Embedding trials in evidence-based clinical practice
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CHAPTER 4

WHY DO SOME CENTRES RECRUIT BETTER THAN OTHERS?

AN ANALYSIS OF RECRUITMENT RATES IN 17 RANDOMISED CLINICAL TRIALS IN OBSTETRICS AND GYNAECOLOGY

Katrien Oude Rengerink, Lotty Hooft, Noortje M. van den Boogaard, Birgit Y. van der Goes, Patrick M.M. Bossuyt, Ben Willem J. Mol
ABSTRACT

Introduction A commonly reported problem with the conduct of RCTs is that recruitment is usually slower than anticipated. We observe large differences between the numbers of patients recruited between different hospitals, even for similar trials. However, it is unclear which factors are associated with these recruitment differences.

Design We aimed to identify centre level factors associated with recruitment in hospitals participating in the Obstetrics and Gynaecology trials consortium in the Netherlands. We sent a web-based questionnaire to local researchers in centres that had recruited in total 14,808 patients for 17 multicentre trials. Our primary outcome was the summed weighted recruitment score of a hospital for all 17 studies, while the average weighted recruitment score per trial was a secondary outcome. The recruitment score was adjusted for the size of the catchment area. Using regression analysis we evaluated associations between recruitment scores and factors motivating centre decisions about participation in trials, the research orientation of the department, and the (perceived) logistic support by research personnel.

Results From 57 of 83 (69%) centres at least one questionnaire was returned. In univariable analysis, participating in trials because ‘expecting others to recruit in return for their studies’ was associated with higher recruitment scores, participating ‘because it is expected from us’ was associated with lower scores. Higher recruitment scores were seen in centres regularly initiating research and in academic medical centres. Weighted recruitment scores were higher in centres where research staff was available for more hours. On average coordinating centres recruited 4.2 times more patients than the median over all centres.

Conclusion Inclusion of patients in clinical trials is dependent on conviction of the value of recruitment for supporting practice and on the number of research staff. Our findings could be used to develop strategies aimed at improving recruitment rates in trials.
INTRODUCTION

Comparative effectiveness research is essential to inform evidence based health care decisions. The randomized controlled trial (RCT) is worldwide considered as the best instrument to evaluate the effectiveness of medical interventions. A commonly reported problem with the conduct of RCTs is that recruitment is usually slower than anticipated. In a cohort of 114 multicentre trials funded by the UK Medical Research Council and the UK Health Technology Assessment Programme between 1994 and 2002, less than one third recruited their targeted sample size within the time originally planned, and around one third needed more time. As a result, trials have less statistical power to detect potentially important differences between groups, which will make them less useful or even not used for guidance of decisions in clinical practice, if the targeted sample size is not achieved. Moreover, if recruitment has to be extended to reach the required sample size, the trial will cost more and take longer to complete.

As relevant adverse clinical outcomes in Obstetrics and Gynaecology are relatively scarce, large sample sizes are typically required to detect or refute relevant differences with limited statistical uncertainty. Therefore, in the Netherlands, up to 70 hospitals are working together in a consortium to recruit patients for a wide range of trials in women’s health. We observed large differences between hospitals in this consortium in the number of patients recruited, even for similar trials. As trial specific factors are the same in all centres, this variability may indicate that centre specific factors in conducting the trial play a role in recruitment for these trials. This phenomenon is not unique for our consortium.

Previous studies have shown that support from research staff positively influences recruitment, but other factors could also be influential. If barriers and facilitators for recruitment in centres could be identified, these could be linked to strategies to improve patient participation in trials within centres and eventually for selection of sites based on their recruitment performance. We collected centre information through a questionnaire and evaluated associations between centre characteristics and recruitment for trials organized by the Dutch Obstetrics and Gynaecology Trials Consortium.
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METHODS

DESIGN
This study was part of the IMPACT study, of which the full protocol has been published elsewhere. We used a web-based questionnaire survey (available from the authors) to identify factors measurable at centre level potentially influencing recruitment in hospitals, both academic and non-academic, participating in the Obstetrics and Gynaecology Trials Consortium in the Netherlands.

