

Technical University of Denmark



Are Clinical Trial Experiences Utilized?: A Differentiated Model of Medical Sites' Information Transfer Ability

Smed, Marie; Schultz, Carsten; Getz, Kenneth A.; Salomo, Søren

Published in:
Proceedings of PICMET '15 Conference

Publication date:
2015

Document Version
Peer reviewed version

[Link back to DTU Orbit](#)

Citation (APA):
Smed, M., Schultz, C., Getz, K. A., & Salomo, S. (2015). Are Clinical Trial Experiences Utilized?: A Differentiated Model of Medical Sites' Information Transfer Ability. In Proceedings of PICMET '15 Conference

DTU Library

Technical Information Center of Denmark

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Are Clinical Trial Experiences Utilized?
– A Differentiated Model of Medical Sites' Information
Transfer Ability

Marie Smed (Corresponding author)*, Carsten Schultz**, Kenneth A. Getz***
and Søren Salomo*

* DTU Management Engineering, Technical University of Denmark. Produktionstorvet,
Bygning 426, DK-2800 Kgs. Lyngby. msm@business.dtu.dk

**Institute for Innovation Research, Christian-Albrechts-Universität zu Kiel (CAU),
Germany

***Center for the Study of Drug Development, TUFT University, Boston, MA US

Abstract

The collaboration with medical professionals in pharmaceutical clinical trials facilitates opportunities to gain valuable market information concerning product functionality issues, as well as issues related to market implementation and adoption.

However, previous research on trial management lacks a differentiated perspective on the potential for information transfer from site to producer. An exploration of the variation in stickiness of information, and therefore the complexity of information transfer in clinical trials, is the main aim of this study. To further enrich the model of the dispersed sites' information transfer ability, their methods of communicating, are included.

The model is studied on a unique dataset of 395 medical site-representatives by applying Rasch scale modeling to differentiate the stickiness of the heterogenic information issues.

The results reveal that economic measures, complementary service issues and usability patterns are all significantly more difficult to transfer in clinical trials than issues related to product functionality.

Keywords: *Information potential, drug application, information transfer, clinical trials, medical sites, pharmaceutical industry*

Introduction

Pharmaceutical product development is highly dependent on effective clinical trials. New product candidates undergo extensive clinical trials conducted by medical sites, such as private clinics, health centers, hospitals and academic medical centers. The main goal of clinical trials is to obtain information concerning a new treatment's safety, medical outcome and efficacy in order to obtain market approval by the regulatory authorities.

Integrating medical professionals into drug testing, however, also represents a unique opportunity to gain insights concerning product optimization, portfolio possibilities and market implementation and adoption. This is for example seen in relation to the increasing development of specialty drugs, where specific knowledge from user are highly valuable [5,66,73]. Application of a new drug candidate in the medical practice can provide information concerning usability patterns [2,10,51], such as patient and staff convenience, for example a tablet vs. an injection, as well as logistical measures, such as when to take the drug and where. This also applies to complimentary service issues [3,44,55,56,75], such as patient education and compliance, and staff skills and training necessary to support a treatment. Further, medical sites can gain information concerning economic measures, such as users' reaction to the branded name [27,54,78], and the cost effectiveness of the new drug [28,53]. Such usability, service and economic measures do not directly influence the approval of a product, which is based on safety and efficacy measures, but can contribute to the drug application post launch.

The new product development (NPD) literature has pointed to the importance, but also the challenge, of information transfer from external expert partners in optimizing the development process and products [1,39,47,81]. The information present in the external environment varies in complexity, as some information is highly context-dependent [16,57]. Further, not all information is explicit and therefore easy to articulate, but is more tacit in nature [48,61], making it more sticky to transfer [15,19,40,41]. As such, there are various issues beyond structural patterns that influence optimal information sharing. The ability and opportunity to transfer gained information is a key factor; both issues that essentially also influence the motivational factors for sharing gained information [69].

Clinical trials represent a history of collaboration between the industry and practical health care, which exemplifies the information potential from external relations as described in NPD literature. However, there is a gap in the health care management literature in understanding whether the information potential of clinical trials is utilized. Literature on site-sponsor

relations focuses on; Sponsor biased publication patterns [49,80] or the influence of sponsor' previous experiences in clinical trials [20,71] There is limited research focusing on the management of information transfer in drug development [30,46,52,60]. Further, existing research does not differentiate between the information possibilities, but observes information generated by health care organizations as a homogenous mass. There is a need for a differentiated model of information transfer in drug development in order to understand whether some information is more easily transferred between health care professionals and the pharmaceutical industry, and if some information is thereby lost in the extensive trial process.

When studying the transfer of information in clinical trials it should also be considered that collaborating partners are globally dispersed, as clinical trials are conducted in natural settings at local health organizations. This determines that the methods of communication between partners consist of either standard written trial reports, face-to-face meetings, or ongoing virtual methods, which will influence the character of the information transfer process. The research model therefore also includes how predefined communication methods influence the transfer of the different information topics.

The objective of the paper is therefore, to explore if all information is utilized from collaboration partners in clinical trials. This is done by differentiating between types of information, and also types of information transfer methods. . In order to structure this study the following two research questions are therefore guiding the research: 1) *Can a difference in medical users' ability to transfer information to pharmaceutical firms be detected when differentiating between clinical trial topics – functionality issues, usability issues, complementary service issues and economic issues?* And 2) *Which patterns of communication support the transfer of information from medical sites to pharmaceutical producers?*

The method applied to explore the study questions is survey data collected from 395 respondents at medical sites participating in clinical trials. To differentiate the information transfer ability of these medical sites to producers in clinical trials, Rasch scale modeling [63] based on item response theory (IRT) [45,70] is applied. The Rasch model has the advantage of analyzing related items on a common scale and then determining the location (difficulty) of the items in the continuum of low to high degree of information transfer ability.

