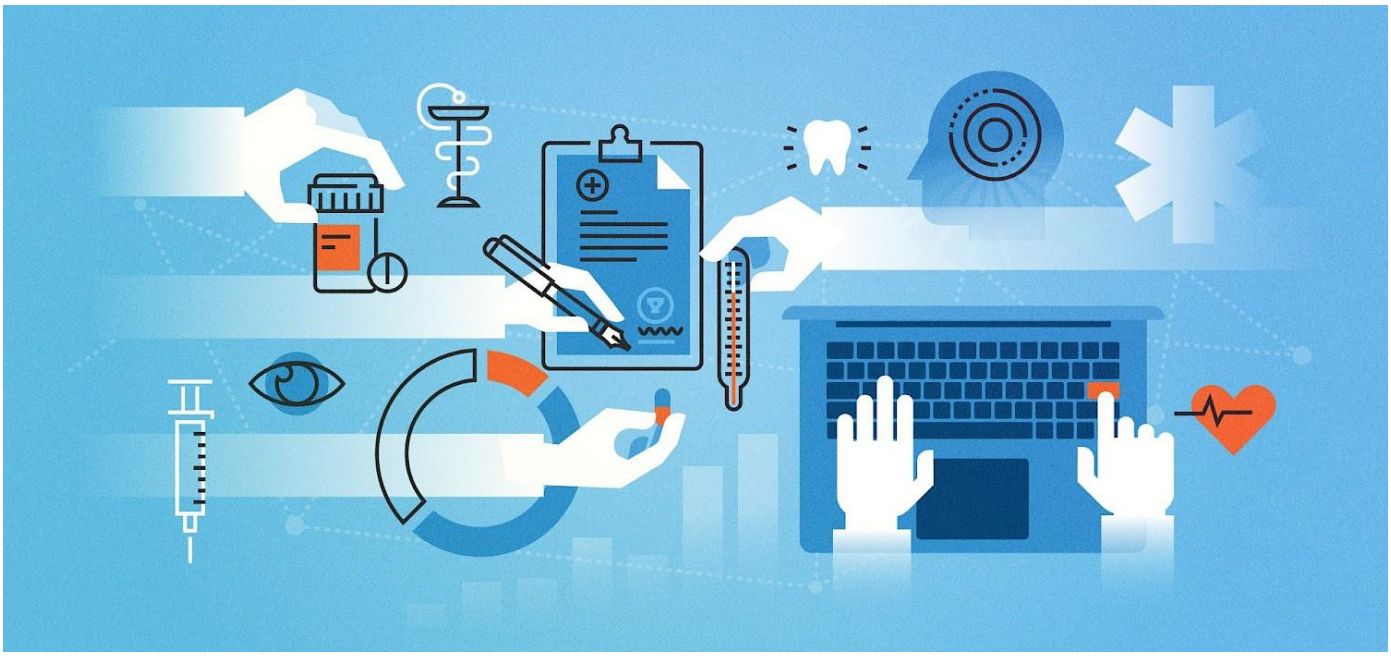
Patient recruitment and participation in the Netherlands – an exploration of factors and views



Student: Huibin Zhou

Studentnumber: 5657466

Master's Program: Drug Innovation, Utrecht University

Host Institution Supervisor: Dr. Francisco Hernandez

UU Examiner: Prof. dr. A.K. (Aukje) Mantel-Teeuwisse

Date: July 28th, 2023

Table of Contents

Abstract

Clinical trials are crucial for evaluating the efficacy and safety of new pharmaceutical treatments, and the Netherlands has the potential to be a world leader in clinical research with its high-quality hospitals, facilities, and healthcare professionals. However, the country lags behind its neighbors in the number of clinical trials conducted, possibly due to longer administrative and more difficult clinical trial processes and requirements, which increase costs for pharmaceutical companies. On the other hand, the prominent role the Medicines Evaluation Board (MEB) is playing within the EU regulatory network represented by the European Medicines Agency (EMA) has not resulted in significantly more studies conducted in NL compared with other member states. Another important issue is the slow pace of patient recruitment, which can delay drug development, potential treatments and have financial consequences for the accessibility of innovative therapies. Further research is needed to identify the factors that delay patient recruitment and hinder the full development of the Netherlands' potential in clinical research. In the present study we show that many factors are involved in patient participation and recruitment speed. While some factors have a negative influence on the Dutch clinical trial situation, other factors do not seem to be as relevant. We identified several barriers for clinical trials in The Netherlands, such as the comprehensibility of patient consent, and the availability of personnel. To overcome these barriers, all stakeholders in clinical trials (e.g., patients, pharmaceutical industry, regulatory authorities, healthcare, and academics) have to come together and explore options to improve the clinical trial situation in The Netherlands for the benefit of all patients and the Dutch innovative environment.

Introduction

New pharmaceutical treatment options are evaluated for their efficacy and safety by means of clinical trials (especially randomized clinical trials)(1). These clinical trials involve a series of intensive testing and approval procedures to ensure that safe and effective medication becomes available to individuals globally. The requirements for clinical trials are recorded in the guidelines and requirements of the International Council for Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use (2). Even before market approval, clinical trials might provide a group of patients with an additional treatment option in an investigational setting (3). Furthermore, having more clinical trials in various countries, including the Netherlands, improves representation of different populations and national clinical practices (4). Therefore, having (more) clinical trials in the country would be beneficial to patients on a national level. In addition, the execution of clinical trials creates the opportunity to nationally increase scientific, clinical, and medical expertise regarding innovative therapies.

The Dutch Association for Innovative Medicines (Vereniging Innovatieve Geneesmiddelen) has an initiative called "Boston by the North Sea". The purpose of this initiative is to make The Netherlands the medicine hub of Europe. The proposal is modeled after the thriving medical and biotechnological sector in Boston, which is the dominant innovative biomedical area of the United States. Strengthening the Dutch biomedical sector would have many benefits for the Netherlands as a country and possibly Europe as a whole. First, establishing a life science hub could attract investment, create new jobs, and stimulate economic growth in the Netherlands. Second, it could strengthen collaboration between academic institutions, research centers, and pharmaceutical companies to advance scientific knowledge and develop new therapies and treatments. Third, it would provide an opportunity to find therapies for unmet medical needs and improve patient outcomes. Lastly, it could improve the Netherlands' reputation in the biomedical field (5) and the world.

Boston by the North Sea would be an achievable mission due to the world leading potential in the field of clinical research that the Netherlands has. The nation has many high-quality hospitals within a 200 km radius, facilities to perform cutting edge research, and several worldwide renowned healthcare professionals in various therapeutic areas (6). A comparison of hospitals by Statista Inc. created a ranking of the 200 best hospitals globally. The Netherlands appeared in the top 200 ranking list with 7 out of 8 of its prestigious academic hospitals in 2021. In comparison, Belgium had only 3 academic hospitals in this list and France has 13 out of 32 university hospitals on the 2021 list. In addition to its prestigious academic hospitals, the Netherlands has 26 state-of-the-art hospitals, multiple (bio)pharmaceutical laboratories, and a rising biotechnology industry in general and all are located within a radius of 200 km (7). Furthermore, with the relocation of the European Medicines Agency (EMA) from London to Amsterdam, the Netherlands set a tone to demonstrate the essential role the Medicines Evaluation Board (MEB) is playing within the EU-regulatory network, after the Brexit and departure of the MHRA, as well as to display the myriad of opportunities the Dutch pharmaceutical industry has, and potential to grow (8,9). Therefore, development of the Dutch pharmaceutical sector would lead to not only economic growth in the Netherlands but also earlier availability, experience, and access to investigational treatment options, meaning faster interventions for patients and improved health perspectives.

Research into the number of clinical trials from clinicaltrials.gov revealed that The Netherlands gets outperformed by many surrounding countries (e.g., Belgium, Germany, France, etc.) in terms of number of clinical trials in phases I, II, and III. Although the Netherlands is smaller than both Germany and France, which complicates patient recruitment and enrollment due to travelling distances, it seems that even Belgium is more often involved in actively participating in clinical trials. We are intrigued to know the reasons why the Netherlands has not been fully utilized as a country to conduct clinical trials in different phases despite of its abundance in high quality medical facilities and its resemblance with Belgium in terms of infrastructure of healthcare and travelling distances (10).

There are many different factors, such as the relatively complex regulatory process and relatively high cost of clinical trials, which may negatively influence the process of conducting clinical studies in the Netherlands, hampering the

full development of its potential in clinical research. Due to longer administrative and/or more difficult clinical trial processes and requirements, costs for clinical trials performed in the Netherlands have increased (11). Another important issue concerns the recruitment pace of patients. There are signs indicating that the patient recruitment process could be significantly improved from several perspectives. Enrolling could be exhausting and demotivating; it can take months before the first patient is enrolled after approval of the clinical trial. This is not only disadvantageous for the sponsor and the speed of drug development, but also delays potential treatment for patients. It also has financial consequences for the further development of the products and decreasing the rate of success in cases where other competitors will win the race by starting and finalizing clinical studies faster in another countries. Several factors affecting clinical trial patient recruitment speed have been identified before, such as patient burden and time investment(12). The purpose of this research aims to identify the factors that are relevant to the clinical trial situation in the Netherlands, in particular factors that have a potential delaying factor in the recruitment of the first patient in a clinical trial and patient recruitment speed in general. With this information, we want to improve the knowledge about barriers related to patient recruitment in The Netherlands and inform/stimulate various stakeholders to make changes to the clinical trial situation in The Netherlands.

Methods

Literature Search

Literature search was performed in PubMed with the keyword “clinical trials” as a basis. The search term “clinical trials” was combined with other search terms to get more specific results, first it was combined with “participation” and “recruitment”. Based on the hits found this combination of keywords, more specific searches were performed to elucidate the factors found and to find additional factors affecting the patient recruitment for clinical trials. Other keywords used in combination with “clinical trials” were “awareness”, “Netherlands”, “Burden” and “physicians”.

Survey

Based on the information obtained from the literature search, a questionnaire was created to gather information about the situation of clinical trial patient recruitment in the Netherlands. This survey was used to identify factors that could potentially have a delaying factor in the Dutch patient recruitment process. Various stakeholders (e.g., Regulatory authorities, pharmaceutical industry, physicians, and patients participating in clinical trials) were approached to identify what the factors are respective from different perspectives. Stakeholders were approached through different national trade, clinical, and medical associations (such as: Vereniging van Innovatieve Geneesmiddelen - VIG, Dutch Clinical Research Foundation - DCRF, Nederlandse Vereniging voor Farmaceutische Geneeskunde - NVFG, etc.) and from LinkedIn (professional network/social media). These stakeholders were invited to participate in an anonymous online survey assessing their views on factors influencing clinical trial startup speed.

The complete survey form can be found in the annex. First, the responders’ experience with clinical trials was investigated to see how much to weigh their opinion as someone with years of experience in the field of clinical studies might have a clearer overview of the clinical trial situation in the Netherlands. This was done using experience eliciting questions, such as the number of clinical trials they have been involved in, and how they were involved in clinical trials.

Thereafter was a section asking about the responders’ opinion on known factors that influence patient recruitment and how much they think this affects the Dutch clinical trials. Responders had to indicate how much of a positive or negative influence a factor had on the willingness of a patient to participate in a clinical trial. Furthermore, responders’ opinion on the implementation of these factors in the Netherlands was investigated. Responders were asked which factors they thought were properly implemented in the Netherlands and which factors could be improved.

Analysis

Responses to the questionnaire were collected and analyzed manually. Categories and subcategories of responses were compared to one another using frequencies analyses. The results are reported as absolute numbers and percentages to improve the interpretation of the results. The results are described in text form and/or visualized in either table form or graphical formats.

Results

Distribution of responders

In a 3-month period, various individuals, and organizations in the field of pharmaceutical sciences were approached and 40 responses were collected in total. Out of 40 responders, 20% indicated that they did not have any experience in the field of clinical trials but did have experience within the pharmaceutical/scientific sector. These individuals did not answer the remaining questions as we were interested in the opinion of the individuals that did have experience with clinical trials. Therefore, only the remaining 75% of responders that do have experience with clinical trials were thoroughly analyzed and subsequent reporting of the results represent the 75% of responders (30 out of 40 responders) as the 100% value.

Responses are subdivided in 76.7% of responses from the pharmaceutical industry, 6.7% from the academic field, 6.7% from a patient perspective (patients/family of patients/patient representative), 6.7% from clinical regulatory authorizations, and 3.3% from healthcare sector (figure 1). A third of responders (36.7%) were directly involved in clinical trials (e.g., patient, physician, nurse, statistician, methodologist). Of those who have directly participated in clinical research, the majority have participated in more than 8 clinical trials (26.7%), while 10% have participated in one or max 3 clinical trials. Of those who have participated in clinical trials/research, there was a difference in terms of years of experience.

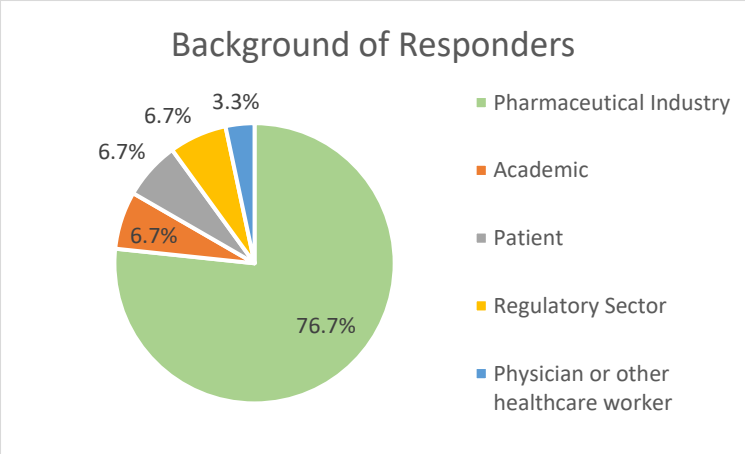


Figure 1 Distribution of responders with backgrounds in the pharmaceutical industry, academics, patients, regulatory sector, and physician or other healthcare workers.

