Cancer Clinical Trials in Finland: Challenges and Opportunities

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Edited by Jeroen Pouwels and Juha Klefström
Cancer rates are increasing worldwide as the population ages. In Finland alone, 32,799 people were diagnosed with cancer in 2015 and 12,338 people succumbed to the disease (Finnish Cancer Registry; [https://cancerregistry.fi](https://cancerregistry.fi)). The total cost of cancer in Finland was 927 million € in 2014. These costs do not just include primary and secondary care, but also the cost of cancer screening, the indirect costs for sick leave (exceeding 10 working days) and disability pensions.

Finland is among the 8 countries in the world with the highest 5-year net survival when all cancers are considered, which is a testimony to Finland’s high standard
of early diagnosis, cancer care and functional public health care system. The current rapid development of new cancer drugs, especially the emerging immunotherapies, is transforming cancer diagnosis and care. On the other hand, the new treatments come with a number of challenges - new drugs are costly and their therapeutic actions against cancer are mediated via complex biological mechanisms. In addition to providing opportunities for cancer treatment, utilization of these novel therapeutics thus creates unmet challenges for the whole health care ecosystem to offer the best possible care and individualized treatments for future cancer patients.

Cancer clinical trials seek to determine the safety and efficacy of new drugs or treatment methods, and to personalize the treatments. Such trials not only offer outstanding benefits to cancer patients and hospitals in the form of access to novel drugs and savings in drug costs, they also offer possibilities to define the methods for optimal use of new drugs. The take up of new drugs in routine clinical care will be fastest in hospitals that have been active in organizing cancer clinical trials. Due to the significant impact of cancer clinical trials on cancer care, research, society and the economy, many large-scale efforts have been undertaken around the world to create clinical trial-facilitating environments on a local, regional and national level. Currently, 64651 cancer clinical trials are registered at clinicaltrials.gov.

This report provides an analysis of the current and past cancer clinical trial landscape in Finland and, for comparison, statistical figures of cancer clinical trials in other member states of the European Union (EU) and the European Free Trade Association (EFTA). For simplicity the EFTA and EU are together referred to as EU throughout the report. The landscape analysis shows that in spite of currently having high standard of care, in cancer clinical trials Finland is significantly lagging behind many socio-economically similar countries throughout Europe. The current low level of cancer clinical trials in Finland may slow down the uptake of new cancer drugs to routine care. Increasing the number of cancer clinical trials in Finland will provide patients with better treatment options, create jobs, reduce health care costs, contribute to the Finnish economy and move Finland to the forefront of clinical cancer research. The report provides recommended actions to increase the number of cancer clinical trials as part of the national growth strategy in health sector.

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Summary of the methods

The publicly available database www.clinicaltrials.gov was mined for European cancer clinical trials registered between the 1st of January 2000 and the 31st of December 2017. Clinicaltrials.gov was chosen due to the ease with which data can be extracted compared to the EU Clinical Trials Register. We note that not all European cancer clinical trials are registered in clinicaltrials.gov. However, this is expected to affect all European countries equally. Thus, while the absolute cancer clinical trial numbers reported here might be lower than the reality, the data provide an estimation of the cancer clinical trial numbers over time and comparison between European countries. The whole trial database for selected countries was downloaded for analysis. Cleaning and filtering of the data was performed in the R programming environment. Trials were included as cancer trial if the stated trial indication had one of 17 cancer specific words (e.g. “cancer”, “neoplasia”, “malignancy”). To reveal the cancer type under investigation, the dataset was annotated by searching for cancer specific terms in the condition label, e.g. for breast cancer the search terms were: “breast”, “ductal”, “lobular”. The same trial was counted in all countries with at least one study center and, thus, most trials are counted in multiple countries. All countries belonging to the European Free Trade Association (EFTA; Iceland, Norway, Liechtenstein and Switzerland) and the European Union (EU) were included in this study. For simplicity the EFTA and EU are together referred to as EU throughout the report. More detailed methods are provided in appendix 1.
What is a cancer clinical trial?

Cancer clinical trials:

- are scientific studies that involve volunteer cancer patients. Any cancer patient who meets certain conditions (the “inclusion criteria”) can participate.
- usually test the safety and efficacy of a new treatment in groups of patients.
- are intended to add to medical knowledge. For example, finding better ways to treat cancer or to find and diagnose cancer.