The results show, that medical sites ability to transfer information can be differentiated according to topic are, and that some issues are harder to transfer than others. Issues related to economic-, service. And usability measures are more difficult to transfer than issues

relating to the functionality of the product. Further, the transfer of information are in general better supported by face-to-face methods as well as virtual methods, illustrating that methods supporting more tacit information topics are important in order to utilize external knowledge sources in product development.

Theoretical framework

In product development processes, such as clinical trials, professional users are integrated in a close collaboration with producers, creating a unique opportunity to access product and market information [1,47,81]. The medical professionals have unique expertise in the therapeutic area [29], which represents an opportunity for companies to tap into cutting edge knowledge developed in natural settings of the future market [24,68]. Through the application of the drug candidate in medical practice, clinical trials can contribute with information relevant for approval, and therefore concerning product functionality. However, data concerning issues such as usability patterns, economics measures and complementary services can also be provided by clinical trials.

Usability issues relate to both patient and staff convenience in using the product, and can be exposed when the new product is applied in natural settings. Usability issues are therefore often referred to as context-of-use measures [2,11,51], and include patients' convenience of tablet vs. injection, treatment on site or at home etc. Complementary service issues [3,55,56,75] relate to training and maintenance measures. In drug development and later drug application such service issues could relate to patient education and compliance of drug use, as well as the staff skills and training necessary to support a treatment. Information concerning economic measures can contribute with a coherent value-adding product perspective [3,44]. Classical market analysis issues include the end-user's reaction to the brand name [27,54,78] and the cost-effectiveness of the new product relevant for adoption processes [28,53].

However, the information generated by professional medical partners in clinical trials can be challenging to transfer. It is recognized that external information from development collaboration is beneficial [1,47,81], but also that the transfer of such information is not always easy [7,19,26,77]. The extensive information generated by expert partners [26,33] is often tacit [61] and therefore hard to externalize [48,74]. The tacit character of information can contribute to the stickiness of some information [15,19,41,40]; whereas more explicit knowledge is easier to de-code and thereby articulate [19,74]. Further, information which is more complex in nature will require a higher degree of overlapping existing knowledge among collaborating partners [21,37,57,59,76]. Context-dependence, and therefore prior experience in partnerships and product area, can affect the difficulty of transferring information [16,17,58].

The information potential from external collaboration should therefore not be observed as a homogenic mass transferring among collaborative partners. Rather, it should be seen as a differentiated model, where some information is more easily transferred than other. Previous literature points to product-embedded information as having a larger degree of articulability and therefore ease of transfer, as this information is more specific in nature [25,82]. However, the literature is insufficient in supplying a concrete model of which information is then more difficult to transfer. There is a need for further understanding of the information transfer process between medical professionals and pharmaceutical producers in clinical trials, and the extent to which some issues are more easily transferred than others. This will extend our knowledge concerning the information potential in clinical trials and the extent to which this potential is utilized. We therefore propose the following research question:

Research question I: *Can a difference in medical users' ability to transfer information to pharmaceutical firms be detected when differentiating between clinical trial topics – functionality issues, usability issues, complementary service issues and economic issues?*

Communication methods

The medical professionals participating in clinical trials are by definition located in dispersed global settings, as drugs should be tested on location in the health care practice. To add to our differentiated model of information transfer in clinical trials the analysis is therefore extended with a study of the partners' communication methods, as these methods are closely connected to the character of the information being transferred.

The standard communication method in clinical trials is written protocols, where medical sites supply predefined information issues to the pharmaceutical companies. In order to communicate information in written documents the information needs to be explicit and de-codified [48,74], which may thereby influence the transfer of tacit knowledge. Geographical proximity supporting face-to-face communication is often mentioned as a stimulating factor for information transfer [35,42,62], as both formal and informal interactions can occur [35,62]. It is argued that co-location creates a shared belief system and common understanding, which promote both explicit and tacit information transfer [9,33,72]. However, meeting face-to-face in clinical trials will only occur at on-site meetings or at other planned settings, generating a time consuming and logistically challenging task, which will postpone discussion points and feedback. Previous literature points to the opportunities of collaborating cross-distance through virtual methods created by IT tools [6,8,65,67], as

partners can communicate directly and give immediate feedback, similar to co-location processes [4,17,18].

Dispersed collaboration structures in clinical trials are therefore included in the research model, by studying if medical professionals' ability to transfer information is influenced by communication patterns created by 1) Face-to-face methods, 2) Virtual methods, or 3) Written communication methods.

Research question II: *Which patterns of communication support the transfer of information from medical sites to pharmaceutical producers?*

Research methodology

Data collection

To answer the research questions, a study among medical professionals participating in clinical trials in pharmaceutical drug development processes was carried out. Medical site representatives are difficult to locate and identify, as there are no public listings of clinical trial sites and the industry is reluctant to disclose their important site contacts. A unique contact list of 2300 clinical sites was therefore developed through previous research projects within the industry. An online questionnaire was sent to the 2300 clinical sites. 395 site representatives responded to the questionnaire, representing a substantial sample size and a satisfactory response rate of approximately 17%.