Influence of several factors on patient recruitment

Several factors, as mentioned in the introduction, have been identified and are known to be related to patient recruitment. These factors include, but are not limited to, patient burden and time investment. Responders were asked to give their opinion on various factors and their effect on patient recruitment. These factors were subdivided into factors related to healthcare, benefits and risks of clinical trials, personal reasons, and some other factors.

Healthcare related factors influencing patient recruitment

Responders gave their opinions on factors that influence patient participation in clinical trials. Factors related to healthcare, such as “quality of hospitals” or “expertise of physicians and other healthcare personnel” were indicated

to be the most positive aspects to aid clinical trial participation. 90% of responders indicated that “quality of hospitals” had a positive influence on clinical trial participation (figure 2). The majority of responders (96.7%) said that “the expertise of the physicians and other healthcare workers” was important for a swift recruitment process. On the other hand, 86.7% and 73.3% of responders noted that “difficulties in understanding the process of a clinical trial” and “fear and/or distrust in clinical trials” respectively were major negative factors to patient recruitment.

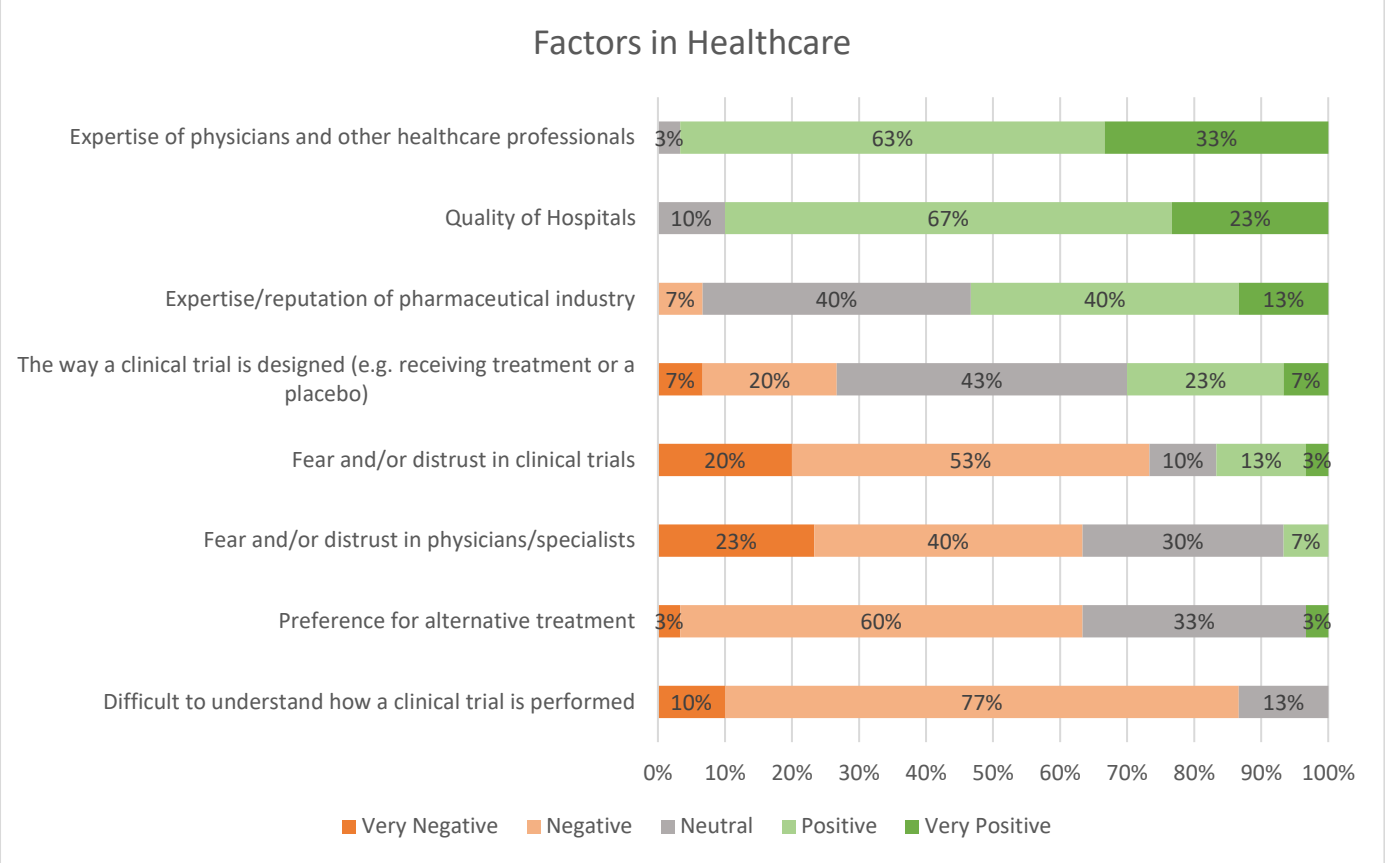


Figure 2 Opinions of responders on factors' influence on patient participation related to healthcare.

Influence of factors related to benefits and risks of clinical trials on patient recruitment

Concerning the factors related to benefits and risks of clinical trials, responders considered “access to an alternative treatment option” and “earlier access to an innovative medication” as the most positive factors. “Unknown side effects” and “burden on patients” were noted as the most negative factors influencing patient recruitment speed. For the positive factors, in the case of “access to an alternative treatment option” and “earlier access to an innovative medication”, 86.7% and 96.7% of responders respectively indicated these factors to have a positive influence on patient recruitment (figure 3).

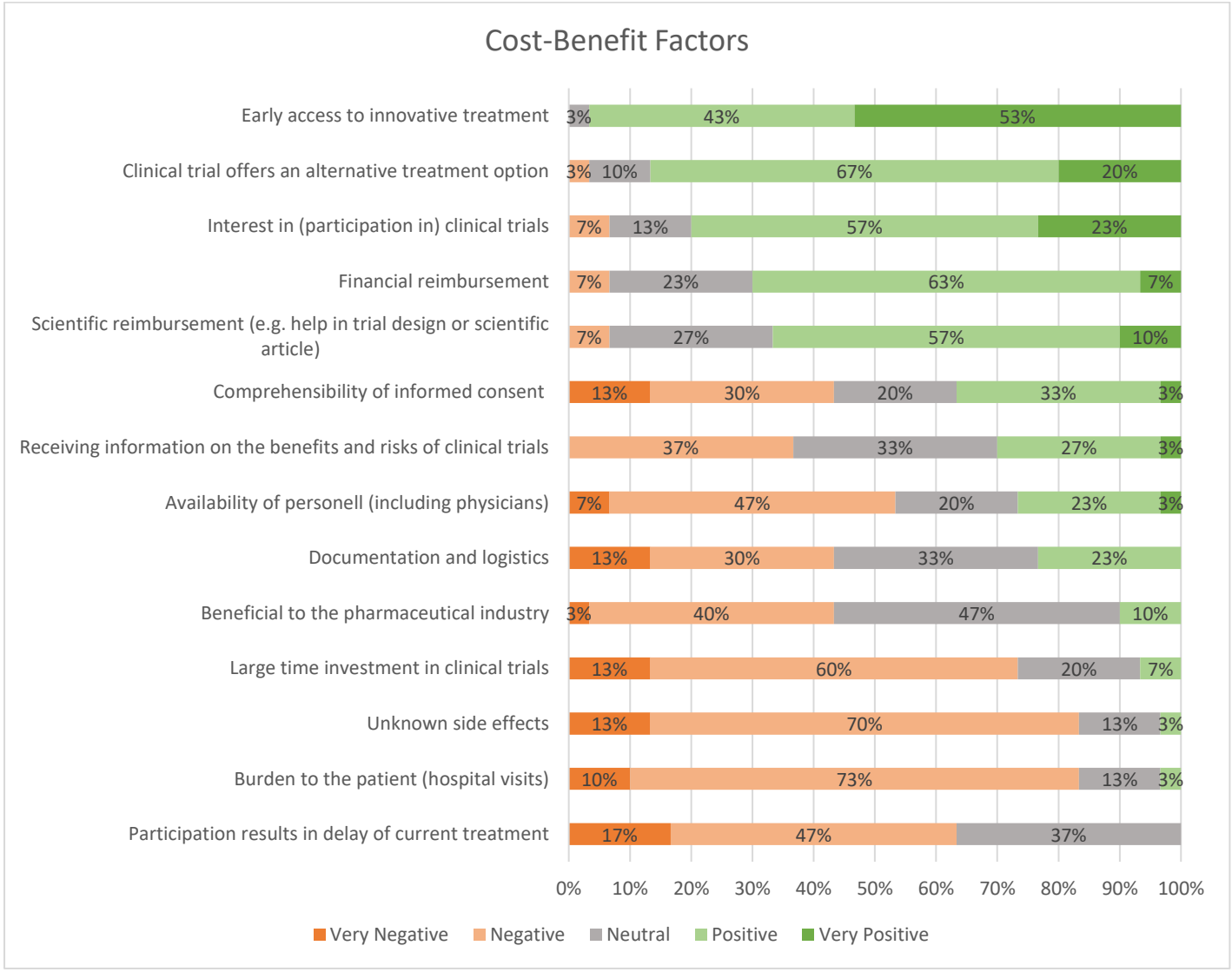


Figure 3 Opinions of responders on factors' influence on patient participation about costs and benefits related to clinical trials.

Influence of personal factors on patient recruitment

Our responders also gave their opinions on a list of personal factors that could influence the willingness of patients to participate in clinical trials. “Support of family and friends” (e.g., motivating to join a clinical trial or support throughout the clinical trial process) and “intention to help innovation of healthcare” were the most positive factors, both having 86.7% positive responses (figure 4). Then “motivation to participate from the clinical researcher” also seemed to be a positive factor in patient recruitment with 63% positive responses. On the other side, many personal factors were found to have a negative effect on willingness to participate. The most negative influences are “inability to combine clinical trials with work” and “dropping out of the clinical study”, both with 90% of responders indicating that it has a negative influence on patient recruitment. Slightly below these factors but still very negative is “Belief that the medication in clinical trials is worse than conventional medication” also had a negative influence according to 87% of the responders.

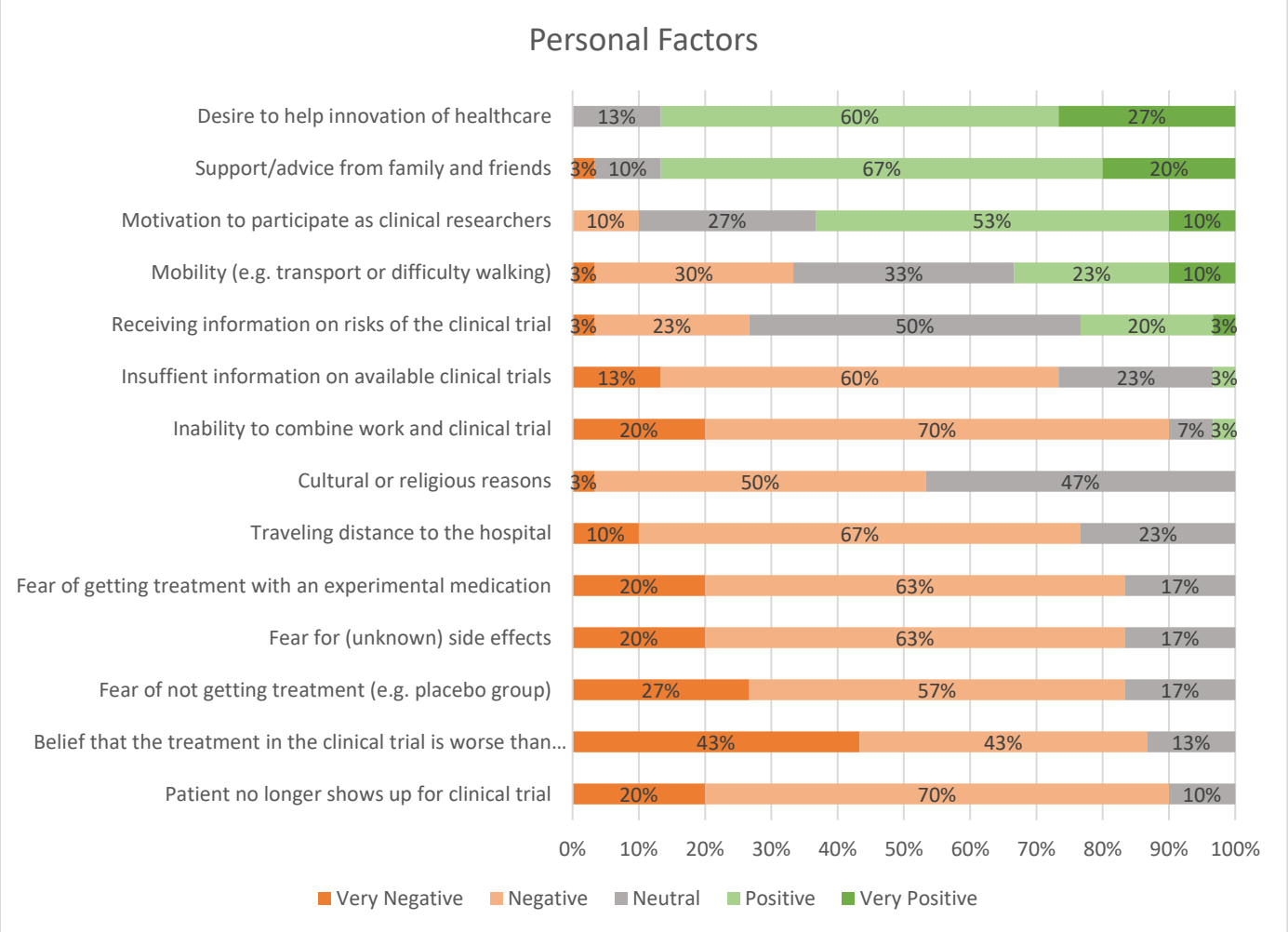


Figure 4 Opinions of responders on factors' influence on patient participation related to personal factors of clinical trial participants.