Why do cancer clinical trials exist?

Clinical trials are one of the requirements for regulatory approval and granting of marketing authorization in the EU. Thus, a new medical treatment, procedure or equipment can only be used in the clinic and enter the market if its efficacy against cancer and safety to the patients have been scientifically proven in cancer clinical trials.

Who runs cancer clinical trials?

Cancer clinical trials are usually organized either by the pharmaceutical industry or academic investigators. Importantly, cancer clinical trials are large programs that require input and support from a range of people and organizations. In addition to patients and clinicians, important input is required from regulatory organizations, researchers, funders, hospitals, statisticians, data managers and patient organizations. Regulatory authorities (the Finnish Medicines Agency (Fimea) in Finland) and ethics committees (the National Committee on Medical Research Ethics (TUKIJA) in Finland) ensure that the trial complies with all ethical and regulatory guidelines. Mostly pharma companies and/or public funding agencies finance the cancer clinical trials, which can be very expensive. Data managers, researchers and statisticians take care of data collection and interpretation as well as data storage. Patient organizations are increasingly involved in clinical trials to look after the interests of the patients.
How do cancer clinical trials prove that a new treatment is better than the current ones?

The clinical trial process traditionally takes place in three distinct phases (I-III). Each phase studies the drug in larger numbers of patients than the one before. In recent years, regulators have occasionally granted market authorization based on Phase I and Phase II data alone.

**Phase I** trials may test a new treatment for the first time in humans. Before this stage is reached, the treatment has already been studied for many years in simulations, cell line models and experimental animals. Usually only a small group of 20-100 patients is enrolled in these studies. The main purpose of Phase I studies is to assess the safety and pharmacokinetics (how the drug is affected by the human body) of a new drug. Phase I studies assess the possible side effects of the treatment, for example, determining how often it causes fever or nausea or what is the effect of the drug on blood cell counts. Many laboratory tests will be performed during the trial. In addition, the study may ask what is the optimal dose and dosing scheme of the treatment.

**Phase II** trials follow after Phase I studies, in case those have shown that a new drug is mostly safe and has acceptable pharmacokinetics. Phase II trials recruit a larger group of patients, typically 100-300. Here, the main goal is to study if the drug has anti-tumor activity and, if so, could indicate what type of cancers should be treated. In addition, patient survival is measured over longer periods of time. Phase I and Phase II studies often also look for specific biological markers; selective indicators that predict which patients are most likely to benefit from the treatment.

**Phase III** trial is the final phase in the process, which aims to obtain market approval from the regulatory authorities (the European Medicines Agency for Europe). Phase III studies recruit large numbers of patients, typically 300-3000, with most phase III clinical cancer trials recruiting closer to 300 patients. Phase III trials are large collaborative efforts, which include many different hospitals in countries around the globe. Besides assessing anti-tumor activity and safety, Phase III trials record patient survival over longer periods of time. Other endpoints may include for example progression-free survival, disease-free survival and time to tumor progression. Such extensive studies will give the ultimate verdict on the benefits of the drugs for treating cancer patients. When novel treatments enter the clinic without a Phase III study, the verdict is ultimately given after extensive use in the clinic.
**Benefits from cancer clinical trials to patients**

For patients, clinical trials can offer access to cutting-edge medication and treatment that is not available in hospitals through standard care. These medications are paid by the clinical trial, not by tax-payers or the patient. Clinical trials often provide the only possibility to receive experimental treatment in case standard care options are not effective. However, participation in a clinical trial is not a guarantee for the patient to receive any therapeutic benefit; this is a fundamental part of the informed consent, which the patient is required to sign to participate in a clinical trial. In clinical trials, all patients are often entitled to very close monitoring of their disease. Patients commonly experience a sense of satisfaction knowing that by entering a trial they contribute to the advancement of medical science and they can help to improve the prospects for future cancer patients.