PARTICIPANTS
A web-based questionnaire was sent to local research coordinators of all hospitals that had recruited for randomized trials ran by the consortium, both academic and non-academic centres. To compare centre characteristics, we included all national multicentre randomized trials from our network, in which at least 5 centres had recruited patients, and that had finished or nearly finished recruitment when sending the questionnaire in September 2011. The selected trials were Allo, Amphia, Apostel2, Digitat, Hypitat, IUPC, Ppromexil, Probaat, STAN, Womb, ProTWIN, Ines, LifeSTYLE, Portret, Vusis1, Vusis2, and Trudil. All studies were performed in the field of Obstetrics and Gynaecology: 11 in obstetrics, 2 in reproductive medicine and 4 in urogynaecology. All studies had only recruited patients in hospitals in the Netherlands.

Table 1 specifies the number of centres participating and the number of patients recruited for each trial. In total 14,808 patients had been included in these 17 trials, with a range of 60 to 5715. Eighty-three centres intended recruitment for at least one of these trials and were therefore eligible. Per trial between 6 and 52 centres had recruited for the trial. We sent the questionnaire to the local investigator or research coordinator in each of these 83 centres.

If required, we differentiated between obstetrics, reproductive medicine and urogynaecology, which implicated that in most cases questionnaires were sent to three subspecialties in a single centre and in some cases to one person responsible for all subspecialties. If the contact person did not feel he or she was the one best informed to answer questions, we asked to forward the questionnaire to a better informed colleague in the same centre. The questionnaire was not anonymous, which allowed us to send targeted reminders to non-responders. In case of non-response, two reminders were sent after the initial invitation.
QUESTIONNAIRE
The web-based questionnaire (available from the authors) was constructed based on literature and presented during a research meeting at the Academic Medical Centre for input from residents, research nurses and gynaecologists (in training). This questionnaire was then pilot tested by 3 research nurses, 4 gynaecologists and 4 residents, working in different subspecialties of Obstetrics and Gynaecology in a range of hospitals and adjusted based on the pilot experiences. The final questionnaire was then distributed to the above described participants with Survey Monkey [www.surveymonkey.com].

In the questionnaire we asked for three sets of factors potentially influencing recruitment in trials: A) Factors motivating centre decisions about participation in new trials; B) The research orientation of the department; and C) The (perceived) logistic support by research personnel.

Table 1: Subspecialty, sample size and number of centres of the trials included in the analysis