Influence of several other factors on patient recruitment

Lastly, responders were asked to give their opinion on few factors unrelated to previously mentioned categories, such as media coverage and government stance towards the pharmaceutical industry. “Feedback from the researchers”, as part of discussing the outcomes from the study, was found to be the most positive factor with 76.7% of responders appreciating this approach (figure 5). “Coverage by the media on the pharmaceutical industry” was seen as the most negative factor for participants, with 73.3% of responders, to influence the willingness of patient participation in clinical trials.

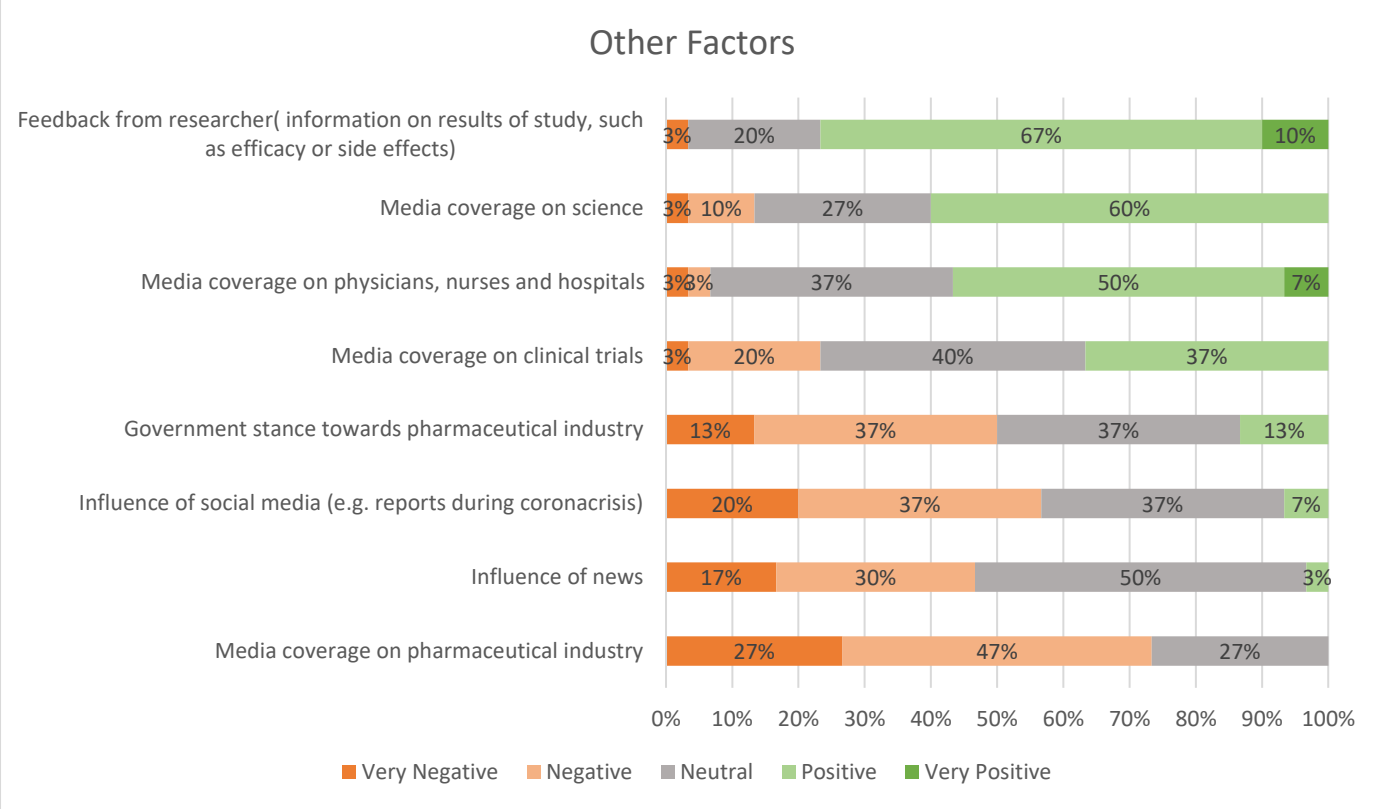


Figure 5 Opinions of responders on influence of factors unrelated to previous categories (healthcare, cost-benefit, and personal factors) on patient participation.

Differences of views between participants

Of all responders, approximately a third (36.7%) had directly worked in a clinical trial (e.g., as a physician, statistician, etc.). Of this 36.7%, 20% of responders were from the pharmaceutical industry, 6.7% from an academic field, 6.7% from a patient perspective, and 3.3% physician or other healthcare worker. For the remaining 63.3% of responders without direct clinical trial experience, 56.7% of responders were from the pharmaceutical industry and 6.7% from the regulatory sector of clinical research. A comparison between responders with and without direct involvement in clinical trials was made to see if direct involvement in clinical trials could give a different viewpoint on the involvement of factors regarding patient participation.

Differences of views in the healthcare sector

Regarding factors in healthcare, responders who had direct involvement in clinical trials had relatively similar opinions compared to those who did not, except for one factor which was “the expertise/reputation of the pharmaceutical industry”. Responders with direct involvement in clinical trials had a total of 72% positive rating while indirect responders only had a positive rating of 42% on “the expertise/reputation of the pharmaceutical industry” (figure 6). One notable difference between the groups is the use of the option “very positive”. Responders who were directly involved in clinical trials were 4 times more likely to answer with “very positive” than responders without direct involvement in clinical trials.

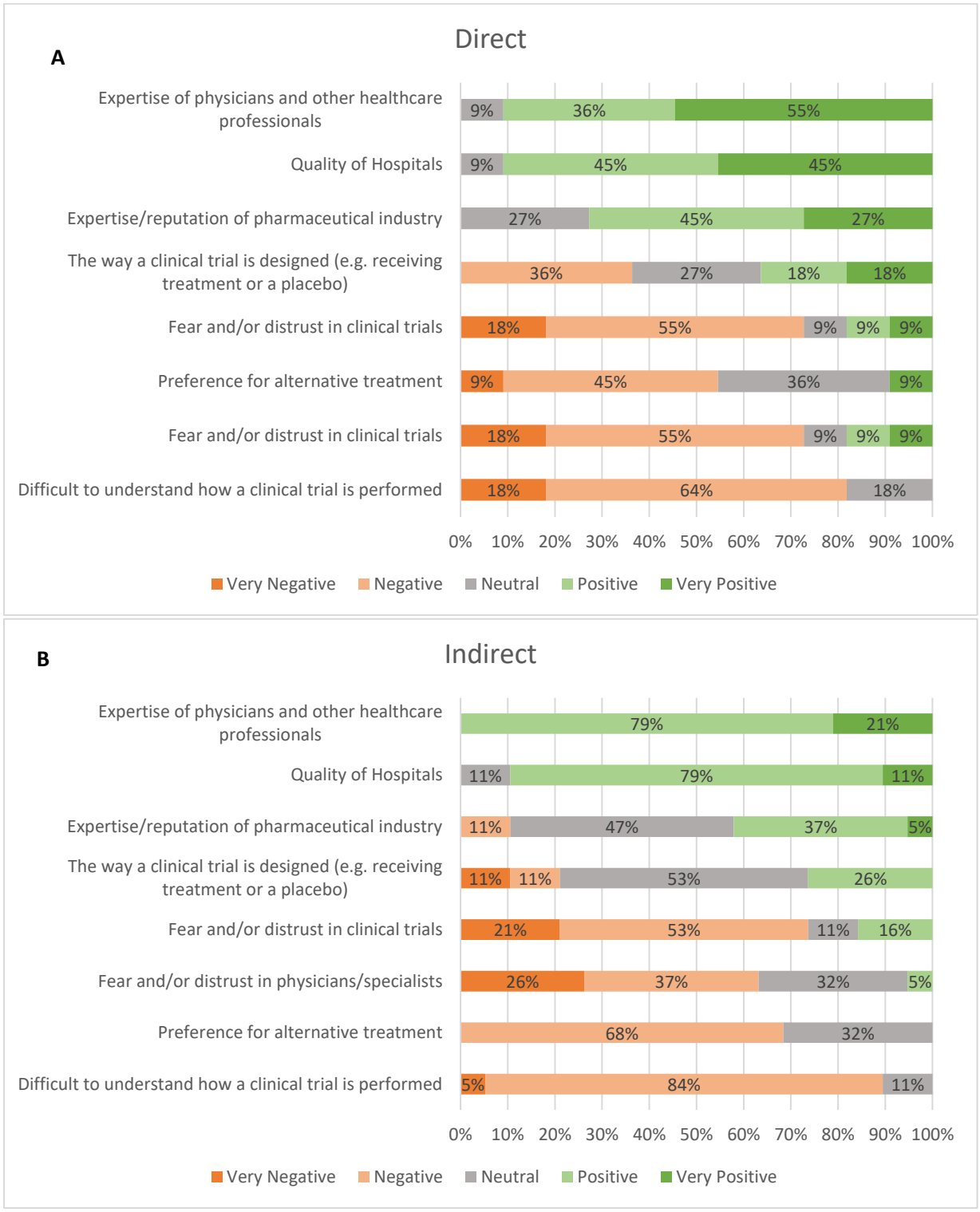


Figure 6 Comparison of responses on the effect of factors in healthcare on the willingness of patients to participate in clinical trials from responders, based on direct or indirect involvement in clinical trials. (A) Direct involvement (B) Indirect involvement

Differences of views regarding benefits and risks of clinical trials

Views on patient participation were similar in responders with or without direct experience in clinical trials. Two factors that differed between the two groups are "Receiving information about the benefits and risks of clinical trials" and "Availability of personnel (Including physicians)" (figure 7). In the case of "Receiving information about the benefits and risks of clinical trials" responders without direct experience in clinical trials had a more negative opinion compared to those with direct experience. The same could be seen in the case of "Availability of personnel (Including

physicians)". Only 27% of responders with direct experience gave a (very) negative opinion of the availability of personnel compared to 68% of responders without experience.

Figure 7 Comparison of responses from responders based on direct or indirect involvement in clinical trials. (A) Direct involvement (B) Indirect involvement

Differences of views regarding personal factors

Another group of factors important to patient participation in clinical trials are personal factors. Both type of responders with or without direct clinical trial experience agree on the positive or negative influence a factor has on clinical trial participation in most cases (figure 8). One difference seen in the two groups is regarding "mobility (e.g., transport or difficulty walking)". On the topic of "mobility", opinions of responders were mostly neutral or divided. Responders with direct clinical trial experience were more positive towards "mobility", with 45% of responders having a positive view, while only 18% viewed this negatively. Those without direct experience were more negatively inclined with 26% positive votes against 42% negative votes.

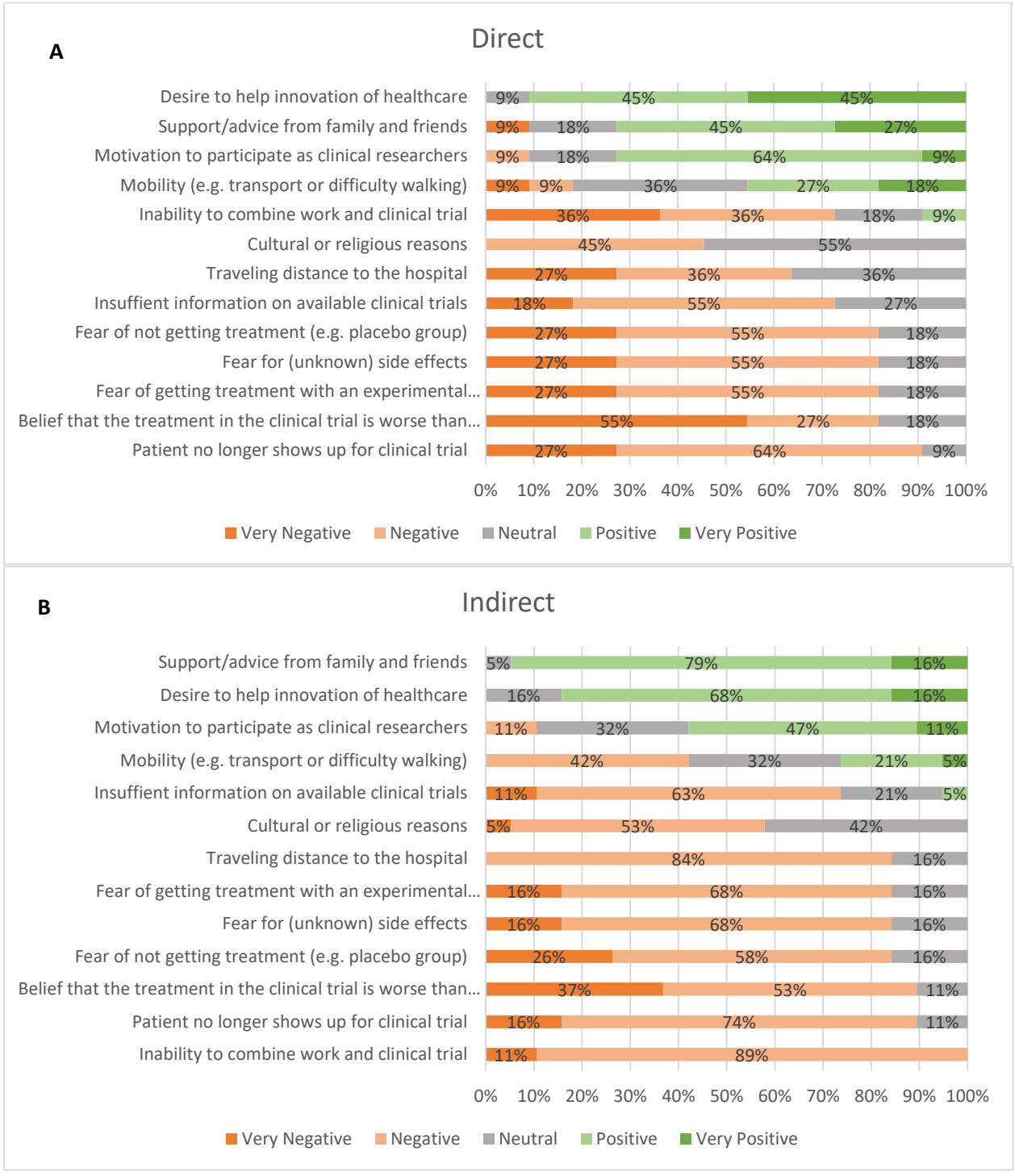


Figure 8 Comparison of responses from responders based on direct or indirect involvement in clinical trials. (A) Direct involvement (B) Indirect involvement

Differences of views regarding several other factors

Finally, there are some "other" factors that did not fit in the previous categorizations but are nonetheless important, such as media coverage on clinical trials, science, and the pharmaceutical industry. From these "other" factors, responders with and without direct clinical trial experience generally had a similar overall opinion on the influence of these factors on the patient participation in clinical trials (figure 9).

