating, and if there is a significant difference, we could somewhat quantify the exact effect clinical trials have. However, this requires a long period of time, so it must be implemented as a standard tool in annual monitoring of employee well-being.

In general, long-time monitoring of the variables studied in this study is the most important thing for the future research into this topic. Incorporating the findings of this study into annual monitoring and ensuring that the measurements can be done easily and automatically is critical, as only through that can we gain solid insight into the total effects.

Lastly, based on this study it is vital to note that the beneficial effects of sponsored clinical trials are not limited to drug costs. Indeed, most effects are outside that. This has one major implication: the relative importance of different specialties

changes. If drug cost avoidance was the only noteworthy benefit, only those fields which have expensive drugs – usually oncology and related specialties – should be focused. However, as the benefits are far wider based on this study clinical trials are very beneficial also in those specialties where drugs are relatively inexpensive. Therefore, all specialties that conduct clinical trials – whether sponsored or not – should be included in future studies.

## 5.4 Managerial implications

As we can see from the results conducting sponsored clinical trials is highly profitable for university hospitals, and thus should be maximized. This has several implications, shown in table 5. The table shows the finding and aim that this study has, as well as some tools that this study suggests should be utilized to achieve that goal. On top of what is shown here, it should be noted that cutting-edge research is a core responsibility of HUS, and clinical trials are a part of that. Indeed, it might be the only responsibility HUS has that is profitable and not a cost.

## 5.4 Managerial implications

| Aim | Methods |
|---|---|
| Maximizing number of clinical trials | Optimizing the process for quality and throughput<br>Centralize research nurses to the extent that is possible in order to even workload of research nurses<br>Influencing policymakers to increase the total number of trials in Finland<br><br>Increasing the number of clinical trials, sponsored or not, in other specialties |
| Leverage the potential effects on nurses | Give nurses more ownership of the clinical trials where possible<br>Incorporate more nurses into clinical trials |
| Increase the well-being of doctors | Ensure doctor workloads are reasonable<br><br>Agree that all tasks which can be performed by nurses are performed by nurses to decrease the workload on doctors<br>Automate reporting and processing where possible to decrease meaningless, tedious work related to clinical trials |
| Spread knowledge more efficiently | Informal displays of results and ongoing trials at the ward in breakrooms etc.<br><br>Use clinical trials in nurse training |

*Table 5 Managerial implications*

Firstly, the hospital should endeavor to maximize the number of trials performed at the hospital. This is important not only for the reason that it is profitable, but also because being a research hospital is a core part of what makes a university hospital a university hospital. The management should try to convince other university hospitals and governmental institutions to invest in clinical trials facilitation, in order to

increase the number of clinical trials performed in Finland. This kind of co-operation and investments on a national level would also increase the number of trials at HUS. Simultaneously, HUS should take action to ensure the quality of clinical trials at HUS is high, and agreements are met. Ensuring that the output of clinical trials at HUS is of high quality is the best method of maximizing the number of trials at HUS in the long term.

Our interviews suggest that combining all of the clinical trial administration under one organization might be an efficient method for increasing the quality of the trials performed. Ensuring research nurses are available when needed is easier when they all share a workload. HUS has already combined administration to HUCH, and it might be beneficial to similarly centralize research nurses in order to even the workload and ensure throughput stays constant and no single individual becomes a bottleneck for the clinical trials. Also the barriers for nurses to partake in clinical trials should be lowered in order to increase the flexibility of the staff. The workload is uneven over a single year and over multiple years, and some sort of flexibility is required always to ensure efficiency.

If the amount of clinical trials could be increased to the level they were at in 2007, it would create cost-savings of 3 to 6 million euros annually in HUS alone. When considering the cost avoidances received in other institutions too it can be clearly seen that even rather expensive investments in order to increase the number of clinical trials is financially profitable for the government. Also, the effects shown in this study are not the only effects of clinical trials, as they have positive effects in the economy on a larger scale too. Thus, based on this study Finland should endeavor to create a unified strategy that aims to increase the standing of Finnish hospitals as top-tier clinical trial facilities, especially so for all different types of cancer drugs. When discussing benefits on a societal level, the relative value of drug cost avoidance increases, as it is a major tool that could be used to decrease the costs of healthcare in Finland, which is a hot topic at the moment. Thus, on a national level striving to create top-level clinical research in fields where new drugs are expensive, mainly in cancer treatment, could decrease the costs of healthcare quite substantially.

Further study should be conducted on the topic of clinical trial drug cost avoidance in HUS, as well as in other university hospitals in Finland, outside of the oncology and hematology departments. Despite the value of drugs received free of cost being relatively small in HUS outside of oncology and hematology, we should be careful to not assume that it has to be this way. It could very well be that the oncology and hematology departments at HUS have highly skilled individuals and have a good reputation, which causes more clinical trials. Further research into the state of other

specialties in other Finnish university hospitals could give insight into whether it is possible to achieve more cost savings in other specialties too.