Designing the questionnaire

To design the eleven domains the clinical trial study guidelines were studied. The study guidelines focus primarily on product functionality, as the prime goal is regulatory approval information [34,43]. To quantify the industry-designed study guidelines telephone interviews with industry representatives were conducted. The interviews confirmed that producers' prime focus in drug testing is the safety and efficiency of the new drug. However, some of the industry respondents also emphasized the need for additional information concerning economic measures related to marketing issues.

To include a post-market launch perspective the clinical practice guidelines were studied [34,43]. Clinical practice guidelines are applied to support the clinical personnel at hospitals and health centers in the application of a new treatment after market launch. These guidelines include issues of complementary service, which are relevant for the application of the drug in

practice, as well as usability issues related to end-user (patient) comfort and possibly economic measures, which are relevant for the medical center in general.

Based on the explorative studies about the information relevant from clinical trials – both from an industry perspective and a market perspective post-product launch eleven domains were outlined. Based on the theoretical model described in this paper the eleven domains were categorized into areas addressing the four overall topics; 1) Issues related directly to the product's functionality, 2) Issues concerning related services, 3) Usability related issues, and 4) Economic issues. All of these areas are found to be key elements in the development for new products and especially in the adaptation of new product areas on the marketplace.

The topic items are outlined in table 1. All of the eleven issues were to be answered on a four-point scale; 1= Is not passed on, 2=To a very little degree, 3=To some degree, 4=To a high degree. They were categorized randomly in the questionnaire.

Method – research question I

To answer research question one, and therefore how the transfer of information from medical users may be differentiated by topic area, Rasch scale modeling [63], which is part of IRT [45,70], is applied. Instead of focusing on dependent and independent variables, IRT focuses on measuring how related items are positioned on the same scale [70]. By applying probability statistic modeling, Rasch scale analysis evaluates the difference in difficulty between items [63,70]. This makes it possible to observe respondents' relative responses directly against each other. The scale thereby assigns a relative measure on a common continuum defining how difficult certain information is to transfer relative to other items.

The scale output (variable map, figure 1) outlines the sample distribution. By outlining the sample distribution on one side (left) and the item difficulties on the other side of the scale (right) the floor and ceiling effect can be observed [13]. If the item-sample scale does not correspond and a high portion of the sample falls above or below the item locations (floor/ceiling effect), an under-identifying power can be observed implying that the chosen items do not alone describe the issue area in question [13,63]. Item fit statistics supply information concerning the fit between the Rasch scale model and the observed data [13,63]. Such infit/outfit measures can be identified in the analysis and will be elaborated on in the result section, together with the specific difficulty measures of the individual items.

Method – research question II

To explore research question two a cluster analysis [22,79] is applied to group the respondents in clusters of similar communication patterns. When determining the number of categories, balancing the heterogeneity of the clusters is a key measure. As the number of clusters decreases, the heterogeneity increases, and it is therefore the goal to identify the amount of relevant categories and simultaneously maintain a low level of heterogeneity [38]. A method commonly applied for this purpose is to evaluate the distance between unclustered observations [23,36]. In this study the Euclidean distance method is applied, which is the most common method for hierarchical cluster analysis using Ward's method [22,36]. The results of the cluster analysis are entered into a one way ANOVA together with the Rasch scores that identify a site's general ability to transfer information.

Measures

All of the three measures of communication were to be answered on the same three point Likert scale (1=never, 2=rarely 3= often) indicating how often respondents communicate with the producer via these methods;

Communication method – F2F. Face-to-face (F2F) communication includes on-site meetings where pharmaceutical representatives visit the site, as well as professional conferences or related forums.

Communication method – virtual. Virtual communication methods are defined as telephone conferences and web-based meetings, where partners have the opportunity to communicate directly with each other.

Communication method – Written. Written communication is defined as email exchanges and other written documents, such as reports and clinical trial protocols.

Information transfer ability. Besides presenting a differentiated scale, the Rasch method also produces a single measure representing the whole scale. The Rasch measure can be defined as the likelihood of the respondents to score high on the information ability scale, and therefore the ability of the medical user to transfer information [13].

Results

Fit statistics

Fit statistics are computed in the Rasch analysis and supply information concerning the fit of the data in relation to the Rasch output map. The mean square values should have an expected value around 1, but values above and below may occur. If the MNSQ *infit* values

are significantly lower than 1 some dependencies are present in the data, and if higher than 1 some noise should be considered in the model [50]. Further, an MNSQ *outfit* level significantly lower than 1 also implies dependency in the data, while an MNSQ *outfit* level significantly above 1 indicates that there are some unexpected outliers in the chosen variables.

Table 1. Fit statistics, Rasch analysis (Winstep output)

Description	Issue Type	Difficulty	MNSQ	
			Infit	Outfit
Cost effectiveness of new drug (<i>CostEff</i>)	<i>Economy</i>	1.61	1.15	1.16
Patients' and professionals' reaction to branded name (<i>BrandName</i>)	<i>Economy</i>	1.19	1.19	1.23
Patients' access to the drug (<i>PatientAcc</i>)	<i>Service</i>	.76	.90	.88
Workforce required for drug administration (<i>Workforce</i>)	<i>Service</i>	.37	.78	.76
Delivery form (tablet, capsule, injection etc.) (<i>Delivery</i>)	<i>Usability</i>	.12	1.02	1.06
Administration of the new drug (e.g. taken with meal, taken in the evening, on empty stomach etc.) (<i>AdmDrug</i>)	<i>Usability</i>	-.18	.94	.96
Clinical skills necessary for successful drug administration (<i>ClinSkill</i>)	<i>Usability</i>	-.29	.76	.71
Dosage of new drug (<i>Dosage</i>)	<i>Product</i>	-.38	1.00	.98
Risk/benefit from intervention (<i>RiskBen</i>)	<i>Product</i>	-.58	.92	.85
Concomitant drug interactions (<i>DrugInter</i>)	<i>Product</i>	-.71	.92	.89
Drug side effects (<i>SideEff</i>)	<i>Product</i>	-1.90	1.33	1.31

Difficulty: degree of users' ability to share with producer reflected in the specific item.