Responders with direct clinical trial experience indicated that "media coverage on the pharmaceutical industry" and "government stance towards the pharmaceutical industry" were greatly negative, with 63% and 67% of responders giving a negative or very negative answer respectively. "Media coverage on science" and "feedback from the researcher" were voted very positively by responders with direct clinical trial experience. Responders without direct clinical trial experience had similar opinions, however their opinion on "government stance towards the pharmaceutical industry" was much less negative than that of the responders with direct experience.

Figure 9 Comparison of responses from responders based on direct or indirect involvement in clinical trials. (A) Direct involvement (B) Indirect involvement

Opinions of various stakeholders

This survey was performed among various stakeholders, including the pharmaceutical industry, regulatory organizations, patients/family of patients/patient organizations, physicians and other healthcare personnel, and academia. In general, all these stakeholders held similar opinions on most of the factors, with a few exceptions that will be reported below.

Amongst all stakeholders, responders had similar opinions on the influence of most factors on patient participation in clinical trials. Nonetheless, differences in opinion between stakeholders were noted in two factors: “Beneficial to pharmaceutical industry” and “Large time investment in clinical trials”. Both had a negative influence on clinical trial participation. In contrast, half of responders from a patient perspective thought that clinical trials being “beneficial to the pharmaceutical industry” and “clinical trials having a large time investment” were positive factors to patient participation.

The factor “Availability of personnel (including physicians)” showed divergent opinions amongst stakeholders. Most stakeholders said this would have a positive influence on the patient participation in clinical trials, whereas 70% of responders from the pharmaceutical industry disagreed and gave a negative opinion.

Regarding “Comprehensibility of patient consent”, there were mixed opinions from the stakeholders. Among responders in the pharmaceutical industry, half of responders had a negative opinion about the effect of “comprehensibility of patient consent” on patient participation. However, a third (34%) of responders from pharmaceutical industry also thought this would have a positive effect. All surveyed physicians believed this would have a negative effect on patient participation, while all surveyed patients said this would have a positive effect on patient recruitment.

“Receiving information about benefits and risks of the clinical trial” was a factor with varied opinions, whereby physicians (and other healthcare personnel) and pharmaceutical industry had a negative opinion. On the other hand, academics, patients and regulatory sector had a positive opinion about this factor.

When it is just about “Receiving information about risks of the clinical trial” some differences can be seen compared to “Receiving information about benefits and risks of the clinical trial”. Physicians and the pharmaceutical industry have a less negative opinion on this and tend to lean towards a more neutral opinion. Among patients and regulatory sector, the opposite can be observed. While they were positive regarding the benefits and risks, however when it is only about the risks, they start having a more negative opinion on the factor’s effect on patient participation in clinical trials.

Regarding “Motivation to participate from the clinical researcher” most responders said that this factor had a positive influence on patient recruitment. A small percentage (9%) of the pharmaceutical industry and 50% of responders from a patient perspective did not agree and said it had a negative influence on patient recruitment.

Most responders found that the “government stance towards the pharmaceutical industry” had a negative influence on the willingness of patients to participate. One exception was the responders from the regulatory sector. In contrast to the negative opinion of most stakeholders, the regulatory sector had a neutral (50%) to positive (50%) opinion on this factor regarding its influence on patient participation.

Finally, the “influence of news and social media” has an overall negative influence on patient recruitment, according to stakeholders. Responders from a patient perspective also had divided perspectives on the influence of news and social media on the willingness of patients to participate in clinical trials but were more positive on this aspect compared to other stakeholders.

Factors influencing patient recruitment in the Netherlands and their implementation status

Besides the effect of the abovementioned investigated factors and their effect on the patient recruitment of clinical trials, we were also interested to see how well these factors were nationally implemented and their effect specifically on the clinical trial situation in The Netherlands.

Factors related to healthcare and their status in the Netherlands

In the list of factors regarding healthcare in the Netherlands, all responders (100%) agree that "the quality of hospitals", and "the expertise of physicians and other healthcare personnel" is of high quality in the Netherlands (figure 10). Factors that are less relevant in the Netherlands are "fear and/or distrust in clinical trials" and "preference for alternative medication" (89.5% and 81.3% of responders respectively).

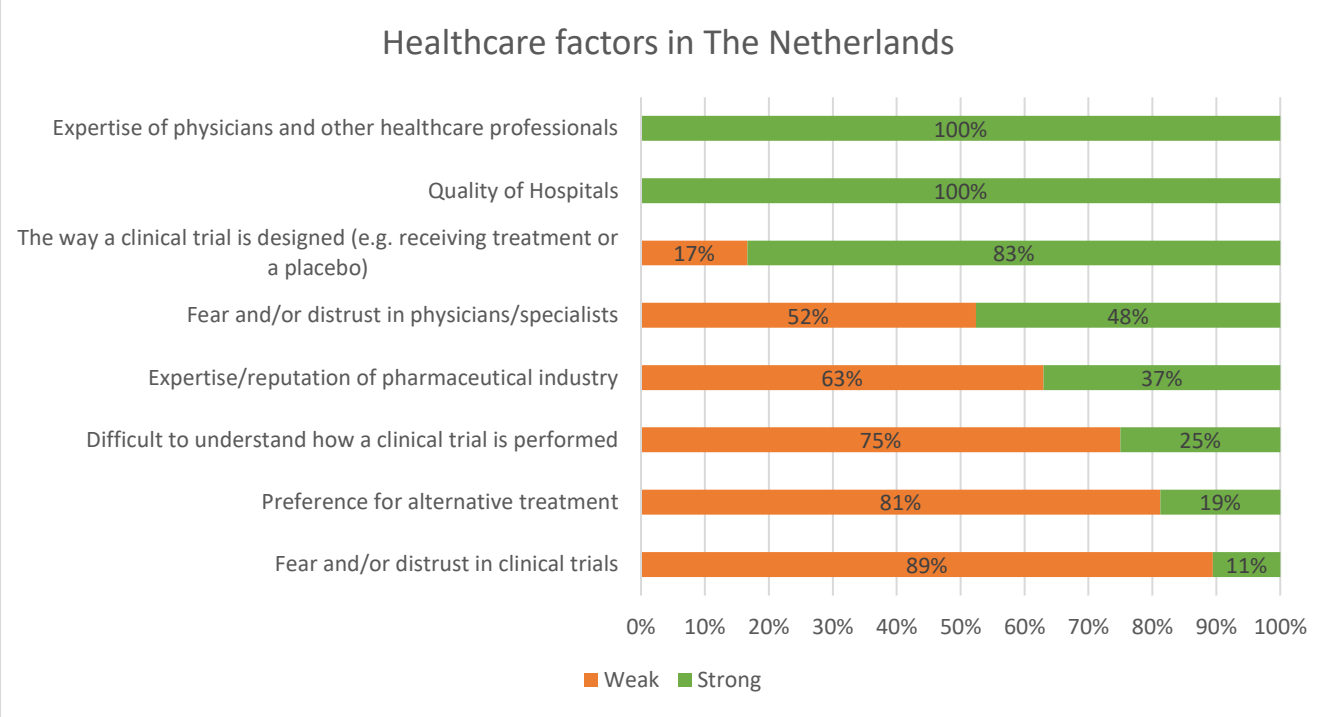


Figure 10 Opinions of responders on factors' influence on patient participation related to healthcare in The Netherlands

Factors related to benefits and costs of clinical trials and their status in the Netherlands

Regarding the benefits and costs of clinical trials, most of the responders have a positive opinion towards "the provision of alternative treatment options" through clinical trials, and "clinical trials providing earlier access to innovative medication", with 81.3% and 100% respectively (figure 11). However, there are also a few problems regarding clinical trial benefits and costs. One factor for objection is the time consumption for (medical) personnel. 76% of responders indicated that "the availability of personnel" in the Netherlands was insufficient.

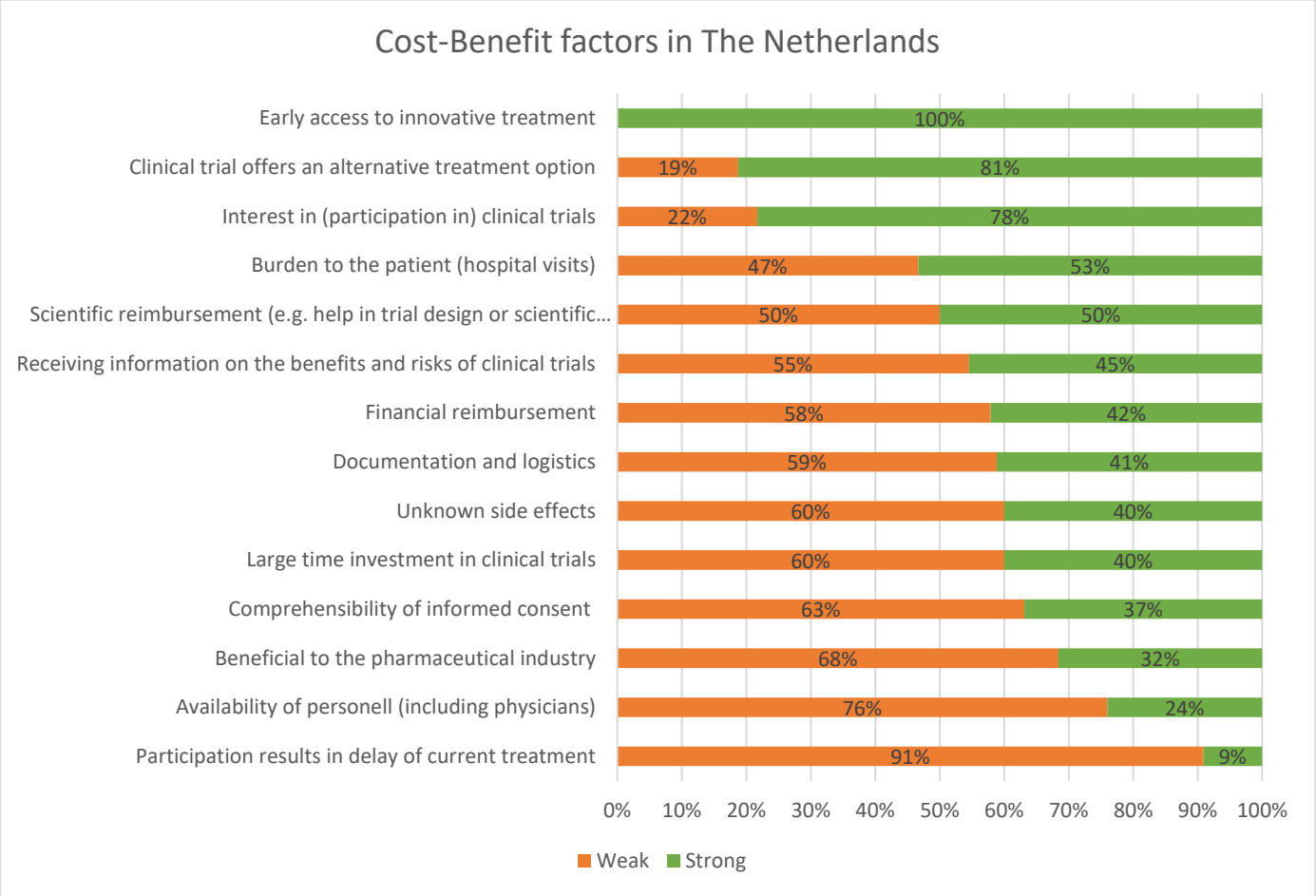


Figure 11 Opinions of responders on factors' influence on patient participation related to costs and benefits in The Netherlands

Factors related to personal reasons and their status in the Netherlands

According to the results of the survey, the most important personal reasons for individuals to participate in clinical trials in the Netherlands concern “the willingness to help innovation of healthcare” (88.2%) and “support/advice from family and friends” (85%) (figure 12). Also, “mobility”, as being impeded to reach a clinical setting, seemed to be not a hampering reason for Dutch patients to participate in clinical trials, supported by 80% of the participants. Inversely, these results indicate that in the Netherlands there is trust in the medication that is used in the clinical trial setting and ample possibility to combine work with clinical trials.