<table>
<thead>
<tr>
<th>Trial</th>
<th>Subspecialty</th>
<th>Sample size (N)</th>
<th>Centres (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allo²</td>
<td>Obstetrics</td>
<td>210</td>
<td>11</td>
</tr>
<tr>
<td>Amphia⁹</td>
<td>Obstetrics</td>
<td>665</td>
<td>44</td>
</tr>
<tr>
<td>Apostel²¹⁰</td>
<td>Obstetrics</td>
<td>406</td>
<td>10</td>
</tr>
<tr>
<td>Digitat¹¹</td>
<td>Obstetrics</td>
<td>650</td>
<td>42</td>
</tr>
<tr>
<td>Hypitat¹²</td>
<td>Obstetrics</td>
<td>756</td>
<td>35</td>
</tr>
<tr>
<td>IUPC¹³</td>
<td>Obstetrics</td>
<td>1456</td>
<td>6</td>
</tr>
<tr>
<td>Ppromexil¹⁴</td>
<td>Obstetrics</td>
<td>739</td>
<td>52</td>
</tr>
<tr>
<td>Probaat¹⁵</td>
<td>Obstetrics</td>
<td>1176</td>
<td>21</td>
</tr>
<tr>
<td>STAN¹⁶</td>
<td>Obstetrics</td>
<td>5715</td>
<td>10</td>
</tr>
<tr>
<td>Womb¹⁷</td>
<td>Obstetrics</td>
<td>500</td>
<td>38</td>
</tr>
<tr>
<td>ProTWIN¹⁸</td>
<td>Obstetrics</td>
<td>695</td>
<td>37</td>
</tr>
<tr>
<td>INeS¹⁹</td>
<td>Subfertility</td>
<td>573</td>
<td>17</td>
</tr>
<tr>
<td>LifeSTYLE²⁰</td>
<td>Subfertility</td>
<td>475</td>
<td>23</td>
</tr>
<tr>
<td>Portret²¹</td>
<td>Urogynaecology</td>
<td>463</td>
<td>23</td>
</tr>
<tr>
<td>Vusis 1²²</td>
<td>Urogynaecology</td>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>Vusis 2²³</td>
<td>Urogynaecology</td>
<td>128</td>
<td>20</td>
</tr>
<tr>
<td>Trudii²⁴</td>
<td>Urogynaecology</td>
<td>141</td>
<td>9</td>
</tr>
</tbody>
</table>
OUTCOME
Our primary outcome was the weighted recruitment (self-designed) score of a centre, summed over all studies. This score gives an overall score for recruitment within a centre, taking into account both centre size and the total number of trials that are recruiting concurrently at a centre. The summed weighted recruitment score was calculated as shown in Box 1. Higher scores indicate better recruitment. To adjust for the size of the catchment area, we standardized these numbers based on the number of clinical deliveries, fertility workups or urogynecological surgeries. The numbers used for standardization for centre size were provided to us by the local research coordinator in each centre. As an additional outcome measure we calculated an average recruitment score for each centre, by dividing the total weighted recruitment score by the number of trials performed in a centre. The analysis of these average recruitment scores was restricted to centres that had recruited for at least 3 trials.
We also looked at the potential for increasing recruitment, by looking at how the recruitment was in the coordinating centre compared to the other centres.

Box 1: How is the weighted summed and average recruitment score calculated?

- Take the number of patients recruited for the trial in the centre
- To adjust for the size of the catchment area, standardize this number by dividing it by the number of deliveries (for trials in obstetrics), number of fertility workups (fertility) or number of urogynaecological operations (urogynaecology).
- The standardized measure is the centre and trial specific recruitment score.
- Calculate the trial-specific mean recruitment score over all centres participating in the trial.
- Calculate the deviation of the recruitment score from the trial-specific mean recruitment score, expressed in standard deviations
- For the summed score: sum the mean recruitment score over all trials in which the centre has participated.
- For the average score: divide the sum over all trials by the number of trials the centre had recruited for.

STATISTICAL ANALYSIS
The analysis was performed at level of the centre. The first part of the questionnaire could be completed by more than one respondent, if in a centre there were different coordinators for the different subspecialties. If this was the case, only one answer per centre was selected. If answers were incongruent between respondents, the category most frequently mentioned was selected. If every one of the respondents in a centre had chosen a different response option, then the intermediate category was selected. Or, if it was a subspecialty specific question the answer of the person filling in the questionnaire for that subspecialty...
was selected if answers were incongruent.
When questionnaires were returned with missing response, we made no attempt at
imputation of missing values. We calculated the number of centres selecting each
response option in the questionnaire, and calculated percentages relative to the number
of centres responding to the corresponding question.

We performed linear regression analysis, using the natural logarithm of the summed
weighted recruitment score, as defined above, as the dependent variable. We have chosen
the summed weighted recruitment score to be able to take into account the number of
trials a site had recruited for, otherwise if a site recruited very well for only one trial will
receive a high score, while a site that had recruited very well for nine trials but recruited
average for one trial would receive a lower score. As independent variables we evaluated
the factors potentially affecting recruitment mentioned earlier.
In a secondary analysis, we looked at the association between the factors and the average
recruitment score recruited, in the subgroup of centres that had actually recruited patients
for at least three trials.