A rule of thumb is a level within 1+/- .2 (.80/1.2) [13]. Item number 1 (*side effects*) shows some sign of noise and outliers (MNSQ Infit level 1.33/MNSQ outfit level 1.31), and item 10 (*Workforce*) shows a tendency to dependency in the data (MNSQ Infit level .78/MNSQ outfit level .76). Therefore the MNSQ fit statistics show that item 1 has a limited fit to the model. However, it is retained in the model, as drug side effects are a key issue for the approval process and therefore a standard element in the protocol design of a clinical trial. To exclude this measure would be to neglect a central element of the testing process in drug development. Item 10 (*Workforce*) is slightly below .80 and may therefore be redundant for the model. However, item 10 is also retained, as the borderline result in itself is interesting. This is because the issue is an integrated part of the clinical practice guidelines applied in medical sites after launch of a product, but is not a key focus for the pre-launch process on the producer side. The issue may therefore appear redundant due to the producers' lack of focus

on the issue, but as this study aims to recover knowledge potential, which may be neglected, item 10 is retained in the model.

Besides item 1 (*Side effects*) and item 10 (*Workforce*), which reflect some fit challenges to the model, the other nine items are well represented within the fit limits in the Rasch analysis. This indicates that users transfer relevant information concerning product functionality, related services, usability issues and economic measures by participating in test phases in drug development.

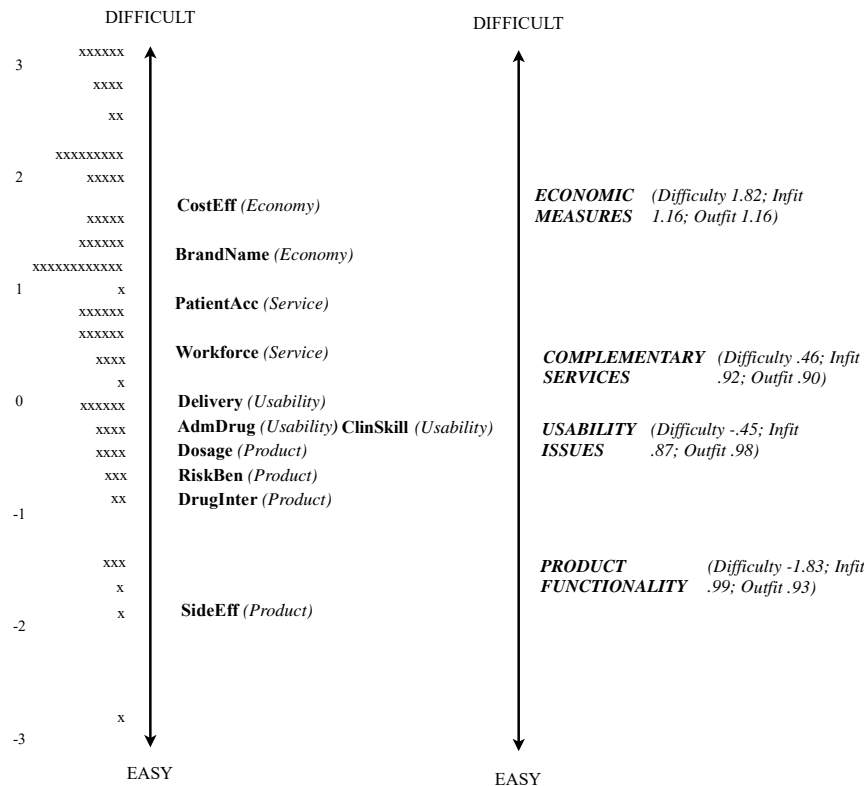


Fig. 1. Item–person (variable) map, Winstep output

Difficulty of transferring information between user and producer by topic item

The result of the Rasch analysis reveals which item issues are more difficult to transfer from user to producer relative to each other. The variable map in figure 1 illustrates how the 11 item issues are located on the continuum on the right side, and on the left-hand side of the scale the person measures can be identified. The variable map thereby illustrates how the respondents (person measures) represent the items on the scale. The specific difficulty levels

of the 11 items are presented in table 1, and the difficulty of the four categories, functionality; usability; service and economy, can be observed in figure 1.

Product functionality issues. The scale reveals that issues related to product functionality (Category difficulty -1.83) are easiest to transfer, as item 1 (*Side effects*), item 3 (*Drug Interaction*), item 8 (*Risk/Benefit*) and item 5 (*Dosage*) can be observed at the lowest end of figure 1. These four items all relate directly to product functionality, and therefore the safety and efficacy of the new drug. Issues relating directly to the approval process of the new drug are therefore easiest to transfer.

Economic measures. At the other end of the continuum, and therefore representing the most difficult issues to transfer to the producer, are the issue items related to economic measures; items 6 (*Cost effectiveness*) and 11 (*Branded Name*) (Category difficulty 1.82). These issues at the highest end of the difficulty continuum are not crucial to regulatory approval, and therefore tests for them are not required in the clinical phases. Therefore these issues are not a standard measure in the study protocols, but are mentioned in the clinical practice guides and by industry interviews as important issues for market application.