**Benefits from cancer clinical trials to high-quality medical research**

Cancer clinical trials are a fundamental clinical research activity, which contributes to the advancement of modern therapies. Clinical trials educate and train doctors, research nurses and scientists and therefore, every cancer clinical trial adds to the professional skills and competence of the participating hospital. Cancer clinical trials bring together clinical teams, research teams and, increasingly, patient organizations. In addition, clinical trials involve a close collaboration between the performing hospital and global pharmaceutical companies, who manufacture the drugs under investigation. Every successfully conducted cancer clinical trial also increases international collaborations and visibility of the highly developed Finnish health care system and increases attractiveness of Finland as a site for the next cancer clinical trial.

**Benefits from cancer clinical trials to innovation and employment**

Every cancer clinical trial brings resources to the hospitals and the health care system from public and private sources. These resources allow doctors to reserve dedicated time for the clinical research, which adds to their professional skills as both clinical researchers and as medical practitioners. These skills will transfer to other doctors in the hospital and lead to improved cancer care. In addition, cancer clinical trials generate overheads, which cover ongoing expenses of the hospital apart from direct labor or materials used in the trial. Among other things, these overheads fund new equipment and the adaptation of new treatment and research methods, which will remain in the hospital and benefit all cancer patients.
Benefits from cancer clinical trials to society

Several transformative novel cancer therapies have been developed recently, such as the 2018 Nobel Prize winning immunotherapies. They offer effective treatments for many cancer types once considered incurable. However, the costs of novel cancer treatments have increased so dramatically in recent years\(^1\) that even highly developed countries like Finland cannot afford the optimal treatment for all cancer patients. Therefore, Finland and other countries face an increasing risk of serious treatment inequality. Will effective cancer treatments be available only for rich patients who can afford hundreds-of-thousands of euros? While organizing cancer clinical trials will not directly solve this problem, such trials do cover the costs of the medication and diagnostic procedures for the patients. This provides an opportunity for patients to receive state-of-the-art experimental treatment at no cost. Therefore, cancer clinical trials improve patient care, provide patients with state-of-the-art treatments and save on treatment costs.

In summary, cancer clinical trials are not a cost or burden to health care but rather investments to future health and the future of society.

Cancer clinical trials for a healthier society in Denmark

In Denmark, the impact of company-sponsored clinical trials was recently quantified. Denmark resembles Finland in terms of population size, GDP (Gross Domestic Product), healthcare system and socioeconomic status but Denmark has clearly higher numbers of cancer clinical trials than Finland (see below).

The Danish investigation showed that the 175 company-initiated trials organized in Denmark in 2015:

1. Had a significant impact on the GDP
2. Improved health care: Better doctors and nurses and access to state-of-the-art medicine
3. Created jobs: 5 FTEs (full-time equivalent) per trial
4. Lowered health care costs: 157,000€ invested in healthcare per trial
5. Contributed to research and development activities, which strengthens the life science industry in Denmark

Cancer clinical trials in Finland according to cancer type

Most cancer clinical trials in Finland and in the EU focus on either hematological (blood) cancers, for example leukemias, or common solid cancers such as lung, breast and prostate cancer. Due to the large market size, most cancer therapies are developed for common solid cancer types. Clinical trials in such cancers have the added benefit that patient recruitment is easier due to the larger patient populations. Hematological cancers are not the most common cancer type (they account for 8% of all cancers) but from a clinical research standpoint, hematological cancers provide easy access to tumor material. A simple blood draw provides enough material for disease monitoring and chemical analyses, which for example allows precise monitoring of the effect of the treatment on the number of cancer cells in the blood stream.

A comparison between Finland and the EU shows a similar distribution of cancer clinical trials over the different cancer types. In Finland, prostate cancer trials are more common than in the EU, while colorectal cancer trials are less common in Finland. The relatively high number of prostate cancer trials can be attributed to active Finnish research in the field; 14 out of 37 trials were (co)sponsored by Finnish universities such as the University of Turku (7) and Tampere University (3). In addition, prostate cancer is one of the focus areas of Orion, the biggest Finnish pharma company. However, one should bear in mind that the total number of cancer clinical trials in Finland is low, and therefore, the percentage figures should be interpreted with caution. For example, only four colorectal cancer trials were registered in clinicaltrials.gov in Finland during 2012-2017.
Most cancer clinical trials test drugs

Cancer clinical trials are usually performed to test new drugs or drug combinations, medical devices, dietary choices or procedures, as well as known treatments that warrant further study or comparison. In Finland, 80% of the cancer clinical trials are focused on cancer drugs. Trials on medical devices (7%), medical procedures (3%) and others (10%, including radiation, dietary supplements and behavioral studies) are less common. The distribution of cancer clinical trial types in Finland is similar as the average in EU countries.