RESULTS

At least one questionnaire was returned by 57 from the 83 (69%) centres for Obstetrics
and Gynaecology. Data on recruitment rates of the 14,808 inclusions were available for
all 17 trials and all centres. For data on recruitment we used all available data; for asso-
ciations between factors in the questionnaire and recruitment data provided by the 57
responding centres were used.

Figure 1a shows the number of patients each centre had recruited for each trial, for 16/17
trials. For clarity and interpretability of the figure we excluded the STAN trial with over
5,000 inclusions. The median number of patients recruited was 62, with the 25th and 75th
percentile being 5 and 139.
Figure 1b shows the recruited number of patients per hospital. As can be appreciated from
this figure, the number varied widely both between hospitals and between studies. Of the
9403 inclusions shown, the 10 best recruiting centres had recruited 4968 (53%) patients,
more than half of the total number of patients recruited. The 10 least recruiting centres
did not recruit any patients, although they had expressed their intention to recruit for
these trials. Below we will discuss the strength of the associations separately for the three sets of factors defined earlier.

**Figure 1:** Overview of a) number of recruited patients for each of 16 trials; b) Number of recruited patients ranked for all centres for 16 trials

a. Number of recruited patient for each of the 16 trials*

* The x-axis shows the different studies, with on the y-axis the number of patients recruited for that study. Same colours represent the same centres. For clarity of the figure the STAN trial including over 5000 patients were excluded.

b. Number of recruited patients per hospital ranked for all centres for 16 trials, excluding STAN

* The y-axis shows the number of recruited patients. The x-axis shows the recruiting centers ranked in order of the number of recruited patients (y-axis).
A. Decisions regarding participation in trials

The decision to recruit patients for a trial was most often made during a staff meeting (47 centres; 79%), and/or by the person most specialized in that subspecialty (n=30; 53%). Twenty-one centres (38%) reported discussions between colleagues about participation; while 29 others (29%) indicated there was seldom such discussion. When asked to indicate how important the reasons to recruit for a study were, finding a solution for the clinical problem was selected as (very) important by all 56 responding centres. Other (very) important reasons for recruitment were authorship (n=28, 50%) and because they feel it is expected (‘It is expected from us’) (n=19; 34%). Three centres mentioned that participation depended on financial compensation, 9 centres reported it did not. In 41 centres the necessity of a financial compensation was dependent on other factors, mostly mentioned the actual costs. Six (11%) of the responding centres indicated they participate only if the research fits within the research priorities set by the hospital.

The number of studies running concurrently in a department was reported as limited in 24 centres; mostly to 2-3 trials, depending on work load. In the other 31 hospitals there was no such maximum. In 36 centres (63%) the number of trials a patient is asked for was limited, mostly to 1 or 2 studies.

Table 2 shows the results of the univariable analysis. Recruiting because ‘expecting others to recruit in return for their studies’ was significantly associated with higher recruitment scores. Recruiting because it was ‘expected to do so’ was significantly associated with lower scores. Authorship, financial compensation and being acquainted with the investigator were not influential.

When looking at the average recruitment score, restricting the analysis to the centers that had recruited for at least three trials, both ‘expecting others to recruit in return for their studies’ and ‘expected to do so’ were associated with the average recruitment scores.

B. Research orientation of the department

Twelve centers (21%) indicated never to initiate research themselves, but to participate in studies initiated by other hospitals. Regular discussions about research, as in journal clubs or research meetings, were organized weekly in 19 centers (34%), less than weekly in 33 (59%) and never in 4 (7%) of the centers. In 30 centers (53%) there was no time reserved for counseling during regular outpatient visits, but a special outpatient clinic run by the research staff was organized. In 1 (2%) there was always time reserved for counseling, in
6 (11%) at some occasions, and in 15 (26%) never. In 50 centers (89%) patient recruitment was discussed at the handover session: in 9 (25%) always and in 33 (63%) irregularly. Significantly higher recruitment scores were seen in centers regularly initiating research (Table 2). Higher scores were also seen in tertiary care centers. Having a research meeting was not found to be influential.