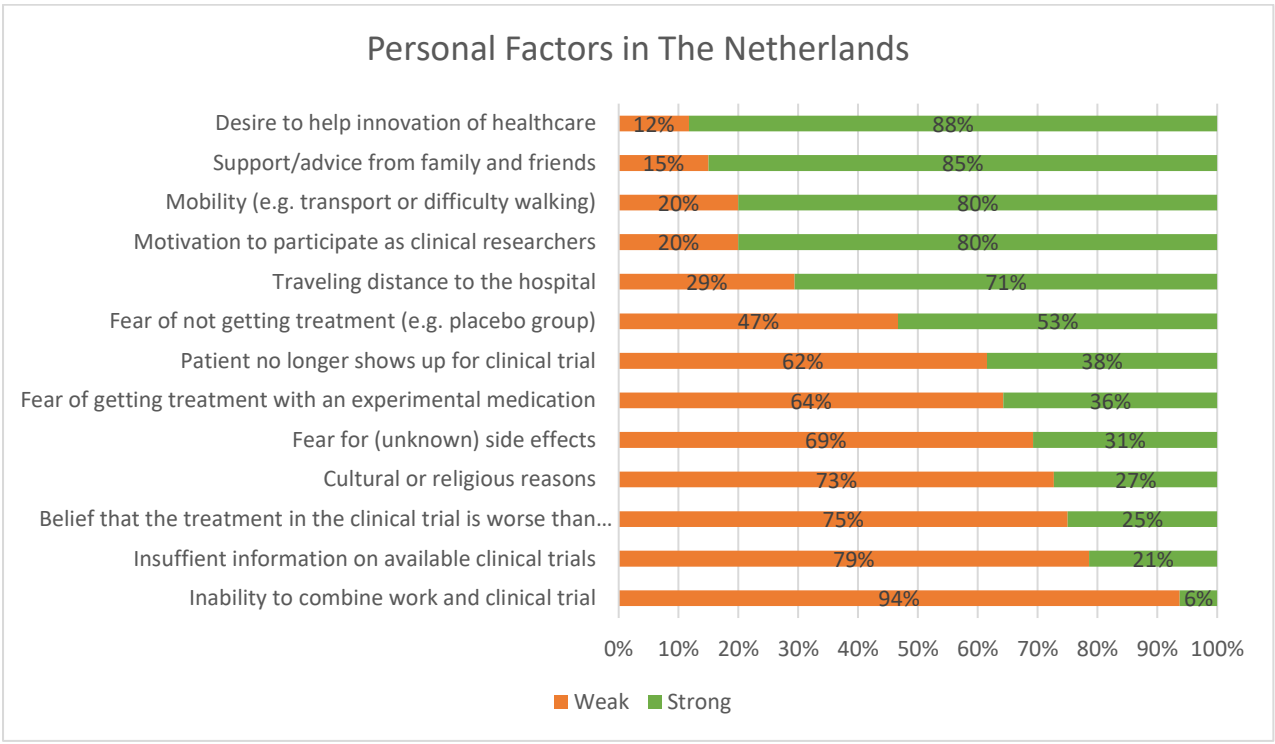


Figure 12 Opinions of responders on factors' influence on patient participation related to personal factors in The Netherlands

Other factors and their status in the Netherlands

Lastly for the group of "other factors", responders had a good opinion on the media coverage of science and healthcare. Most of responders (81%) agreed that the Netherlands performs strongly on the "media coverage regarding science" and 83.3% of responders rated the "media coverage on physicians, nurses, and hospitals" positively present in the Netherlands (figure 13). For "media coverage of the pharmaceutical industry" in The Netherlands, on the other hand, 85.7% of responders reported this as weak. Furthermore, a similar score is seen for "influence of social media and news", with 84.2% and 80% respectively.

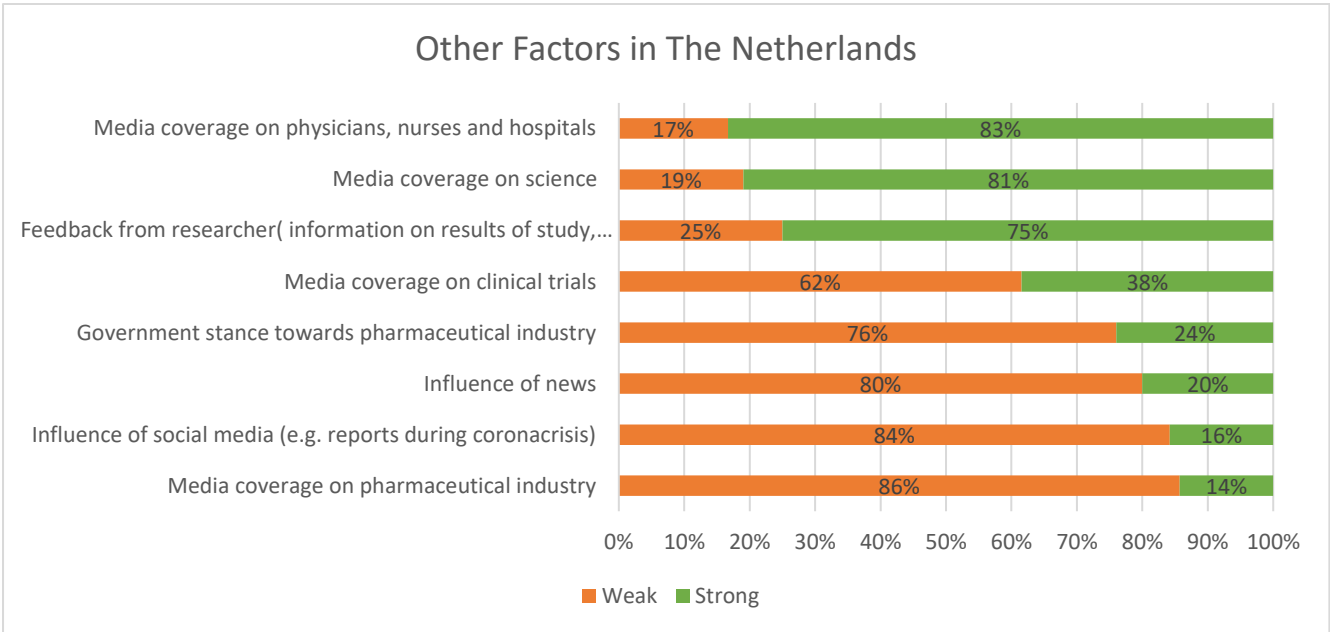


Figure 13 Opinions of responders on factors' influence on patient participation in The Netherlands unrelated to previous categories (healthcare, cost-benefit, and personal factors) on patient participation

Differences of views between Participants

In this section, we analyzed whether having direct experience in clinical trials influenced the opinion of responders regarding some of our abovementioned investigated factors and their effect on the patient recruitment of clinical trials in The Netherlands.

Differences of views regarding healthcare in the Netherlands

In a comparison between responders with and without direct involvement in clinical trials, responders from both groups largely had the same opinions on these factors related to healthcare. One notable difference is in their opinion on "Fear and/or distrust in Physicians/Specialists" (figure 14). Responders with direct experience in clinical trials stated that The Netherlands has a good performance in this aspect, while those without experience mostly think the opposite.

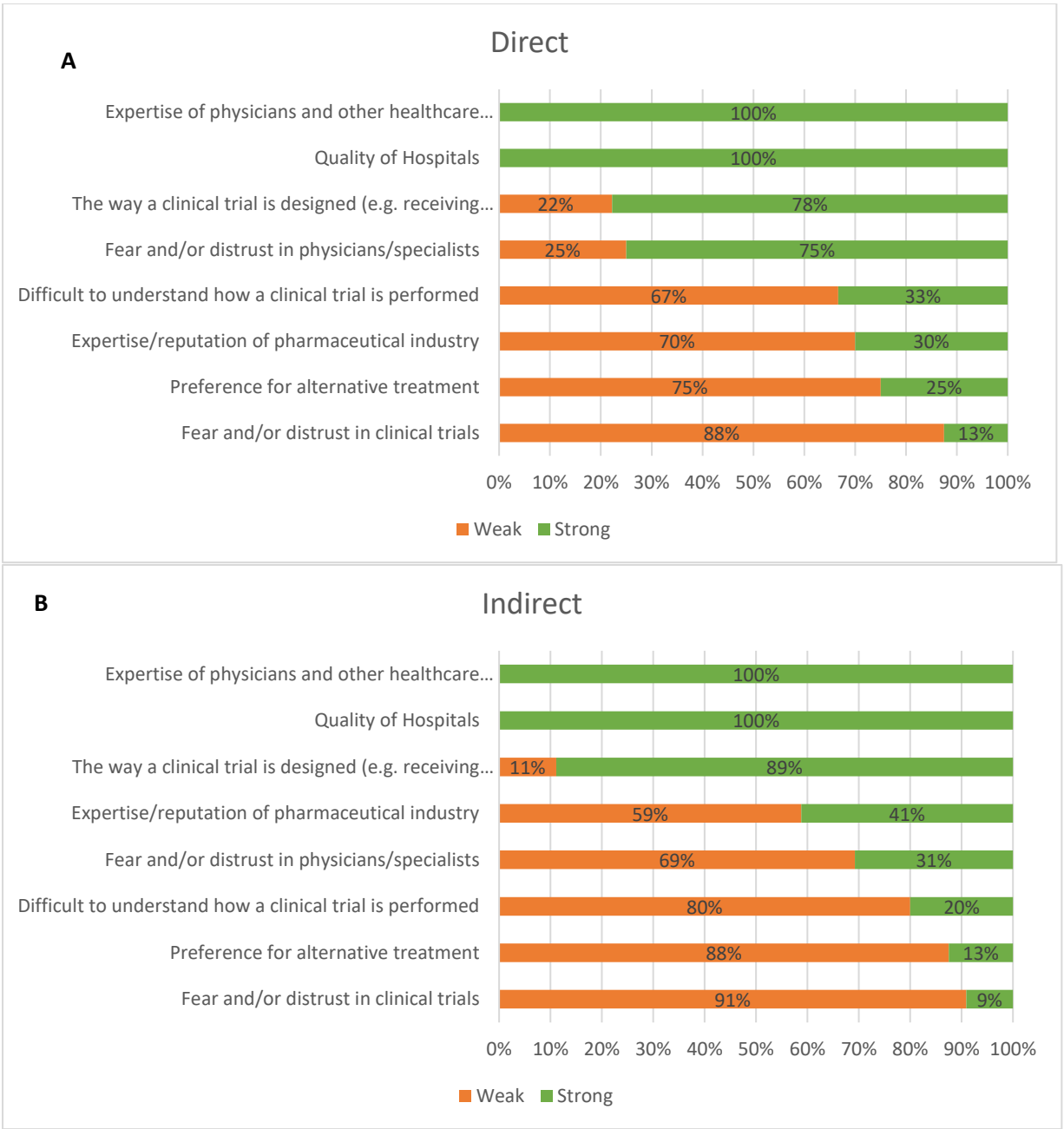


Figure 14 Comparison of responses from responders based on direct or indirect involvement in clinical trials. (A) Direct involvement (B) Indirect

Differences of views regarding benefits and risks of clinical trials in the Netherlands

Responders without direct involvement in clinical trials seem to have a more negative opinion on "The comprehensibility of patient consent" compared to those with direct experience. Contrary to this, responders without direct experience seem to be more positive on the "Unknown side effects" compared to those with direct experience in clinical trials (figure 15). Furthermore, responders with direct experience in clinical trials have a more positive opinion on the "Scientific reimbursement" (such as getting to aid in the clinical trial design or a publication) in The Netherlands and a less positive opinion on "Financial reimbursement" (such as being rewarded with a financial compensation for your time) compared to the responders without direct experience. Finally, responders without direct clinical trial experience have a more negative opinion on the "Large time investment in clinical trials" in The Netherlands.