**Intervention Types in Clinical Cancer Trials in the whole EU**

- Drugs (incl. biologicals): 86%
- Devices: 3%
- Procedures: 4%
- Other: 7%

**Intervention Types in Clinical Cancer Trials in Finland (2012-2017)**

- Drugs (incl. biologicals): 80%
- Devices: 7%
- Procedures: 3%
- Other: 10%
Cancer clinical trials take place throughout Finland

A National Finnish Comprehensive Cancer Centre (FICAN) will be established and coordinated from a central unit in Helsinki. Five local cancer centers, which are part of the five University Hospitals, are in charge of operations and share national responsibilities for specialized health care. These hospitals provide high-quality technology and medical care throughout the country. All Finnish University Hospitals organize clinical trial activities through separate research units called University Hospital District Clinical Trial Units (CTU).

177 cancer clinical trials were registered in Finland during 2012-2017. The most active study sites (participation in the highest number of trials) were the University Hospitals of Helsinki, Tampere, Turku, Oulu and Kuopio. However, patients were also recruited by other sites throughout the country. The map shows the nationwide distribution of cancer clinical trials. In most cases, Finnish hospitals contributed to large multicenter clinical trials that recruit patients in many countries - sometimes in over 60 locations in more than 30 different countries. During 2012-2017, 40 Finnish cancer clinical trials were registered with no involvement of foreign sites.

Finnish Clinical Cancer Trials per city (2012-2017)

* University hospital.
Cancer clinical trials in Finland and the EU

Finland contributes to 1.4% of all cancer clinical trials performed in the EU region

Around 26 000 cancer clinical trials were registered in the European Union during 2000-2017. Most of those cancer clinical trials were registered in France, Germany, the United Kingdom, Italy and Spain. The share of Belgium and the Netherlands is also large. The 362 cancer clinical trials registered in Finland comprise 1.4% of all EU-based cancer clinical trials.
The number of cancer clinical trials in Finland and other northern European countries during 2000-2017

The number of cancer clinical trials in Finland (registered from 2000 to 2017) was compared to other Nordic countries, Belgium and the Netherlands. These Northern European countries have a similar socioeconomic status and population base as Finland. Finland has 5.5 million inhabitants, Norway 5.3, Sweden 10.0, Denmark 5.8, Belgium 11.4 and the Netherlands 17.0. In Belgium, the Netherlands and Denmark a strong increase in cancer clinical trials can be observed till 2015, followed by a sharp decline after 2015. In Sweden cancer clinical trial numbers increased similarly as in Denmark until 2013 but have strongly declined since then. Cancer clinical trial numbers in Norway and Finland modestly increased until 2009, but have remained more or less constant since then, with a marked 31% decrease in Finland after 2015 (from 36 to 25 cancer clinical trials). In most years, Finland had the lowest number of cancer clinical trials among the comparator countries.

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<tr>
<th>Country</th>
<th>Number of annually registered cancer clinical trials</th>
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<td>Belgium</td>
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<td>Netherlands</td>
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**Belgium**
- Number of trials: 200
- Yearly distribution from 2000 to 2017

**Denmark**
- Number of trials: 200
- Yearly distribution from 2000 to 2017

**Norway**
- Number of trials: 200
- Yearly distribution from 2000 to 2017

**Finland**
- Number of trials: 200
- Yearly distribution from 2000 to 2017

**Netherlands**
- Number of trials: 200
- Yearly distribution from 2000 to 2017
Cancer clinical trials in EU countries with different-sized economies

A comparison of cancer clinical trial numbers in different EU countries in relation to their Gross Domestic Product (GDP; a commonly used measure of economic performance) shows that in general those countries with high GDP perform more cancer clinical trials than countries with low GDP. The small graph shows the data across all countries and the large graph shows the same data for all EU countries without the UK, Germany, France, Spain and Italy. The trendline shows the average relationship between GDP and cancer clinical trial number across all EU countries. Countries that appear above the trendline perform more cancer clinical trials than average based on the size of their economies, while countries below the trendline underperform.