Table 2: Univariable association between factor and weighted recruitment score

<table>
<thead>
<tr>
<th></th>
<th>Natural log of sum of z-scores per trial (N=57)</th>
<th>Average z-score if participating in ≥ 3 trials (N=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (95% CI) Ln transformed</td>
<td>P-value</td>
</tr>
<tr>
<td><strong>A Decision regarding recruitment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissension about participation</td>
<td>0.20 (-0.03-0.44)</td>
<td>0.09</td>
</tr>
<tr>
<td>Finding a solution for a clinical problem</td>
<td>NA*</td>
<td>0.04</td>
</tr>
<tr>
<td>We get an inclusion fee</td>
<td>0.15 (-0.08-0.38)</td>
<td>0.22</td>
</tr>
<tr>
<td>Authorship of scientific article</td>
<td>0.18</td>
<td>0.18</td>
</tr>
<tr>
<td>Recruitment is expected from us</td>
<td>-0.20 (-0.44-0.03)</td>
<td>0.09</td>
</tr>
<tr>
<td>We know the (principal)investigator of the study</td>
<td>-0.06 (-0.31-0.19)</td>
<td>0.62</td>
</tr>
<tr>
<td>We expect others to recruit in return</td>
<td>0.34 (0.11-0.58)</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>A maximum number studies in department concurrently</strong></td>
<td>0.09 (-0.15-0.32)</td>
<td>0.463</td>
</tr>
<tr>
<td><strong>A maximum number patient is asked for concurrently</strong></td>
<td>-0.11 (-0.36-0.14)</td>
<td>0.375</td>
</tr>
<tr>
<td><strong>B Research orientation of the department</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital type tertiary care versus other</td>
<td>0.53 (0.23-0.84)</td>
<td>0.001</td>
</tr>
<tr>
<td>Regular research initiation of department yes/no</td>
<td>0.30 (0.09-0.51)</td>
<td>0.006</td>
</tr>
<tr>
<td>Regular research meeting in department yes/no</td>
<td>0.12 (-0.14-0.37)</td>
<td>0.37</td>
</tr>
<tr>
<td>Extra time for counselling during outpatient clinic yes/no</td>
<td>-0.01 (-0.35-0.33)</td>
<td>0.95</td>
</tr>
<tr>
<td><strong>C (Perceived) logistical support research staff</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of hours research staff appointed (hour)</td>
<td>0.01 (0.002-0.02)</td>
<td>0.03</td>
</tr>
<tr>
<td>Research staff counsels patients in sub specialism Obstetrics yes/no</td>
<td>0.07</td>
<td>0.24</td>
</tr>
<tr>
<td>Fertility yes/no</td>
<td>-0.131</td>
<td>0.12</td>
</tr>
<tr>
<td>Urogynaecology (yes/no)</td>
<td>-0.013</td>
<td>0.88</td>
</tr>
</tbody>
</table>

*The clinical problem was mentioned by all, therefore a measure of association could not be calculated.
Centers in which recruitment was always discussed during the handover session had the highest weighted recruitment score, followed by centers that discussed patient recruitment on an irregular basis during the handover session, but the difference was not significant.

When looking at the average recruitment scores, where the analysis was restricted to centers that had recruited for at least three trials, regularly initiating research was associated with higher average recruitment scores. Higher scores were also seen in academic medical centers.

C. (Perceived) logistical support by research personnel

In 47 centers (85%) research support staff was appointed for 1 up to 90 hours a week, mostly research nurses (N=24) and research midwives (N=15). Centers that did not have research support staff appointed all mentioned that it would be too costly, in view of the number of patients that was to be randomized.

Research nurses were reported to be working in 44 centers for studies in obstetrics, in 32 centers for subfertility trials, in 27 centers for trials in urogynaecology, and in three for oncology trials. Research staff was in 78% [28/36] available on fixed days only. Research staff was always available for counseling outside office hours in 2 centers (6%).