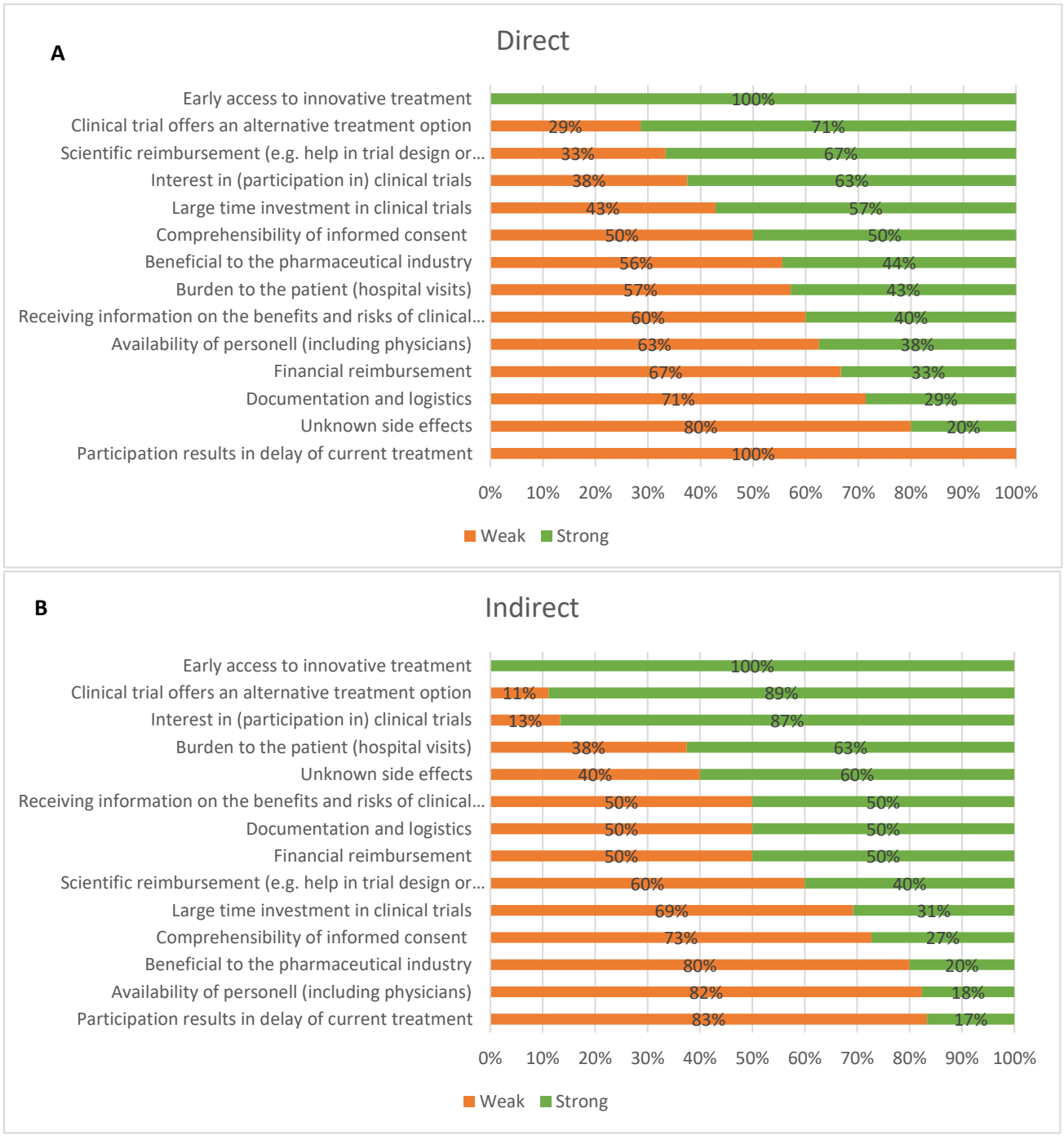


Figure 15 Comparison of responses from responders based on direct or indirect involvement in clinical trials. (A) Direct involvement (B) Indirect involvement

Differences of views regarding personal factors in the Netherlands

Regarding personal factors, a large contrast can be seen in “Fear of not getting treatment (e.g., Placebo Group)” (figure 16). Responders with direct experience showed strong perspectives on the fear for not getting treatment compared to those who were indirectly involved; their fear was weaker. A similar trend can be seen for the “Fear of (unknown) side effects)” and “Fear of treatment with an experimental medication”, those without direct clinical trial experience have a stronger opinion on this aspect in The Netherlands than responders who do have direct clinical trial experience. Finally, responders with direct experience in trials think that there is “Insufficient information on available clinical trials” while those without direct experience do not seem to have this issue.

Figure 16 Comparison of responses from responders based on direct or indirect involvement in clinical trials. (A) Direct involvement (B) Indirect involvement

Differences of several other factors in the Netherlands

Finally, in the remaining "Other factors", two differences could be observed between the groups (figure 17). Responders with direct experience in clinical trials were more positive on the "Media coverage on clinical trials" and "Feedback from the researchers" than the responders without direct clinical trial experience. In both groups, we observed that "government stance towards-, and media coverage on the pharmaceutical" weakens their possible willingness in participating in clinical studies.

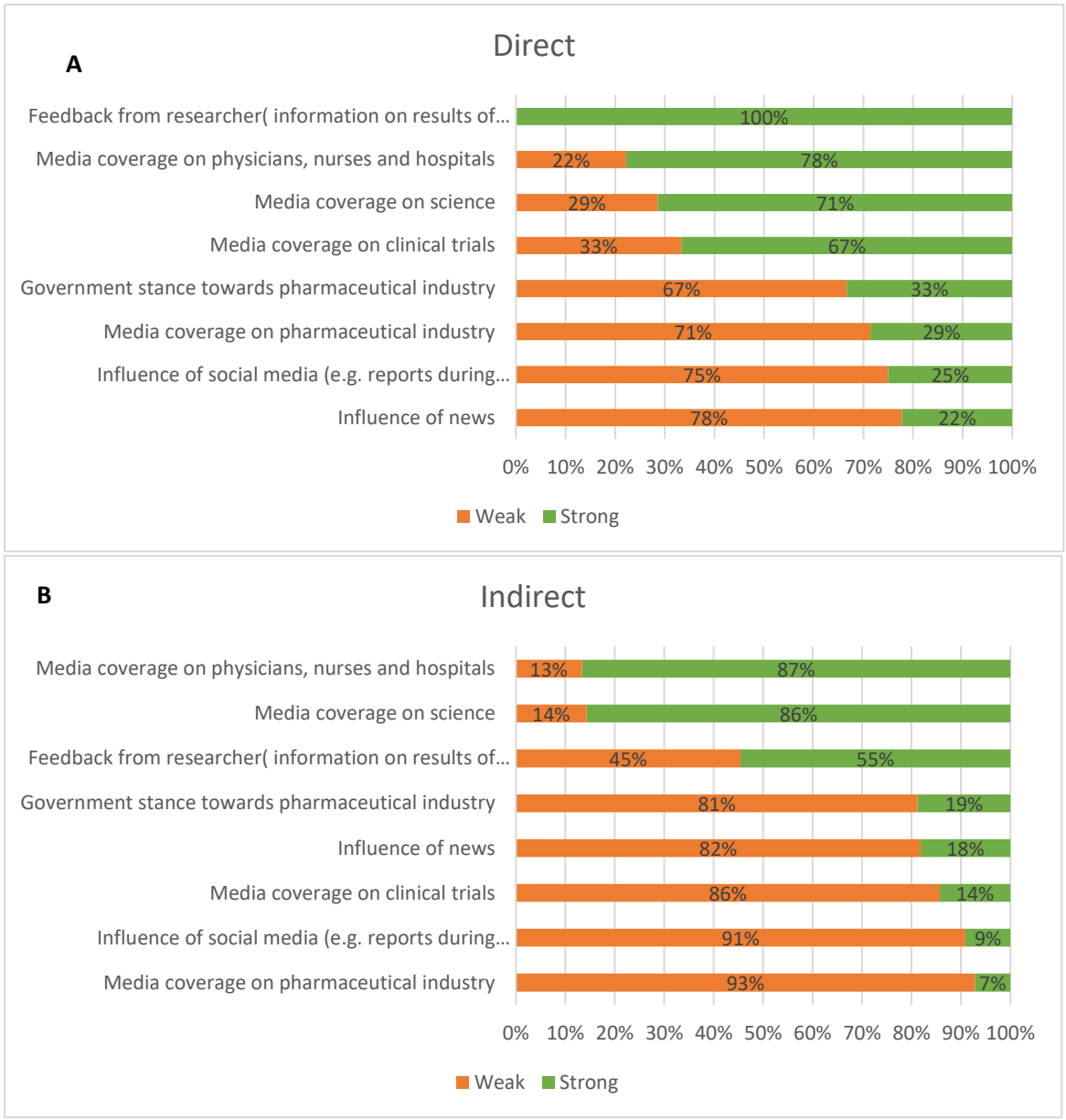


Figure 17 Comparison of responses from responders based on direct or indirect involvement in clinical trials. (A) Direct involvement (B) Indirect involvement

Opinions of various stakeholders

First, there was a division of opinions regarding the "Expertise/reputation of the pharmaceutical industry". Many stakeholders had a negative opinion on the "expertise and/or reputation of the pharmaceutical industry" in The Netherlands. According to the survey, 100% of responders from academic, patient, and regulatory sectors said that the "expertise and/or reputation of the pharmaceutical industry" was weak in The Netherlands. Responders from the pharmaceutical industry also had a divided view on this point; less than half (43%) of responders from the pharmaceutical sector said that their expertise and/or reputation was good in The Netherlands. Instead, Physicians

and other healthcare workers had a unanimous positive view (100%) about the expertise and/or reputation of the pharmaceutical sector specifically in conducting clinical studies.

Most stakeholders agree that a “preference for alternative treatments” does not apply to the situation in The Netherlands. Responders from a patient perspective had an opposite view all of them indicating a strong presence of preference of alternative treatments in The Netherlands.

Another factor patients disagreed on was “The design of a clinical study”. According to 50% of patients this was not properly implemented in The Netherlands, likely related to the understandability of the clinical trial design, whereas this was only supported by a third (17%) of respondents from the pharmaceutical industry and none from academia, healthcare, and regulatory stakeholders.

Understanding of the clinical trial process (i.e., “Difficult to understand the clinical trial process”) in the Netherlands seemed not to be an issue for most responders from regulatory and healthcare sector (100%), and the pharmaceutical industry (78%). However, half of patients (50%) and all responders from academia (100%) think that the process is indeed difficult to understand.

In the case of “Benefits for the pharmaceutical industry”, the regulatory sector and pharmaceutical industry are mostly in agreement that the (financial) benefits for the industry is not the main focus for clinical trials and not a problem in The Netherlands. However, 50% of academic and 100% of patient and healthcare responses indicate that according to them this is surely an issue in The Netherlands.

Concerning “Large time investment in clinical trial”, all patient and academia responders (100%) think this is an issue in The Netherlands. Contrarily, 50% of the regulatory responses, 33% of the pharmaceutical industry and none of healthcare personnel indicate this is the case in The Netherlands.

Responders have reported the “Interest in participating in clinical trials” from patients, but also for example physicians, as very positive in The Netherlands. All responses from academia, healthcare, and regulatory stakeholders indicate a positive interest in The Netherlands when it comes to clinical trials. However, responders from the pharmaceutical industry (24%) and patients (50%) indicate that this factor is not as positively present as the other stakeholders indicate.

Regulatory and academic stakeholders responded very positive about the “Comprehensibility of informed consent” in The Netherlands (100% for both), indicating this is well implemented. For patients, this was only the case for 50% of the responders, whereas only 23% of responders from the pharmaceutical industry thinks this is properly implemented in The Netherlands.

When it comes to clinical trials giving “Access to an alternative treatment option” most stakeholders agree that this reason is of interest in The Netherlands. The only stakeholder that disagrees is the healthcare sector, with a complete majority (100%) disagreeing the proper implementation in The Netherlands.

Most stakeholders do not see any issues concerning patient participation due to “cultural or religious reasons” in The Netherlands. Notwithstanding, all responders (100%) from the regulatory sector disagree with this view, acclaiming that this is a problem in The Netherlands.

Furthermore, responders from pharmaceutical industry, patients, and healthcare do not see any issues concerning the “information given on available clinical trials”. However, 100% of academic and 50% of regulatory responses indicate that the information on available clinical trials is not sufficient in The Netherlands.

In the case of “Motivation of clinical researchers to participate in clinical trials” only the patient responders think this is not (sufficiently) present in The Netherlands, while the other stakeholders seem satisfied with the Dutch clinical trial situation in this regard.

Responders from all sectors/groups do not see a problem with the “traveling distance to the hospital” in The Netherlands, except for patient responders which indicate that travelling distance to the research site is longer than expected and hence not adequately implemented in The Netherlands.

Regarding “Feedback of the researchers”, except for regulatory (50%) and pharmaceutical (29%) responders, all other stakeholders agree that this is well implemented in the clinical trials situation in the Netherlands.

All academic and regulatory responders (both 100%) indicate that the “attitude of the government” towards clinical studies in The Netherlands is positive. This perception is halved (50%) among patients. Healthcare and pharmaceutical responders do not agree (100% and 85% respectively) indicating that the government attitude towards clinical research is negative in The Netherlands.

Then about the influence of news, social media, and media coverage about the pharmaceutical industry on patient participation in The Netherlands. Pharmaceutical industry, regulatory sector, physicians and other healthcare workers, and academics agree that “influence of news and social media”, and “media coverage about the pharmaceutical industry” does not have a huge impact on the patient participation in The Netherlands. Patients on the other hand think that these surely are affecting the situation in The Netherlands. Half of patient responses indicate “that news” has influence on patient participation in The Netherlands and 100% of patient responses indicate that “social media” and “media coverage about the pharmaceutical industry” influences patient participation in The Netherlands. All responders from patient, academic, and healthcare perspectives (100%) agree that the “Media coverage on science” is sufficiently present and/or has a positive effect on the Dutch clinical trial situation. While 81% of pharmaceutical responders agree, only 50% of regulatory responders agree with this view. On the other hand, “Media coverage on clinical trials” seems to be sufficient according to academics and patients, and insufficient according to healthcare, regulatory, and pharmaceutical responders. Finally, regarding “Media coverage on physicians, nurses, and hospitals”, pharmaceutical, academic, patient, and regulatory responders agree that this is sufficiently present and/or implemented in The Netherlands. All responders from the healthcare sector seem to disagree and think this is not sufficiently present/implemented in The Netherlands.

Discussion

In the present study, we have identified and studied several factors that are likely to be related to the delayed patient recruitment in clinical trials in The Netherlands. We subdivided these results into groups with factors being related to healthcare, cost-benefit, personal, or other reasons that could influence participation in clinical trials. Many factors in different categories were found to have either a positive or negative effect that may play a role in the willingness to participate in clinical trials in The Netherlands. Factors such as quality of hospitals and expertise of physicians were found to be positive aspects in the Netherlands regarding willingness of patients to participate in clinical trials. On the other hand, factors such as fear and/or distrust in clinical trials, physicians, and specialists were found to be negative for the willingness of patients to participate. Furthermore, many of the factors within and in between groups (i.e., healthcare, cost-benefit, etc.) seem to be related to each other and have a combined positive or negative effect on the clinical trial patient participation and recruitment speed.