Overperforming countries include France, Spain, the Netherlands, Belgium, Poland, Denmark, Czech Republic and Hungary. These countries organize more cancer clinical trials than one would expect based on the size of their economies. Sweden and Norway organize fewer trials than expected from the size of their economies. Among countries with similar GDPs, Finland clusters together with Greece, Portugal, Ireland and Romania. These countries clearly are cancer clinical trial underperformers.
European cancer clinical trial numbers have stopped increasing

Cancer clinical trial numbers increased globally until 2014, then growth has stopped in the EU

From 2000 to 2014 the annual number of registered cancer clinical trials in the EU increased rapidly (almost 7-fold). Cancer clinical trial numbers also increased in the USA and China during this time period, which coincides with the development of the first targeted therapies for clinical testing, such as Trastuzumab for HER2-positive breast cancer and Imatinib for certain types of leukemia and intestinal cancer. Since 2014, however, cancer clinical trial numbers in the EU have remained stable, as opposed to the USA and China, where cancer clinical trial numbers have continued to increase between 2014 and 2017 (19% and 71%, respectively). The strong increase in cancer clinical trials in China might be partly due to increased requirements by China's regulatory authority to perform trials specifically in China to obtain marketing authorization.
Cancer clinical trial numbers have decreased in most EU countries since 2014

The number of cancer clinical trials has decreased in almost all EU countries between 2014 and 2017. The changes in trial numbers varied greatly, from reductions of more than 30% in Slovakia, Portugal and Austria to modest increases in Bulgaria and Greece. The reduction in cancer clinical trials in Finland (7%) is similar to the EU per country average (11%). It seems contradictory that the total number of trials in the EU remains constant from 2014 to 2017 while clinical trial numbers decrease in almost every country. This could be due to smaller trials (Phase II and Phase III) or increased centralization of studies to fewer countries. In conclusion, the stabilization in cancer clinical trial numbers in the EU between 2014 and 2017 is accompanied by an almost EU-wide reduction in cancer clinical trial numbers per country.

Change in Cancer Clinical Trial number (2014-2017)

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1 Only those EU countries with 10 or more cancer clinical trials started in 2014 are shown in this graph.
Conclusions

• Cancer clinical trials are mainly organized in the five university hospitals in Finland (Helsinki, Kuopio, Oulu, Tampere and Turku), but also several other locations throughout Finland, suggesting nationwide commitment to and capabilities for cancer clinical trials. The incorporation of local hospitals into the FICAN regional cancer centers will increase the importance of local hospitals.

• The number of cancer clinical trials in Finland has stagnated for the last decade and is lagging behind many other EU countries.

• Denmark, the country with the socio-economic status and number of inhabitants most similar to Finland, is the only Nordic country with more cancer clinical trials than expected for its economic size. Denmark strongly outperforms Finland with almost 4 times the number of cancer clinical trials in 2017. Also, Belgium (2x the Finnish GDP but 6x the number of cancer clinical trials) and Hungary and the Czech Republic (Both 2x the number of cancer clinical trials than Finland despite having smaller GDPs) strongly outperform Finland.

• After an explosive growth in cancer clinical trial numbers in the EU between 2000 and 2014, this number has not grown between 2014 and 2017, a phenomenon not observed in the USA or China. This suggests that the EU might be losing its competitive edge for cancer clinical trials. This development, should it continue, could cause pharma company activity and cancer science in the EU to severely lag behind, and could negatively impact patient care in the EU.

• Based on data from Denmark, increasing the number of cancer clinical trials in Finland would provide patients with better treatment options, create jobs (average of 5 jobs per trial), reduce health care costs (150,000€ per trial) and contribute to the Finnish economy (every trial adds 120,000€ to the GDP).

• As a final conclusion, there is an urgent need to realize that Finland conducts fewer cancer clinical trials than its European peers. This situation has a negative impact on health, the economy and progress of clinical research. To improve both the capabilities and attractiveness of Finland as a preferred site for future cancer clinical trials, this report demands urgent improvements in the situation through decisive actions in the political arenas and funding organizations, and through significant improvement at the infrastructural level.