Complementary service issues. In the middle of the continuum, but still at the difficult end of the scale, issues related to complementary services (Category difficulty .46) can be observed. Item 7 (*Patient Access*) and item 10 (*Workforce*) are, like the economic measures, not requirements according to the regulatory protocol; however they are highly integrated in the clinical practice guidelines that are applied by health care actors.

Usability measures. In the middle of the continuum, and therefore close to a moderate difficulty of zero, item 4 (*Delivery*), item 2 (*Administration of Drug*) and item 9 (*Clinical Skills*) can be observed. The administration of the drug (taken with meal, empty stomach etc.) and delivery form (tablet, capsule, injection etc.) apply to end-users' convenience in using the treatment, whereas the clinical skills necessary applies to medical site personnel's convenience and possibilities in using the new product. The necessary clinical skills are also relevant as a service measure, as this could create demand for training activities. However, all three issues are closely related to product application, and therefore to the expert knowledge of the doctors participating in the trial.

Floor/ceiling effects

The results of the Rasch analysis illustrate that all items can be measured on the same scale; therefore supporting the reliability of the model. A tradeoff generated by the similarity of the items on the same scale may be an under-identifying power of the model, implying that the scale may not cover some issues [13,70]. The sample distribution and item issues should correspond in the Rasch scale model (figure 1). If an over- or under-representation of the sample can be identified, a floor or ceiling effect is present [13]. Figure 1 shows that at the bottom of the scale the sample distribution and the item issues correspond to a high degree, as only 3% of the person measures can be identified below the lowest difficult to transfer information (Item 1, *Side effects*). However, at the other end of the continuum, an over-representation of the sample distribution can be detected, and a ceiling effect identified, as 41% of the person measures are above the most difficult to transfer on the scale (Item 10, *Workforce*). This rather high ceiling effect draws attention to issues not represented at the difficult end of the model, and therefore potential issues beyond product functionality that are not covered in this study. This issue will be further discussed in limitations and future research.

Information transfer and patterns of communication

The agglomeration procedure of the cluster analysis illustrates an incremental change (elbow) at the stage of four clusters [36]. A model of four clusters is therefore chosen, as this will represent a within-group homogeneity, as well as a balanced between-group heterogeneity [22,38]. The four-cluster measure was applied in a one-way ANOVA in order to determine a descriptive communication profile of the four clusters. A post-hoc comparison applying the Tukey HSD indicated a significant difference between the four groups ($p < 0.5$). The profiles of the four groupings of medical respondents' communication patterns are defined and described here:

All-round intense communicators. The first cluster of medical sites applies all three methods of communication to a relatively high degree – face-to-face (2.70), virtual (2.54) and written (3.00). This cluster also represents the second highest level of information transfer ability (1.32).

All-round low communicators. The second cluster of medical sites represents a generally low information transfer ability (1.05), and also shows a generally low use of all communication methods – face-to-face (2.07), virtual (2.16) and written (2.32).

Virtual communicators. The third cluster represents a group of medical sites that to a high degree apply virtual communication methods (face-to-face [2.09], virtual [2.75] and written [3.00]), and therefore technological tools that enable collaborating partners to communicate across distance at any point in time. This group represents the medical sites that express the highest ability to transfer information to drug producers (1.57); notably to a higher degree than cluster one where all three methods of communication were relatively high.

Traditionalist communicators. The fourth group of medical sites primarily applies the required methods of communication (face-to-face [1.92], virtual [1.92] and written [3.00]), which is the written documentation often observed in the mandatory protocols and trial reports. This group is also the group showing the lowest ability to transfer information to the industry partner (.68).

Discussion

The results showing a positive effect of both face-to-face and virtual communication methods emphasize the settings where informal information transfer can occur. Through direct interactions partners can create joint understanding, stimulating the context-dependent information [35,72], and a dialogue of tacit and explicit knowledge through socialization [48]. It is interesting to observe that previous arguments for the importance of co-location [9,33,72] are challenged by the strong positive association between virtual communication methods and information transfer ability in clinical trials. The group of medical sites that apply virtual communication methods to a high degree have a high degree of information transfer ability. In clinical trials a relocation of partners at face-to-face meetings will delay ongoing communication and may thereby challenge continuous feedback loops and reflections [14,32].

The positive association of virtual and face-to-face methods in general supports the notion that the transfer of information requires circumstances for partners to communicate issues that may not be explicit, but require interaction to stimulate the often complex and context-dependent issues. While the analysis of communication methods supports previous arguments in NPD literature, both provide no insights on which information areas are stickier than others. Here the results of the Rasch analysis contribute with a specific scale, differentiating issue areas relative to each other.

The scale of information issues

The result of the Rasch analysis reveals that all of the suggested information topics in the questionnaire are relevant within the same scale, and it is therefore relevant to pursue all of these information outcomes from the clinical trials. However, the Rasch scale also clearly illustrates that some of these information issues are stickier in character and therefore harder to transfer from medical site to producer.

At the easy end of the continuum the issue areas representing product functionality are clearly represented. This clear representation of product functionality issues as easiest to transfer is probably due to the main task of the medical professionals in clinical trials being monitoring of the medical reaction of a new treatment. However, it is interesting to observe that even though usability issues are closely linked to medical practice they are significantly more difficult to transfer. This also applies to the complimentary service category, which is even more difficult to transfer between site and producer. These issues can be argued to be slightly further from the individual professional expertise of medical staff, and more related to a department's organizational measures, but still directly linked to the aim of clinical trials. Information related to workforce competences and patient access to the drug is issues relevant to everyday practice at the medical site, and therefore issues closely related to respondents' interest and competence areas.