Experts agreed that, of the factors related to healthcare, the Netherlands performs well on the factors that have a positive influence on patient recruitment in clinical trials, such as the expertise of physicians and other healthcare professionals, and the quality of hospitals. Patients have trust in the capabilities of healthcare professionals and their expertise, which is a factor that enables enrollment and increases clinical trial participation.

One of the factors having a positive influence on patient recruitment in the Netherlands, whereby there was room for improvement, was the expertise/reputation of the pharmaceutical industry. Over half of responders indicated that the expertise/reputation of the pharmaceutical industry has a positive influence on patient recruitment in clinical trials. On the other hand, a slight majority also indicated that the expertise/reputation of the pharmaceutical industry was negative. Reputation damage of the Dutch pharmaceutical industry might have occurred as a result of negative

media coverage, controversies, or a critical attitude from parts of the government towards the sector, such as discussions about high prices of drugs (13,14). This negative perception of the industry in the public sphere could be one of the delaying factors in patient recruitment as there could enable distrust. Nonetheless, the negative perception of the pharmaceutical industry in the Netherlands seems to be related to reputation issues and not about the expertise of the industry (15,16) Hence, it's important to work on initiatives to clarify the positive role of the industry in clinical research, focusing on patient safety, availability of innovative therapeutical options, and scientific competence to develop new medicinal products. To achieve a positive impact on patient's participation, these initiatives should be supported by multi-stakeholder collaborations. Governments benefit from medical innovations studied during clinical research in terms of financial gains, employment, investments, medical and scientific expertise gains, generation of start-ups, or worldwide scientific/medical recognition. These benefits have been highlighted by the Dutch trade organization (VIG), Health Holland, Netherlands Enterprise Agency (Rijksdienst voor Ondernemend Nederland - RVO), and the Netherlands Foreign Investment Agency (NFIA) in their Bidbook Life Sciences Healthcare (LSH) sector, and fully endorsed by the ministries of Economic Affairs and Climate Policy and Health, Welfare and Sport (i.e., EZK & VWS) (17,18).

Clinical trials comprehend both benefits and risks for participants. According to our responders from various sectors, the main driving reasons for participation seem to be interest, an alternative treatment option, and an innovative treatment option. Mostly, an innovative treatment option is the main motivator for patients to participate in a clinical trial (3). This is one of the greatest societal and scientific impacts that trials have. This is not an exception for the Netherlands. For this reason, the importance of having studies in the Netherlands increases the treatment options for patients to improve their conditions.

Responders indicated that the comprehensibility of informed consent and clinical trial design are difficult to understand. There seems to be a disconnect between responders who have directly worked/being involved in clinical trials and those who have worked with clinical trials, but were not directly involved in one (e.g., working as a physician, statistician, nurse, etc). This is also the case for patients participating in a clinical trial. This is a well-known problem for clinical trial patient recruitment since a patient might be unwilling to join because of the lack of understanding, or misunderstanding about the conditions or details of the clinical trial the patient is to participate in (19). A study by Phelps et al. showed that the decision to participate in a clinical trial is influenced by, among others, the patients' ability to understand the clinical trial and clinical trial process (20). According to previous research in combination with our results (e.g., fear of unknown side effects or not getting treatment), fear and negative beliefs seem to be a significant limiting factor to the willingness of patients to participate in clinical trials (21). Although these beliefs are not as strongly present in our sample, they are still present and surely play a role in the diminished patient recruitment. With the introduction of the summary for laypersons, understandable information for patients is ought to be achieved to support them in the decision-making process to weigh the benefits and risks of participation to clinical studies. This initiative dates from 2017 and the consequences of its implementation in the Netherlands regarding understandable information to patients must be further evaluated. Patients struggle with understanding information about clinical studies, as well as the length of these documents, creating a barrier for participation. Further initiatives assessing the impact and length of understandable patient information to improve clinical trial participation are urgently needed (22,23).

One weak point of the Netherlands regarding clinical trials is the lack of or insufficient personnel, as indicated by most responders. This is a major and severe limiting factor as also most responders (78%) indicated that there is plenty of interest in clinical research and there is a strong desire to help the innovation of healthcare in the Netherlands. In other words, the understaffed healthcare setting is impeded in bringing innovations to patients due to the current system and choices. This finding is in accordance with previous literature in which they found various reasons, including lack of resources, limiting physician participation in clinical research (24). Furthermore, responders indicated that the expertise of physicians and quality of hospitals is very high in The Netherlands. Therefore, creating more opportunities for physicians and other healthcare workers to participate in clinical research would improve the

clinical trial scene in The Netherlands. In addition, it will expose healthcare professionals to the latest innovations and contribute to building up the Dutch expertise to eventually strengthen the healthcare system. More importantly, the Medicines Evaluation Board (MEB), as national competent authority, plays a dominant role within the European Medicines Agency (EMA) in the evaluation of new marketing authorizations (i.e., CHMP), post-marketing safety monitoring (i.e., PRAC), and in the provision of scientific advice (i.e., SAWP) (9). As for this, the expertise and authority of the MEB within the EMA should be reflected in the number of clinical studies and a reason to prioritize the Netherlands above many other Member States. Part of this strategic reasoning was key in the decision for the EMA to move from London to Amsterdam after the Brexit. This key clinical asset for the Netherlands has not been yet fully optimally utilized. Hence, more studies are required to map the financial and scientific/medical benefits of having clinical trials in the Netherlands compared to other similar countries.

Limitations

We observed skewed response rates, which may have different explanations. Accessibility could have played a role since the survey was performed using an online questionnaire. Response rate from certain groups could be lower than others since certain groups of individuals are less likely to have access to the internet or have lower familiarity with technology (25). In our case we approached mostly working professionals and expect that they have sufficient knowledge of technology. Another reason could be financial motivation. According to Artino et al., there are various reasons for individuals to participate in a survey: incentives, altruism, personal interest, social pressure, and obligation (26). In our survey there was no incentive, neither financial or scientific, and there would be no personal rewards for completing the survey.

Also, a low response rate was observed. Involvement during surveys is a common methodological limitation and issue. Due to a low response rate, certain groups could be underrepresented within our stakeholders (27). While not much can be said for the other groups, responders from the pharmaceutical industry had similar answers across different factors. Since the subject is related to expertise, while it is not fully representative, answers from the underrepresented groups could still give an indication of trends within those groups. Nonetheless, our study still holds value as an initial estimation on the state of clinical trial recruitment in The Netherlands.

Future Directions

Communication between stakeholders

First, communication between the different stakeholders needs to be improved. Among our stakeholders a large variety of responses were observed and many differences in opinions between stakeholders. All stakeholders should come together to improve the clinical trial process with the patient's wellbeing as the highest priority. In The Netherlands, the Dutch Clinical Research Foundation has already taken steps in this aspect by collecting the views of different stakeholders in clinical research (15). One improvement to this could be to increase the input from a patient perspective by inviting relevant patient organizations into the discussion. A special committee comprised of these stakeholders (e.g., pharmaceutical industry, government, patients, and physicians) could be created focused on improving patient participation in clinical trials, in particular communication of information about clinical trials.

Communication with patients

Communication with the patient is vital. Understanding of clinical trials and informed consent forms is a known challenging issue among patients (28). Research has shown that a patient's understanding of trial methods and patient safety could improve a patient's willingness to participate in a clinical trial, thereby improving patient recruitment (29). Since the main communication point for patients is healthcare staff, healthcare staff should have sufficient understanding of the clinical trial design, risks, and benefits. Furthermore, there should be sufficient staff to perform these informational activities for patients. Also, there should be ample opportunities for questions and explanations to ensure patient understanding of the clinical trial. Other stakeholders, for example the pharmaceutical industry, could help by making sure the information provided for the clinical trial should be clear and understandable.

This can be achieved by for example a summary for laypersons or a clear and concise overview of the most important points (e.g., responsibilities, risks, benefits, etc.) (30). However, as mentioned before steps should still be taken to assess and improve the impact and length of understandable patient information for improvement of clinical trial participation.

Repetition and expansion of the current study

Next, due to the low response rate in the performed research, a similar study should be performed with an adequate sample size to show statistically relevant response rates. This way the data can be used as a (more) accurate representation for all groups researched. Furthermore, this research could be performed in specific patient groups of interest. It is possible that interest and willingness to participate in clinical trials for disorders where there is limited to no treatment would be higher than in the case of a disorder with an existing treatment. This could allow us to identify which clinical trials could benefit from extra attention in patient recruitment.

Conclusions

The Netherlands has an impressive infrastructure for the execution of clinical studies, which apparently seems to be underutilized. There are several reasons for this. Most of the issues in the Netherlands regarding patient recruitment in clinical trials need cooperation of all the different stakeholders. The clinical trial process cannot be streamlined and improved without collaboration of all parties involved in the clinical trial process. Furthermore, there are major misunderstandings in the perception of and between stakeholders about the execution of clinical studies. These misunderstandings ought to be promptly addressed to guarantee the flow of innovation in the Netherlands. All involved parties should work together to improve patient recruitment in clinical trials and make the clinical trial process as smooth as possible to reach the most benefit for all parties, but most importantly, the patients in need of better treatments.

Conflicts of interest

This research was performed in a collaboration between Utrecht University and Pfizer bv Netherlands. The author received a legal intern fee as compensation, according to Pfizer's guidelines.

Acknowledgments

The author sincerely thanks Francisco Hernandez, Seema Mahabier, and Marianne Groeneveld for their contributions to the manuscript. Furthermore, the author is thankful to all those who took the time to complete the questionnaire.

References

1. Umscheid CA, Margolis DJ, Grossman CE. Key concepts of clinical trials: A narrative review. Vol. 123, Postgraduate Medicine. 2011. p. 194–204.
2. Collignon O, Schiel A, Burman CF, Rufibach K, Posch M, Bretz F. Estimands and Complex Innovative Designs. Vol. 112, Clinical Pharmacology and Therapeutics. John Wiley and Sons Inc; 2022. p. 1183–90.
3. Novitzke JM. The significance of clinical trials. Vol. 1, Journal of Vascular and Interventional Neurology. 2008.
4. Lang T, Siribaddana S. Clinical trials have gone global: Is this a good thing? PLoS Med. 2012;9(6):6.
5. Vereniging Innovatieve Geneesmiddelen. BOSTON BY THE NORTH SEA [Internet]. 2021 [cited 2023 Mar 27]. Available from: https://y6e7t2d5.stackpathcdn.com/production/documents/Boston-by-the-North-Sea.pdf.pdf
6. Vereniging Innovatieve Geneesmiddelen. HOE WORDT NEDERLAND KOPLOPER OP HET GEBIED VAN KLINISCH ONDERZOEK? 2020.
7. Nancy Cooper. World's Best Hospitals 2021 [Internet]. 2021 [cited 2021 Dec 11]. Available from: https://www.davidscottco.com/worlds-best-hospitals-of-2021-top-200-global-ranking/
8. van Agthoven M, Antonisse A. Nederlands Vestigingsklimaat voor Farmaceutische Bedrijven Onder Druk. 2019.
9. Medicines Agency E. ANNUAL REPORT 2022. 2022 May 15;
10. Unknown. clinicaltrials.gov [Internet]. 2022 [cited 2022 May 4]. Available from: https://clinicaltrials.gov
11. Smeets E. Regeldruk bij patiëntgebonden onderzoek. Ned Tijdschr Geneeskd. 2015;
12. van den Brink MJ, Hummel M, Lemstra M, Berger MY, Dekker JH, Blanker MH. Factors affecting patient recruitment to trials: qualitative research in general practice. BJGP Open. 2020 Aug;4(3).
13. de Visser E. Minister Bruins dreigt farmaceuten die woekerprijzen vragen aan de schandpaal te nagelen. De Volkskrant. 2019;
14. BNR Webredactie. Minister Bruins dreigt farmaceutische industrie met naming & shaming. BNR. 2019;
15. Lambers Heerspink H, Buijzen F, Lambers Heerspink H, Visser dr LE, de Zeeuw dr D. STAKEHOLDER OPINIONS ON THE POSITION OF THE NETHERLANDS IN CONDUCTING CLINICAL DRUG TRIALS A SWOT ANALYSIS. 2011.
16. Health Holland. The Netherlands Europe's most attractive and innovative biopharmaceutical environment. 2018.
17. Bosma S, Swieringa J, Vermeulen E, Meeuwisse J, Stallman B, Vink M, et al. LSH bidbook. 2023;
18. Vereniging Innovatieve Geneesmiddelen. LSH-sector presenteert nieuw bidbook [Internet]. 2023 [cited 2023 Jul 11]. Available from: https://www.verenigginnovatievegeneesmiddelen.nl/actueel/nieuwe-bidbook-lsh-sector-is-uit
19. Lidz CW, Albert K, Appelbaum P, Dunn LB, Overton E, Pivovarova E. Why is therapeutic misconception so prevalent? Cambridge Quarterly of Healthcare Ethics. 2015 Feb 26;24(2):231–41.
20. Phelps EE, Tutton E, Griffin X, Baird J. A mixed-methods systematic review of patients' experience of being invited to participate in surgical randomised controlled trials. Soc Sci Med. 2020 May;253:112961.

21. Quinn GP, Koskan A, Wells KJ, Gonzalez LE, Meade CD, Pozo CLP, et al. Cancer Patients' Fears Related to Clinical Trial Participation: A Qualitative Study. Journal of Cancer Education. 2012 Jun 21;27(2):257–62.

22. Summaries of Clinical Trial Results for Laypersons [Internet]. 2018. Available from: http://health.gov/communication/literacy/quickguide/factsbasic.htm

23. Centrale Commissie Mensgebonden Onderzoek. Summary of results [Internet]. [cited 2023 Jul 11]. Available from: https://english.ccmo.nl/investigators/clinical-trials-with-medicinal-products-ctr/end-of-study-ctr/summary-of-results

24. Rahman S, Majumder MAA, Shaban SF, Rahman N, Ahmed M, Abdulrahman K Bin, et al. Physician participation in clinical research and trials: Issues and approaches. Vol. 2, Advances in Medical Education and Practice. Dove Medical Press Ltd; 2011. p. 85–93.