HUS should also take actions to maximize the intangible benefits received from clinical trials. The answers to the questionnaire show that nurses feel currently very outsiders to clinical trials. It would seem that there is potential for both well-being and clinical expertise enhancements if more nurses are integrated to the clinical trial process, and it becomes a shared endeavor of the whole organization. There are two clearly distinct goals the organization should have. Firstly, more effective and even research nurse organization. This means organizing research nurses in such a fashion that the workload, which is very uneven over the calendar year, can be effectively spread to several nurses and the quality and consistency of clinical trials increases. Simultaneously, different types of IT-solutions could be used to increase transparency to the patient material available, which lets HUS both give more realistic estimates of patient recruitment speed as well as speeds up patient recruitment. HUS already has a project underway addressing this, ensuring that project meets its goals and is adopted fully is important for effective clinical trials in the future.

Secondly, clinical trials should be seen as a source of clinical expertise for nurses. Lowering the barriers to partake in clinical trials for nurses is very important here. This could be achieved by measures such as rotations that include a limited time of doing research nurse duties, and similar means. In general, every nurse who is interested in clinical trials should be encouraged to participate and to learn the needed skills that are required by the medical companies and protocols. This might also increase continuity in the long run, as more nurses would have the basic skills for clinical trials which might increase both willingness as well as increase the qualifications nurses have to do clinical trials. Good Clinical Practices (GCP) could be utilized as a starting point for improvement and encouraging more nurses to seek training in them might be beneficial. Medical companies could also look into helping nurse training via funding or collaboration. This would both benefit the hospitals due to increases in nurse satisfaction and skill, and also increase the quality of clinical researches, thereby being valuable to also medical companies.

The well-being of doctors is a major concern for HUS, as it is directly linked to employee retention and it is well known that doctors are often under excessive workload due to multiple reasons. Thus, HUS should endeavor to make clinical trials – which most doctors want to participate in and feel are important – become a more integrated part of the work of doctors. Simultaneously, the workload they cause should be critically examined in order to ensure that clinical trials do not further burden doctors who are already under stress due to workload. Moving all activities related to

clinical trials that do not require a doctor to research nurses might be a good way of approaching this issue. For example, patient recruitment could be performed more cost-effectively by nurses rather than doctors. Whatever the methods, clinical trials are a potential source of employee satisfaction for doctors too, but currently its effect is perhaps even negative due to workload issues.

Similarly, recruitment should try to utilize clinical trials as a more effective tool. It is well possible that resident doctors as well as nurses could be recruited partially thanks to clinical trials, despite current staff not reporting it as a factor in their decisions. For specialists this was an important subject, and as such it should be leveraged. Recruiting specialists by ensuring they have enough time for clinical trials and research might be an effective way of getting highly skilled individuals to work for HUS.

Information should also be spread more effectively. Currently, many nurses and doctors do not hear from clinical trials. By improving how much information is passed down a sense of meaning and pride in their work could be installed in the employees, which could enhance work satisfaction. This could be achieved not only via traditional mailing lists and similar communication channels, which are often not very effective, but through for example posters and notes on walls displaying the amounts and results of clinical trials in HUS. Simultaneously also other types of research should be promoted in order to give everyone working in the organization a sense of accomplishment for new advances in medicine. Those trials could also be used as part of routine staff training whenever applicable, with separate notes given about those new treatments that were studied at HUS. All ways of passing on information and sharing the accomplishments should be explored, as they are a major source of job satisfaction.

When discussing singular factors that HUS should aim for, the most important one is job satisfaction. As cited in the literature review, employee turnover across the whole organization has costs of roughly €100 million. If clinical trials can be utilized as a tool to increase job satisfaction and thus decrease employee turnover, major cost savings could be achieved.

## 5.5 Conclusions

This study had two research questions: how to measure impact of Clinical trials and what that impact is in the case of HUS. The literature review found that no comprehensive studies exist to assess the impact, and thus a new framework was developed based on prior studies and interviews conducted with personnel of HUS. This

framework was then used at HUS to assess the impact and to gain evidence of the validity of the framework.

The results are similar to those in previous literature, but more precise, and thus they are credible. The framework is the answer to research question one, and indicates the complexity of the issue. Research question 2 was studied in chapter 4, with total net positive effects of 4-10 million euros. Of this 3-6 million euros are direct cost savings, and 2-4 million euros are indirect benefits.

## 5.6 Limitations

The framework described in this study aims to be as general as possible, and thus is it applicable for all specialties and different types of scenarios where clinical trials are done on behalf of a sponsor and some sort of renumeration is paid. However, that generality is also a weakness, as it is not very well suited for precise financial analysis. As stated earlier, clinical trials are such an extensive issue that their costs and benefits are impossible to accurately calculate.