The most difficult category to transfer between user and producer, economic measures, is also highly relevant for drug adoption. Cost effectiveness and brand name reactions both refer to considerations conducted by management responsible at the medical site. This is probably the reason for their location at the most difficult end of the continuum, which is nevertheless interesting as these measures were emphasized as important trial outcomes by several of the interviewed industry respondents and the clinical practice guidelines.

Why is some trial information stickier?

The clear focus on product functionality issues in product testing reflects the overall aim in current structures of clinical trials, which to some degree may over-prioritize some issues at the expense of utilizing information on a broader scale from external partners. It can be argued that medical partners in the pharmaceutical industry are primarily perceived as providers of explicit and pre-defined information relevant for trial protocols.

The pharmaceutical industry is under extensive pressure to optimize costly and time-consuming clinical trials, which has resulted in more management layers and outsourcing strategies supporting efficiency of trials [12,29]. The established written protocols are often the prime source of information between sites and companies, and therefore focus on explicit

and easy to transfer knowledge. Certain information may therefore not be recognized and thereby de-coded and transferred. When utilizing the information potential from external collaboration in drug development, tacit knowledge at sites is essential in order to unravel valuable and often concealed medical application know-how [48].

This development can challenge the ability of a process to discover tacit information from medical sites, as many actors are involved, challenging the ongoing relation between partners. The complex information developed at sites can be challenging to unravel if the receivers are in-experienced in the topic areas, and instead are focusing on explicit data collection concerning protocol information. Extant studies on clinical trials have documented that previous collaboration experience among trial partners can stimulate trial outcomes [20,71]. The continuous outsourcing of trial management and increasing in-house layers of management [29,31,64] can thus challenge the development of mutual knowledge and trust among partners of clinical trials. These circumstances may all be contributing to the vast differentiation of information transfer ability in clinical trials.

Managerial implications

The results of this study may guide firms to improve their management of trials, as specific initiatives are necessary in order to capture the large information potential from medical partners. Incorporating routines to identify and utilize medical site input on a broader scale is recommended. The industry could differentiate medical users based on their competences and roles in the clinical process. Such categorization should then be supported by specific protocols aiming outside the functionality issues; therefore explicitly supervising the commercialization and application processes. Stimulating continuous relations between site and industry should then support the focus on complex and tacit information. A model where a few industry representatives are continuously integrated in trials with the prime goal of tapping into information based on an extended trial output agenda is therefore recommended. Further, the gathering of medical experiences should be supported by a focus on virtual communication tools, as these supply opportunities for continuous interaction with these important development partners.

Limitations and directions for future research

The data collection in this study has aimed at a high level of continuity in the information topic items by generating parallel question and answer options, which have met the limitation

of reliability of scale items in the Rasch method. However, the spread of the items in relation to the person distribution represent some under-identification in the model. This is considered in the conclusions of the study, which is kept on the level of differentiating between the four defined groupings: product functionality issues, product service issues, usability issues and economic measures. From the understanding developed in this study we suggest that future studies consider expanding the breadth of topic items at the difficult end of the continuum to include topics such as; *Usability issues*: End-users' convenience and attitude toward the design of the drug, patients' attitude toward intervention time. *Service issues*: Requirements for long-term patient care, required training of personnel to apply treatment. *Economic measures*: the need for organizational changes coming with a new product or treatment plan, fit of treatment to existing treatment opportunities in the national health system.

Future data observations could also include measures exploring global variance in relation to information potential and communication tools. It would also be relevant to incorporate outsourcing measures, and therefore the extent of Contract Research Organizations' (CRO) role in a trial, in order to detect potential consequences of third party agents integrated in the trial business model.

Further, future research may explore the extent to which the existing network of sites applied in a single clinical study may influence information processes, since the heterogeneity of backgrounds may add to the depth and breadth of learning.

References

- [1] Ahuja, G., The duality of collaboration: Inducements and opportunities in the formation of interfirm linkages, *Strateg. Manag. J.* **343** (2000) 317–343.
- [2] Alonso-Ríos, D., Vázquez-García, A., Mosqueira-Rey, E., and Moret-Bonillo, V., A Context-of-Use Taxonomy for Usability Studies, *Int. J. Hum. Comput. Interact.* **26** (2010) 941–970.
- [3] Baines, T. S., Braganza, A., Kingston, J., Lockett, H., Martinez, V., Michele, P., et al., State-of-the-art in product service-systems, *Proc. Inst. Mech. Eng.* **221** (2009) 1543–1552.
- [4] Baker, G., The Effects of Synchronous Collaborative Technologies on Decision Making: A Study of Virtual Teams, *Inf. Resour. Manag. J.* **15** (2002) 15.
- [5] Banaszak-Holl, J., Zinn, J. S., and Mor, V., The impact of market and organizational characteristics on nursing care facility service innovation: a resource dependency perspective., *Health Serv. Res.* **31** (1996) 97–117.
- [6] Barczak, G., Sultan, F., and Hultink, E. J., Determinants of IT Usage and New Product Performance, *J. Prod. Innov. Manag.* **24** (2007) 600–613.
- [7] Barson, R., Foster, G., and Struck, T., Inter-and intra-Organisational barriers to sharing knowledge in the extended supply-chain, *Proc. e2000 Conf.* (2000).
- [8] Bathelt, H., and Turi, P., Geoforum Local , global and virtual buzz : The importance of face-to-face contact in economic interaction and possibilities to go beyond, *Geoforum* **42** (2011) 520–529.
- [9] Berchicci, L., and Tucci, C., There Is More to Market Learning than Gathering Good Information: The Role of Shared Team Values in Radical Product Definition*, *J. Prod. Innov. ...* (2010) 972–990.
- [10] Bevan, N., Usability is quality of use, *Adv. Hum. Factors/Ergonomics* **130** (1995) 115–130.
- [11] Bevan, N., Design for usability, *Proc. HCI Int.* (1999) 22–26.
- [12] Bodenheimer, T., Clinical investigators and the pharmaceutical industry., *N. Engl. J. Med.* **343** (2000) 511.
- [13] Bond, T. G., and Fox, C. M., *Applying the Rasch Model – Fundamental measurement in the Human Sciences.*, (Lawrence Erlbaum Associates, 2001).
- [14] Caffyn, S., Extending continuous improvement to the new product development process, *R&D Manag.* **27** (1997) 253–267.