Weighted recruitment scores were significantly higher in centers when more hours of research staff were available (p=0.03). When adjusted for type of hospital (academic versus non-academic), the difference disappeared. Whether or not research staff also counseled patients did not influence the weighted recruitment score in a statistically significant way. When looking at the average recruitment score, restricting the analysis to the centers that had recruited for at least three trials, the number of hours a research nurse was appointed was also significantly associated with higher recruitment scores. When adjusted for the number of studies performed in a center this effect was no longer significant (p-value of 0.08).

In Appendix 1 the number of patients recruited in the coordinating center is compared to the median number of patients recruited. On average the coordinating center recruits 4.2 times more patients than the median number of patients (calculated over all participating centers), it recruits on average 0.8 time more than the best recruiting center, and 42 times more than the least recruiting center. These numbers were not corrected for any other potentially influential factors, such as the length of the recruitment period (initiating centers typically start earlier).
DISCUSSION

In this study, we found that research oriented departments in which physicians were convinced of the value of recruitment for supporting practice recruit more patients in clinical trials, as do centres with more research staff appointed. Recruitment in trials because their centre primarily feels they were expected to do so was associated with lower recruitment scores. On average the coordinating center recruits 4.2 times more patients than the median number of patients.

Strong points of our study are that we included a variety of trials and a large series of centres, in which in total 14,808 patients were recruited. The high number of centres made it possible to compare recruitment rates between centres for specific trials. We would also like to mention a few potential limitations. We analysed the questionnaires at the centre level, not taking into account the perception of all individuals in that centre. We selected this strategy, as we hoped to get a response from the best informed gynaecologists in a centre, without bothering all of the colleagues.

For most studies the actual number of patients eligible for a trial was unknown. To adjust for the size of the catchment area, we standardized these numbers. These adjustments may not reflect smaller differences in eligibility, due to variability in the prevalence of inclusion and exclusion criteria. We did not take into account the time period a centre was recruiting for a trial. We assumed that all trials could have started the process of getting ethical approval at the same time. We are aware that the coordinating centre often starts the study in its own centre early, to test whether all procedures are clear and running smoothly.

Haidich and colleagues evaluated recruitment in early and late-starter sites in a cohort of 14 randomized trials conducted by the Adult AIDS Clinical Trials Group and found that sites that started recruitment within 5 months from the time the first patient entered the trial were eventually responsible for over 90% of the total enrolment in 11 of the 14 trials.\textsuperscript{25,26} They concluded that the late-starter sites were unlikely to make important contributions to eventual trial enrolment in large clinical trials conducted by groups with a fixed number of sites. Given the common stop date in all trials, this indicates that adjustment for the length of the recruitment period could even unintentionally give a too optimistic picture of the worst recruiters.

We found that centres with research staff appointed recruited better. Studies in different
clinical areas have also shown that support from research staff positively influences recruitment. However, Campbell et al. observed lower recruitment rates in trials with paid local recruitment staff.

Tarnow-Mordi et al. pointed out that government funded clinical research networks, including local site research nurses or coordinators to support clinical trials, could enhance recruitment in sites with an adequate volume of patients. Such networks have already been established for cancer trials in Australia and for pediatric trials in the United Kingdom. Although it seems very promising, it’s cost-effectiveness has not been proven yet. We found that research oriented departments in which physicians were convinced of the value of recruitment for supporting practice recruit more patients. De Wit and colleagues found that in primary care research successful patient recruitment is more affected by the motivation level of the research group than by financial incentives, the research topic, or research experience.