25. Wu MJ, Zhao K, Fils-Aime F. Response rates of online surveys in published research: A meta-analysis. Computers in Human Behavior Reports. 2022 Aug 1;7.

26. Artino AR, Youmans QR, Tuck MG. Getting the Most Out of Surveys: Optimizing Respondent Motivation. Vol. 14, Journal of graduate medical education. NLM (Medline); 2022. p. 629–33.

27. Schouten B, Cobben F, Bethlehem J. Indicators for the representativeness of survey response [Internet]. Vol. 35, Statistics Canada, Catalogue No. 2009. Available from: https://www.researchgate.net/publication/267836796

28. Pandiya A. Readability and comprehensibility of informed consent forms for clinical trials. Perspect Clin Res. 2010 Jul;1(3):98–100.

29. Juan-Salvadores P, Michel Gómez MS, Jiménez Díaz VA, Martínez Reglero C, Iñiguez Romo A. Patients' knowledge about their involvement in clinical trials. A non-randomized controlled trial. Front Med (Lausanne). 2022 Sep 20;9.

30. Summaries of Clinical Trial Results for Laypersons [Internet]. 2018. Available from: http://health.gov/communication/literacy/quickguide/factsbasic.htm

Annex

* Required

Klinische studies in Nederland

Voordat u deelneemt aan dit onderzoek is het belangrijk om te weten of u ervaring heeft met het uitvoeren van klinische studies. Hier maken wij in sommige vragen ook onderscheid tussen **directe** en **indirecte** ervaring. Onder **directe** ervaring verstaan wij actieve deelname tijdens klinische studies, dit kan zijn o.a. als patiënt, arts, methodologen en/of statistici. Onder **indirect** verstaan wij mensen die niet direct hebben deelgenomen maar wel kennis hebben over de werkingen van of onderzoek doen naar klinische studies. Denk hierbij aan academici, maar ook bijvoorbeeld stichtingen die patiënten helpen met klinische studies, zoals vertegenwoordigen of identificeren, o.a.

Bij sommige vragen zult u een ***** vinden en bij andere vragen niet. Dit kunt u negeren en alle vragen invullen die voor u van toepassing zijn.

1. Heeft u ervaring met klinische studies? *

- ◯ Ja
- ◯ Nee

* Required

Ervaring

Hier vragen wij u een aantal vragen om vast te stellen hoeveel ervaring u heeft met klinische studies

2. Wat voor een rol heeft u in klinische studies? *

Select your answer

3. Heeft u direct aan een klinische studie gewerkt/deelgenomen? (denk aan patiënt, behandelend arts, verpleegkundige, methodoloog, statisticus, etc.) *

- ◯ Ja
- ◯ Nee

4. Zo ja, aan hoeveel klinische studies heeft u gewerkt/deelgenomen?

- ◯ 1-3
- ◯ 4-7
- ◯ 8+

5. Voor behandelend arts, andere zorgverlener, statisticus, of (theoretisch) onderzoeker: Als u werkt binnen klinische studies, hoeveel jaar ervaring heeft u al met klinische studies?

- ◯ 1-3
- ◯ 4-7
- ◯ 8+
- ◯ Niet van toepassing

Factoren

In deze sectie vindt u een aantal factoren die invloed kunnen hebben op deelname van patiënten aan klinische studies. Geef voor elke factor aan of deze naar uw mening een **positieve** of **negatieve** invloed hebben op deelname van patiënten aan een klinische studie. Of als u zelf heeft deelgenomen als patiënt, kunt u antwoord geven vanuit uw eigen ervaring of de ervaring van uw medepatiënten.

6. De Gezondheidszorg

Hieronder ziet u een lijst met factoren gerelateerd aan **de gezondheidszorg**.

- Geef voor elk van de volgende factoren aan of deze een **positieve of negatieve invloed** hebben op deelname van patiënten aan klinische studies *

	Zeer Negatief	Negatief	Neutraal	Positief	Zeer Positief
Kwaliteit van ziekenhuizen	◯	◯	◯	◯	◯
Deskundigheid van artsen en andere zorgverleners	◯	◯	◯	◯	◯
Expertise/reputatie van farmaceutische industrie	◯	◯	◯	◯	◯
Angst en/of wantrouwen in klinische studies	◯	◯	◯	◯	◯
Voorkeur voor alternatieve geneeswijzen	◯	◯	◯	◯	◯
Hoe een klinische studie wordt uitgevoerd (bijv. krijgen van een geneesmiddel of een placebo)	◯	◯	◯	◯	◯
Moeilijk te begrijpen hoe een klinische studie wordt uitgevoerd	◯	◯	◯	◯	◯
Angst en/of wantrouwen in artsen/specialisten	◯	◯	◯	◯	◯

7. **baten en lasten van klinische studies**

Hieronder ziet u een lijst met factoren gerelateerd aan **baten en lasten van klinische studies**.

- Geef voor elk van de volgende factoren aan of deze een **positieve of negatieve invloed** hebben op deelname van patiënten aan klinische studies
*

	Zeer Negatief	Negatief	Neutraal	Positief	Zeer Positief
Ten gunste van de farmaceutische industrie	○	○	○	○	○
Grote investering van tijd in klinische studies	○	○	○	○	○
Beschikbaarheid van personeel (onder andere artsen)	○	○	○	○	○
Interesse in (deelname aan) klinische studies	○	○	○	○	○
Documentatie en logistiek	○	○	○	○	○
Belasting voor patiënten (ziekenhuisbezoeken)	○	○	○	○	○
Deelname zorgt voor uitstel huidige behandeling	○	○	○	○	○
Financiële vergoeding	○	○	○	○	○
Wetenschappelijke vergoeding (bijv. inspraak op studieontwerp of publicatie)	○	○	○	○	○
Onbekende bijwerkingen	○	○	○	○	○
De begrijpelijkheid van de patienteninformatie (informed consent)	○	○	○	○	○
Wel/geen informatie ontvangen over de voordelen van de studie (en de risico's)	○	○	○	○	○

Klinische studie geeft een alternatieve behandelingsoptie	◯	◯	◯	◯	◯
Eerdere toegang tot innovatief geneesmiddel	◯	◯	◯	◯	◯
Wel/geen informatie ontvangen over de risico's van de studie	◯	◯	◯	◯	◯

8. **Persoonlijke Factoren**

Hieronder ziet u een lijst met **persoonlijke factoren.**

- Geef voor elk van de volgende factoren aan of deze een **positieve of negatieve invloed** hebben op deelname van patiënten aan klinische studies

*

	Zeer Negatief	Negatief	Neutraal	Positief	Zeer Positief
Steun/advies van familie en vrienden	◯	◯	◯	◯	◯
Mobiliteit (denk aan vervoer of moeite met lopen)	◯	◯	◯	◯	◯
Culturele of religieuze redenen	◯	◯	◯	◯	◯
Onvoldoende informatie over huidige beschikbare klinische studies	◯	◯	◯	◯	◯
Patiënt verschijnt niet (meer) voor klinische studie	◯	◯	◯	◯	◯
Motivatie om mee te doen als klinisch onderzoeker	◯	◯	◯	◯	◯
Geen vrij kunnen krijgen van werk	◯	◯	◯	◯	◯

Reisafstand naar het ziekenhuis	○	○	○	○	○
Overtuiging dat het geneesmiddel in de studie slechter is dan het beschikbare middel	○	○	○	○	○
Angst om behandeld te worden met een experimenteel geneesmiddel	○	○	○	○	○
Angst voor (onbekende) bijwerkingen	○	○	○	○	○
Angst om niet behandeld te worden (bijvoorbeeld placebo groep)	○	○	○	○	○
Mee willen helpen aan innovatie van gezondheidszorg	○	○	○	○	○

9. **Overige factoren**

Hieronder ziet u een lijst met **overige factoren.**

- Geef voor elk van de volgende factoren aan of deze een **positieve of negatieve invloed** hebben op deelname van patiënten aan klinische studies *

	Zeer Negatief	Negatief	Neutraal	Positief	Zeer Positief
Feedback van de onderzoeker (informatie over de uitkomsten van de studie, zoals werkzaamheid of bijwerkingen)	○	○	○	○	○
Houding van de overheid tegenover de farmaceutische industrie	○	○	○	○	○
Invloed van het nieuws	○	○	○	○	○

Invloed van Social Media (zoals de berichtgeving tijdens de coronacrisis)	○	○	○	○	○
Mediabeelden over de farmaceutische industrie	○	○	○	○	○
Mediabeelden over de wetenschap	○	○	○	○	○
Mediabeelden over de klinische studies	○	○	○	○	○
Mediabeelden over de artsen, verpleging en ziekenhuizen	○	○	○	○	○

Verbeterpunten in Nederland

Deze sectie bestaat uit 2 gedeelten, namelijk **verbeterpunten** en **sterke punten**. Hieronder noemen we opnieuw dezelfde factoren als die eerder behandeld zijn.

- Welke van deze factoren kunnen naar uw mening **verbeterd** worden in Nederland?
- Welke van de genoemde factoren zijn voldoende aanwezig of van voldoende kwaliteit in Nederland (**sterke punten**).

10. De Gezondheidszorg

Hieronder ziet u een lijst met factoren gerelateerd aan **de gezondheidszorg**. Selecteer in de lijst:

- **Minstens 2 factoren** waar Nederland **sterk** op presteert
- **Minstens 2 factoren** waar Nederland **zwak** presteert

	Sterk	Zwak
Kwaliteit van ziekenhuizen	◯	◯
Deskundigheid van artsen en andere zorgverleners	◯	◯
Expertise/reputatie van farmaceutische industrie	◯	◯
Angst en/of wantrouwen in klinische studies	◯	◯
Voorkeur voor alternatieve geneeswijzen	◯	◯
Hoe een klinische studie wordt uitgevoerd (bijv. krijgen een geneesmiddel of een placebo)	◯	◯
Moeilijk te begrijpen hoe een klinische studie wordt uitgevoerd	◯	◯
Angst en/of wantrouwen in artsen/specialisten	◯	◯

11. **baten en lasten van klinische studies**

Hieronder ziet u een lijst met factoren gerelateerd aan **baten en lasten van klinische studies**. Selecteer in de lijst:

- **Minstens 2 factoren** waar Nederland **sterk** op presteert
- **Minstens 2 factoren** waar Nederland **zwak** presteert

	Sterk	Zwak
Ten gunste van de farmaceutische industrie	○	○
Grote investering van tijd in klinische studies	○	○
Beschikbaarheid van personeel (onder andere artsen)	○	○
Interesse in deelname klinische studies	○	○
Documentatie en logistiek	○	○
Belasting voor patiënten (ziekenhuisbezoeken)	○	○
Deelname zorgt voor uitstel huidige behandeling	○	○
Financiële vergoeding	○	○
Wetenschappelijke vergoeding (bijv. inspraak op studieontwerp of publicatie)	○	○
Onbekende bijwerkingen	○	○
De begrijpelijkheid van de patiënteninformatie (informed consent)	○	○

Wel/geen informatie ontvangen over de studie (en de risico's	○	○
Klinische studie geeft een alternatieve behandelingsoptie	○	○
Eerdere toegang tot innovatief geneesmiddel	○	○

12. **Persoonlijke Factoren**

Hieronder ziet u een lijst met **persoonlijke factoren.**
Selecteer in de lijst:

- **Minstens 2 factoren** waar Nederland **sterk** op presteert
- **Minstens 2 factoren** waar Nederland **zwak** presteert

	Sterk	Zwak
Steun/advies van familie en vrienden	○	○
Mobiliteit (denk aan vervoer of moeite met lopen)	○	○
Culturele of religieuze redenen	○	○
Geen/beperkte informatie over beschikbare klinische studies	○	○
Patiënt verschijnt niet (meer) voor klinische studie.	○	○
Motivatie om mee te doen als klinisch onderzoeker	○	○

Overtuiging dat het geneesmiddel in de studie slechter is dan het beschikbare middel	○	○
Geen vrij kunnen krijgen van werk	○	○
Reisafstand naar het ziekenhuis	○	○
Angst om behandeld te worden met een experimenteel geneesmiddel	○	○
Angst voor (onbekende) bijwerkingen	○	○
Angst om niet behandeld te worden (bijvoorbeeld placebo groep)	○	○
Mee willen helpen aan innovatie van gezondheidszorg	○	○

13. **Overige factoren**

Hieronder ziet u een lijst met **overige factoren**.
Selecteer in de lijst:

- **Minstens 2 factoren** waar Nederland **sterk** op presteert
- **Minstens 2 factoren** waar Nederland **zwak** presteert

	Sterk	Zwak
Feedback van de onderzoeker (informatie over de uitkomsten van de studie, zoals werkzaamheid of bijwerkingen)	○	○
Houding van de overheid tegenover de farmaceutische industrie	○	○
Invloed van het nieuws	○	○
Invloed van Social Media (zoals de berichtgeving tijdens de coronacrisis)	○	○
Mediabeelden over de farmaceutische industrie	○	○
Mediabeelden over de wetenschap	○	○
Mediabeelden over de klinische studies	○	○
Mediabeelden over de artsen, verpleging en ziekenhuizen	○	○

Bedankt voor uw deelname

Bedankt voor uw deelname aan deze enquête. Wij stellen het zeer op prijs dat u de tijd heeft genomen om deze enquête in te vullen. Als u op de hoogte gehouden wilt worden van de resultaten van deze studie kunt u uw e-mailadres hieronder invullen en dan zullen wij u informeren wanneer de resultaten bekend zijn.

14. E-mailadres

Enter your answer