Recommended actions

This landscape analysis provides numerical information about the status of cancer clinical trials in Finland compared to other EU countries. The data show that Finland performs very few cancer clinical trials in comparison to other countries of similar socioeconomic status, such as Denmark and Belgium, and that the number of cancer clinical trials in Finland has been stagnant over the last decade. Clinical trials are important investments into national health care, economic strength, training of medical professionals and, ultimately, patients’ lives. Therefore, the Finnish clinical trial landscape requires attention, and strategic decisions and actions need to be taken urgently at both national and local levels.

The authors of this landscape analysis wish to stress that several important concrete actions have already been undertaken at both local and national levels. For example, an important step forward is the establishment of the early phase clinical trial unit in the Helsinki University Hospital Comprehensive Cancer Center. On a national level, the establishment of a National Network of Comprehensive Cancer Centers in Finland (FICAN) will be a significant improvement that will integrate many individual and currently somewhat scattered efforts around the country. The coordination of cancer clinical trials will be one of FICAN’s focus areas.

Despite these efforts, to attract industry-sponsored cancer clinical trials to Finland and to facilitate innovative investigator-initiated cancer clinical trials, significant new national resources and investments are needed specifically to this area of health research.

We note that the authors of this landscape analysis do not represent all cancer clinical trial stakeholders and, therefore, broader discussions are needed to find the best strategies and practices to improve the status of cancer clinical trials in Finland. However, based on internal discussions within the TEHO consortium and external expert views (appendix 2 shows opportunities and challenges for cancer clinical trials in Finland identified using a survey among key opinion leaders), some recommended actions are proposed here:

• Establish a Finnish Clinical Trial Office. A Finnish clinical trial office (CTO) would provide a centralized entry point for those organizing a clinical trial, both for the pharmaceutical industry and clinical investigators. The CTO would have intricate knowledge of the Finnish clinical trial ecosystem and would facilitate the search for the most suitable clinical site and oncologists, medical writers, statisticians, data managers, contract research
organizations and clinical project managers. The CTO can engage patient organizations to increase patient involvement and facilitate patient recruitment. In addition, a Finnish CTO should take care of (inter)national communication and marketing. For investigator-initiated cancer clinical trials, a CTO will significantly lower the barrier for scientists to translate their finding to the clinic. For global pharma companies a CTO is an important part of the local ecosystem to facilitate the planning and execution of the trial, and could be a deciding factor to include Finland in company-sponsored clinical studies.

CTOs exist in most European countries, including the Netherlands (Dutch Oncology Research Platform; www.researchplatform-dorp.nl), Denmark (Clinical Trials Office Denmark; www.clinicaltrialdenmark.com) and several in Belgium. Importantly, Sweden has very recently started a similar national initiative (Clinical Studies Sweden; www.kliniskastudier.se/english.html) to increase the number of clinical trials.

• **Provide ‘protected time’ for clinical trialists.** One challenge in organizing clinical trials is the very busy calendars of clinicians and other medical specialists, which leave little to no time for clinical research. This has led to the situation where clinicians use their free time for clinical trials. ‘Protected time’ would allow clinicians to dedicate a certain amount of their working time to clinical research. This will facilitate the organization and execution of clinical trials, increase the clinician’s skills and provide opportunities for the hospitals. The clinician’s time can be added in the clinical trial budget.

• **Facilitate and support investigator-initiated clinical trials.** We propose to establish new Finnish funding programs from governmental resources or to redefine existing programs to provide essential bridge funding to translate research findings to clinical studies. In addition to facilitating the translation of cancer drugs and potentially helping patients, these early phase trials provide a wealth of clinically relevant data that will drive Finnish research and could lead to commercialization activities. In addition, Finnish trial organizers are more likely to engage Finnish companies in the trial and, in case of positive results, Finnish organizations are most likely to play a central role in the much larger follow-up studies, which will be fully paid for by pharma companies.