The application of the framework to the case of hematology and oncology departments at HUS has several further limitations that mostly arise from difficulties in gathering accurate data. Firstly, the drug cost avoidance cost calculations are theoretical, and it is well possible that the patients would have been treated with more expensive treatments than this study assumes. However, for the purpose of this study it was decided that we use an ideal situation in order to arrive at a lower bound. Nevertheless, the results of this study need to be interpreted with thought.

A major limitation of the study is that it was only carried out at one university hospital. Thus, there might be a major skew in the types of clinical trials that are carried out, which might skew the effects. Based on prior research it is clear that oncology has the largest cost savings potential, but whether other specialties could have higher cost savings than this study suggests is left unanswered as this study does not have valid data from other university hospitals to determine which effects are local and which generalizable.

The questionnaire used in this study had relatively limited scope as well as only a limited amount of answers were gained for doctors. This is due to the small total number of doctors the questionnaire was sent to, in comparison to the much larger audience of the nurse questionnaire. When analyzing those answers this study was careful to not overstate anything. Deeper analysis into how, exactly, clinical trials could impact for example nurse well-being at work is required in order to understand the

whole dynamics at work there. The effect of clinical trials is also inseparable from the total workload, especially for doctors. Thus, some of the answers might be more due to working conditions at the wards or even of the individual doctors rather than the clinical trials themselves.

This study suggests that HUS incorporate questions related to clinical trial in their normal annual personnel questionnaires, if such are used, in order to have data over multiple years on the effects of clinical trials. A deeper, comparative study should also be done to determine the strength of the link between different factors of the framework and clinical trials. Despite these limitations, the answers in the questionnaire converged strongly, which suggests that they are indicative of the true state of things at HUS.

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# A. Questionnaire used for nurses

## Questionnaire for nurses about clinical research

**1. I graduated**

- ◯ less than 2 years ago
- ◯ 2-5 years ago
- ◯ more than 5 years ago

**2. I've worked at my current place of employment**

- ◯ less than 2 years
- ◯ 2-5 years
- ◯ more than 5 years

**3. I participate in research either while working or on separate research leaves**

- ◯ Currently
- ◯ Not currently but have in the past
- ◯ Do not participate

**4. I give drugs related to clinical trials to patients**

- ◯ Yes
- ◯ No

**6. Information and knowledge**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| I get information about the clinical research conducted at my specialty in HUS | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | I do not know what clinical trials are conducted in my specialty at HUS |

| | | |
|---|---|---|
| HUS offers the newest treatments available through clinical trials | ○ ○ ○ ○ ○ ○ ○ | HUS lacks the newest treatments |
| Patients or relatives often ask me about clinical trials at HUS | ○ ○ ○ ○ ○ ○ | Patients or relatives never ask me about clinical trials at HUS |

**7. Employee satisfaction**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| Clinical trials cause unnecessary work for me | | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials do not cause unnecessary work |
| Clinical research increases the quality of care at my ward | ○ | | | ○ | ○ | ○ | ○ | Clinical research lowers the quality of care at my ward |
| Clinical trials increase the quality of care I give | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials lower the quality of care I give |
| I would like to participate in clinical research more than currently | ○ | ○ | ○ | ○ | ○ | ○ | ○ | I would like to participate less in clinical researchh than currently |
| I would like to have more information about the clinical trials in my specialty at HUS | ○ | ○ | ○ | ○ | ○ | ○ | ○ | I am not interested in the clinical trials conducted at HUS |
| My ward actively partakes in developing new treatments | ○ | ○ | ○ | ○ | ○ | ○ | ○ | My ward doesn't develop new treatments |
| Clinical trials have an impact on my choice of employer | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials have no impact on my choice of employer |
| New treatments are a part of my job | ○ | ○ | ○ | ○ | ○ | ○ | ○ | New treatments are not a major part of my job |

# B. Questionnaire used for resident doctors

This questionnaire aims to assess the effect sponsored clinical trials have on employee well-being in HUS. Answers are anonymous. The questionnaire only takes a few minutes. Thank you for your time!