Van Kuyvenhoven and colleagues observed that 50% [4/8] of the general practitioners who participated because they knew the researchers did not recruit any patients, compared with 16% [9/58] that participated for other reasons. Wilson and colleagues found that general practitioners that recruited for trials were more interested in knowing more about research than those who did not recruit. Ziebland et al. concluded that it does matter if clinicians do not understand the rationale for the trial or if they view the results as ultimately irrelevant to their practice. Financial incentives as a reason for recruitment were not significantly associated with recruitment rates. A review by Bryant and Powell concluded there is very limited, inconclusive evidence about financial incentives to improve recruitment.

These results also invite a discussion on the optimal number of centers that should be asked to recruit for a trial. Recruiting in more sites might be faster, but might be a less efficient use of resources. In our results, the 10 best recruiting centres recruited more than half of the total, while the 10 least recruiting centres hardly contributed. Therefore, it might be more efficient to select a lower number of centres for recruitment. However, recruiting for a trial can also give a slight increase in implementation of the results of the trial.
Based on our results, we see a large potential for improving recruitment rates at clinical sites. Logistical infrastructure is a prerequisite for executing trials, but not a sufficient condition for trial recruitment. Sites should be convinced of the value of research for practice and encouraged to consider appointing a research nurse in order to increase recruitment rates. Clinical trial recruitment should be embedded in routine patient care, as trials are the foundation for building an efficient, affordable and high quality health care system.

ACKNOWLEDGEMENTS
We would like to thank all respondents to the questionnaire, all study coordinators for using their recruitment rates and the residents, gynaecologists and research staff who pilot tested the questionnaire.
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REFERENCES


### Appendix 1: Number of recruited patients in the coordinating centre compared to the median number of patients recruited.

<table>
<thead>
<tr>
<th>Study</th>
<th>Nr of patients recruited in coordinating centre</th>
<th>Median recruited number over all centres (min-max)</th>
<th>Number of times coordinating centre recruits better than median over all centres (better than best centre-better than worst centre)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allo</td>
<td>53</td>
<td>19 (1-53)</td>
<td>2.8 (1.0-53.0)</td>
</tr>
<tr>
<td>Amphia</td>
<td>36</td>
<td>10 (1-51)</td>
<td>3.6 (0.7-36)</td>
</tr>
<tr>
<td>Apostel2</td>
<td>30</td>
<td>30 (5-87)</td>
<td>1.0 (0.34-6.0)</td>
</tr>
<tr>
<td>Digitat</td>
<td>16</td>
<td>9 (1-74)</td>
<td>1.8 (0.22-16.0)</td>
</tr>
<tr>
<td>Hypitat</td>
<td>52</td>
<td>17 (2-69)</td>
<td>3.1 (0.75-26)</td>
</tr>
<tr>
<td>IUPC</td>
<td>412</td>
<td>173 (73-552)</td>
<td>2.4 (0.75-5.6)</td>
</tr>
<tr>
<td>Ppromexil</td>
<td>31</td>
<td>10 (0-35)</td>
<td>3.1 (0.89-31)</td>
</tr>
<tr>
<td>Probaat</td>
<td>213</td>
<td>43 (10-213)</td>
<td>5.0 (1.0-21.0)</td>
</tr>
<tr>
<td>STAN</td>
<td>1350</td>
<td>435 (13-1471)</td>
<td>3.1 (0.92-104)</td>
</tr>
<tr>
<td>WOMB</td>
<td>68</td>
<td>6 (0-76)</td>
<td>11.3 (0.89-68)</td>
</tr>
<tr>
<td>ProTwin</td>
<td>87</td>
<td>16 (1-87)</td>
<td>5.4 (1-87)</td>
</tr>
<tr>
<td>INeS</td>
<td>88</td>
<td>29 (2-88)</td>
<td>3.0 (1-44)</td>
</tr>
<tr>
<td>LifeStyle</td>
<td>39</td>
<td>18 (2-62)</td>
<td>2.2 (0.7-19.5)</td>
</tr>
<tr>
<td>Portret</td>
<td>136</td>
<td>13 (2-136)</td>
<td>10.5 (1-68)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>4.2 (0.80-42)</td>
<td></td>
</tr>
</tbody>
</table>