• **Broad co-operation**, including exchange of personnel, is **needed** between hospitals, academic researchers, pharma industry, regulatory authorities (Fimea) and patient organizations to meet the future challenges in cancer care. By joining forces in patient recruitment, Finnish cancer centers will be successful in attracting more clinical trials.
All interventional clinical trials with a documented start date between 2000 and 2017 were downloaded separately for each country as pipe delimited text files from https://aact.ctti-clinicaltrials.org, which is daily refreshed to reflect the new submissions to clinicaltrials.gov. The data were downloaded to the R programming environment. The dataset was filtered to include only interventional trials. All clinical trials in the clinicaltrials.gov database have a label for the specific diseases that the trial is targeting. To select cancer clinical trials, the data were filtered in R according to cancer-specific terms in the “Condition” label. The specific search terms were: “cancer”, “neoplas”, “sarcoma”, “carcinoma”, “leukemia”, “lymphoma”, “malignan”, “astrocytoma”, “blastoma”, “melanoma”, “metasta”, “gist”, “gastrointestinal stromal tumor”, “wilms tumor”, “myeloma”. The data were exported to Microsoft Excel for mining and visualization. The pivot tables tool was used to filter the data required for each visualization.
Interventional cancer clinical trials on clinicaltrials.gov are divided into these categories: Behavioral, Biological, Combination Product, Device, Diagnostic Test, Dietary Supplement, Drug, Genetic, Other, Procedure, Radiation. For simplification, Drugs and Biologicals were grouped, and everything except Devices, Procedures, Drugs and Biologicals was grouped as ‘Other’. The graph shows data for cancer clinical trials between 2012 and 2017.

For this analysis, all cancer clinical trials with at least one Finnish site registered between 2012 and 2017 were manually checked for all Finnish cities participating in the trial. Data represent the total number of cancer clinical trials in which one or more sites in that particular city participated. Most cancer clinical trials take place in more than one Finnish city (up to 12 different Finnish cities in one trial).

For this graph, the total number of cancer clinical trials registered between 2000 and 2017 were calculated for each country. Subsequently, for each country that number was divided by the grand total for all countries together.

In this graph the total number of registered cancer clinical trials with at least one trial site in Norway, Sweden, Denmark, Finland, Belgium or the Netherlands was plotted for each year (2000-2017).

For each country, the total number of registered cancer clinical trials (2013-2017) was plotted against the five-year average (2013-2017) nominal GDP (Source: International Monetary Fund (IMF)). The inset shows the data across all countries and the large graph shows the same data for all EU countries without the UK, Germany, France, Spain and Italy. The linear fit model in excel was used to draw the least squares regression line and calculate the coefficient of determination (R2) between nominal GDP and number of cancer clinical trials. The regression line in the enlarged graph is based on the data from all EU countries.

The data for this graph were extracted slightly different than the data for all other graphs. All clinical trials in the clinicaltrials.gov database were downloaded as pipe delimited text files from https://aact.ctti-clinicaltrials.org/ and subsequently loaded in R. The dataset was filtered to include only interventional trials. The dataset was then filtered for cancer trials using the same patterns as described above using the MESH (Medical Subject Headings) terms in the database. In the graph the total number of registered cancer clinical trials with at least one participating trial site in the EU, China or the USA was plotted for each year (2000-2017; duplicates have been removed).

This graph displays the change in registered cancer clinical trial numbers between 2014 and 2017 in EU countries. Only countries with 10 or more cancer clinical trials registered in 2014 were included.
Appendix 2: opportunities and challenges for cancer clinical trials in Finland — a survey among key opinion leaders

An anonymous survey was conducted in parallel with the cancer clinical trial landscape analysis, in which several key opinion leaders in Finland and in central Europe, representing hospitals, pharmaceutical industry and contract research organizations (CROs), were interviewed about the cancer clinical trial situation in Finland. This survey pinpointed several strengths, but also important challenges:

Strengths:

• The application process to obtain permission to conduct cancer clinical trials in Finland is well-handled.
• Finnish patients are compliant and thus drop-outs are rare.
• Finland has an enormous opportunity in the use of its health registers once legislation is updated to allow the secondary use of health data.
• An increasing number of biotechnology companies in Finland in recent years.

Challenges:

• The current lack of functional infrastructure in Finland. A one-stop model was suggested.
• The low authority of Finnish biotech companies and pharma subsidiaries.
• The small size of the Finnish patient population.
• Finland does not (yet) have a reputation as an active site for clinical trials, which emphasizes the importance of communication and marketing.