**1. I graduated**

- ◯ Within 24 months
- ◯ Over 24 months ago

**2. I have worked in my current job**

- ◯ Less than 2 years
- ◯ More than 2 years

**3. I particiapte in clinical research either as a part of my job or on research leaves**

- ◯ Currently
- ◯ I have previously but do not right now
- ◯ I do not participate in clinical research

**4. I am in the process of writing a doctor's thesis**

- ◯ Yes
- ◯ No

**5. Mark your dream job based on how much of your time would be spent doing clinical work vs. research**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| Clinician | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | Researcher |

**6.**

| | 1 | 2 | 3 | Unsure | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| I have enough time for research in my workdays | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | I do not have enough time to do research during my workdays |
| I would like participtae more in clinical research than currently | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | I would like toparticipate in clinical trials less than currently |

**9. Information**

| | 1 | 2 | 3 | Unsure | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| I know what research is done in HUS in my specialty | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | I do not know what research is done in my specialty in HUS |
| In my opinion HUS offers the newest available treatments through clinical trials. | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | In my opinions HUS does not offer enough of the newest treatments that are still in development |
| Patients or relatives of patients often ask me about the clinical trials being carried out at HUS | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | PAtients or relatives of patients never ask me about clinical trials at HUS |

**10. Well-being**

| | 1 | 2 | 3 | unsure | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| Clinical trials cause me unnecessary work | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials do not cause unnecessary work for me |
| Clinical trials enhance the treatment my ward offerts | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials decrease the quality of treatment at my ward |
| Clilnical trials increase the quality of care I give | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials decrease the quality of care I give |
| Clinical trials speed up the adoption of new treatments at HUS | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials slow down the adoption of new treatments at HUS |
| I would like more information about the clinical trials done in HUS in my specialty | ○ | ○ | ○ | ○ | ○ | ○ | ○ | I am not interested in clinical trials performed at HUS ei kiinnosta minua |
| My ward partakes in actively developing new treatments | ○ | ○ | ○ | ○ | ○ | ○ | ○ | My ward does not actively partake in developing new treatments |
| Clinical research has an impact on my choice of workplace | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials do not affect my choice of workplace |
| New treatments are a part of my job | ○ | ○ | ○ | ○ | ○ | ○ | ○ | New treatments are not a major part of my job |
| newest available treatments through clinical trials. | ○ | ○ | ○ | ○ | ○ | ○ | ○ | enough of the newest treatments that are still in development |
| Patients or relatives of patients often ask me about the clinical trials being carried out at HUS | ○ | ○ | ○ | ○ | ○ | ○ | ○ | PAtients or relatives of patients never ask me about clinical trials at HUS |

# C. Questionnaire used for specialists

**1. I have been a specialist**

- ◯ For less than 2 years
- ◯ For 2-5 years
- ◯ For more than 5 years

**2. I have been in my current workplace**

- ◯ Less than 2 years
- ◯ 2-5 years
- ◯ More than 5 years

**3.I participate in clinical trials**

- ◯ Currently
- ◯ Have previously but not currently
- ◯ No

**4. Estimate how many hours weekly you use on clinical trials**

**5. Mark your dream job based on how much of your time would be spent doing clinical work vs. research**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| Clinician | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | Researcher |

**6.**

| | 1 | 2 | 3 | Unsure | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| I have enough time for research in my workdays | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | I do not have enough time to do research during my workdays |
| I would like participtae more in clinical research than currently | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | I would like toparticipate in clinical trials less than currently |

**9. Information**

| | 1 | 2 | 3 | Unsure | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| I know what research is done in HUS in my specialty | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | I do not know what research is done in my specialty in HUS |
| In my opinion HUS offers the newest available treatments through clinical trials. | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | In my opinions HUS does not offer enough of the newest treatments that are still in development |
| Patients or relatives of patients often ask me about the clinical trials being carried out at HUS | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | ◯ | PAtients or relatives of patients never ask me about clinical trials at HUS |

**10. Well-being**

| | 1 | 2 | 3 | unsure | 5 | 6 | 7 | |
|---|---|---|---|---|---|---|---|---|
| Clinical trials cause me unnecessary work | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials do not cause unnecessary work for me |
| Clinical trials enhance the treatment my ward offerts | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials decrease the quality of treatment at my ward |
| Clilnical trials increase the quality of care I give | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials decrease the quality of care I give |
| Clinical trials speed up the adoption of new treatments at HUS | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials slow down the adoption of new treatments at HUS |
| I would like more information about the clinical trials done in HUS in my specialty | ○ | ○ | ○ | ○ | ○ | ○ | ○ | I am not interested in clinical trials performed at HUS ei kiinnosta minua |
| My ward partakes in actively developing new treatments | ○ | ○ | ○ | ○ | ○ | ○ | ○ | My ward does not actively partake in developing new treatments |
| Clinical research has an impact on my choice of workplace | ○ | ○ | ○ | ○ | ○ | ○ | ○ | Clinical trials do not affect my choice of workplace |
| New treatments are a part of my job | ○ | ○ | ○ | ○ | ○ | ○ | ○ | New treatments are not a major part of my job |
| newest available treatments through clinical trials. | ○ | ○ | ○ | ○ | ○ | ○ | ○ | enough of the newest treatments that are still in development |
| Patients or relatives of patients often ask me about the clinical trials being carried out at HUS | ○ | ○ | ○ | ○ | ○ | ○ | ○ | PAtients or relatives of patients never ask me about clinical trials at HUS |