- [15] Chermack, T. J., Improving decision-making with scenario planning, *Futures* **36** (2004) 295–309.
- [16] Cohen, W., and Levinthal, D., Absorptive capacity: a new perspective on learning and innovation, *Adm. Sci. Q.* **35** (1990) 128–152.
- [17] Coombs, R., and Hull, R., “Knowledge management practices” and path-dependency in innovation, *Res. Policy* **27** (1998) 237–253.
- [18] Cramton, C. D., Finding Common Ground in Dispersed Collaboration, *Organ. Dyn.* **30** (2002) 356–367.
- [19] Cummings, J. L., and Teng, B.-S., Transferring R&D knowledge: the key factors affecting knowledge transfer success, *J. Eng. Technol. Manag.* **20** (2003) 39–68.
- [20] Danzon, P. M., Nicholson, S., and Pereira, N. S., Productivity in pharmaceutical-biotechnology R&D: the role of experience and alliances., *J. Health Econ.* **24** (2005) 317–39.
- [21] Dixon, N. M., *The Organizational Learning Cycle: How We Can Learn Collectively.*, (McGraw-Hill, New York, New York, USA, 1994).
- [22] Everitt, B. S., Landau, S., Leese, M., and Stahl, D., *Cluster Analysis*, 5th ed., (John Wiley & Sons Ltd. UK, 2011).
- [23] Franke, N., Reisinger, H., and Hoppe, D., Remaining within-cluster heterogeneity: a meta-analysis of the “dark side” of clustering methods, *J. Mark. Manag.* **25** (2009) 273–293.
- [24] Franke, N., and Shah, S., How communities support innovative activities: an exploration of assistance and sharing among end-users, *Res. Policy* **32** (2003) 157–178.
- [25] Galbraith, C., Transferring Core Manufacturing Technologies in High-Technology Firms., *Calif. Manage. Rev.* (1990) 56–71.
- [26] Galbraith, J., Designing the innovating organization, *Organ. Dyn.* (1983).
- [27] Gangwal, A., and Gangwal, A., Naming of drug molecules and pharmaceutical brands, **7** (2011) 1–5.
- [28] Garber, a M., and Phelps, C. E., Economic foundations of cost-effectiveness analysis., *J. Health Econ.* **16** (1997) 1–31.
- [29] Getz, B. K., and Zuckerman, R., Clinical Research Outsourcing - Moving from transactional to strategic partnership-based outsourcing, *Contract Pharma* (2008) 10–12.
- [30] Getz, K. a., Campo, R. a., and Kaitin, K. I., Variability in Protocol Design Complexity by Phase and Therapeutic Area, *Drug Inf. J.* **45** (2011) 413–420.

- [31] Getz, K., and Vogel, J., Successful outsourcing: tracking global CRO usage, *Appl. Clin. Trials* (2009) 11–12.
- [32] Goffin, K., and Koners, U., Tacit Knowledge, Lessons Learnt, and New Product Development, (2011) 300–318.
- [33] Grant, R., Toward a knowledge-based theory of the firm, *Strateg. Manag. J.* **17** (1996) 109–122.
- [34] Grimshaw, J., Freemantle, N., Wallace, S., Russell, I., Hurwitz, B., Watt, I., et al., Effectiveness Bulletin Developing and implementing clinical practice guidelines, *Qual. Heal. Care* **4** (1995) 55–64.
- [35] Gulati, R., Alliances and Networks, *Strateg. Manag. J.* **19** (1998) 293–317.
- [36] Hair, J. F., and Anderson, R. E., *Multivariate data analysis*, (Prentice Hall Higher Education, 2010).
- [37] Hamel, G., Competition for competence and inter-partner learning within international strategic alliances, *Strateg. Manag. J.* (1991).
- [38] Harrigan, K., An application of clustering for strategic group analysis, *Strateg. Manag. J.* **73** (2006) 55–73.
- [39] Hippel, E. Von, Lead users: a source of novel product concepts, *Manage. Sci.* **32** (1986) 791–806.
- [40] Von Hippel, E., “Sticky Information” and the Locus of Problem Solving: Implications for Innovation, *Manage. Sci.* **40** (1994) 429–439.
- [41] Hippel, E. Von, Economics of product development by users: The impact of “sticky” local information, *Manage. Sci.* **44** (1998).
- [42] Hoegl, M., and Proserpio, L., Team member proximity and teamwork in innovative projects, **33** (2004) 1153–1165.
- [43] Hoyt, D., Clinical practice guidelines, *Am. J. Surg.* **173** (1997) 32–34.
- [44] Isaksson, O., Development of product-service systems: challenges and opportunities for the manufacturing firm, *J. Eng. ...* (2009) 37–41.
- [45] Jong, M. De, and Steenkamp, J., Using item response theory to measure extreme response style in marketing research: A global investigation, ... *Mark. Res.* **XLV** (2008) 104–115.
- [46] Larisch, A., Reuss, A., Oertel, W., and Eggert, K., Does the clinical practice guideline on Parkinson’s disease change health outcomes? A cluster randomized controlled trial, *J. Neurol.* (2011) 826–834.

- [47] Laursen, K., and Salter, A., Open for innovation: the role of openness in explaining innovation performance among U.K. manufacturing firms, *Strateg. Manag. J.* **27** (2006) 131–150.
- [48] Lewin, A. Y., and Nonaka, I. I., A Dynamic Theory of Organizational Knowledge Creation, *Organ. Sci.* **5** (1994) 14–37.
- [49] Lexchin, J., Bero, L. A., Djulbegovic, B., and Clark, O., outcome and quality : systematic review, **326** (2003).
- [50] Linacre, J. M., *Winsteps Help for Rasch Analysis*, (2011).
- [51] Maguire, M., Context of Use within usability activities, in *Int. J. Hum. Comput. Stud.*, (2001), pp. 453–483.
- [52] McGettigan, P., Golden, J., Fryer, J., Chan, R., and Feely, J., Prescribers prefer people: The sources of information used by doctors for prescribing suggest that the medium is more important than the message, *Br. J. Clin. Pharmacol.* **51** (2001) 184–189.
- [53] Meltzer, D., Accounting for future costs in medical cost-effectiveness analysis., *J. Health Econ.* **16** (1997) 33–64.
- [54] Meyers-Levy, J., The Influence of a Brand Name’s Association Set Size and Word Frequency on Brand Memory, *J. Consum. Res.* **16** (1989) 197–207.
- [55] Mont, O., Clarifying the concept of product–service system, *J. Clean. Prod.* **10** (2002) 237–245.
- [56] Morelli, N., Developing new product service systems (PSS): methodologies and operational tools, *J. Clean. Prod.* **14** (2006).
- [57] Nelson, R., The role of knowledge in R&D efficiency, *Q. J. Econ.* **97** (1982) 453–470.
- [58] Nelson, R., Winter, S., *An Evolutionary Theory of Economic Change.*, (Belknap Press, Cambridge, 1982).
- [59] Nonaka, I., Takeuchi, H., *The Knowledge-Creating Company.*, (Oxford University Press, New York, New York, USA, 1995).
- [60] Ploeg, J., Davies, B., Edwards, N., Gifford, W., and Miller, P. E., Factors influencing best-practice guideline implementation: lessons learned from administrators, nursing staff, and project leaders., *Worldviews Evid. Based. Nurs.* **4** (2007) 210–9.
- [61] Polanyi, M., Tacit knowing: Its bearing on some problems of philosophy, *Rev. Mod. Phys.* **34** (1962) 601–616.
- [62] Porter, M. E., The Adam Smith address : Location, clusters, and the “new” microeconomics of competition, *Bus. Econ.* **33** (1998) 7–13.

- [63] Rasch, G., *Probabilistic Models for Some Intelligence and Attainment Tests*, reprint of, (Mesa Press, Chicago, IL, 1980).
- [64] Rettig, R., The industrialization of clinical research, *Health Aff.* **19** (2000) 129–146.
- [65] Revilla, E., Rodríguez-Prado, B., and Prieto, I., Information technology as knowledge management enabler in product development: Empirical evidence, *Eur. J. Innov. Manag.* **12** (2009) 346–363.
- [66] Robinson, J., and Howell, S., Specialty Pharmaceuticals: Policy Initiatives To Improve Assessment, Pricing, Prescription, And Use, *Health Aff.* **33** (2014) 1745–50.
- [67] Schmidt, J. B., Montoya-Weiss, M. M., and Massey, A. P., New Product Development Decision-Making Effectiveness: Comparing Individuals, Face-To-Face Teams, and Virtual Teams, *Decis. Sci.* **32** (2001) 575–600.
- [68] Shaw, B., Gaining added value from centres of excellence in the UK medical equipment industry, *R&D Manag.* **18** (1988) 123–130.
- [69] Siemsen, E., Roth, A. V., and Balasubramanian, S., How motivation, opportunity, and ability drive knowledge sharing: The constraining-factor model, *J. Oper. Manag.* **26** (2008) 426–445.
- [70] Singh, J., Tackling measurement problems with Item Response Theory, *J. Bus. Res.* **57** (2004) 184–208.
- [71] Sismondo, S., How pharmaceutical industry funding affects trial outcomes: causal structures and responses., *Soc. Sci. Med.* **66** (2008) 1909–14.
- [72] Song, M., Determinants of the Level of Knowledge Application: A Knowledge Based and Information Processing Perspective*, *J. Prod. Innov. Manag.* **22** (2005) 430–444.
- [73] Spatz, I., McGee, N., Brennan, T., Berndt, E. R., and Lott, R., Speciality Pharmaceuticals, *Health Aff. Health Pol* (2013) 1–4.
- [74] Teece, D. J., Capturing Value from Knowledge Assets: the new economy, markets for know-how and intangible assets, *Calif. Manage. Rev.* **40** (1998) 55–79.
- [75] Tukker, A., and Tischner, U., Product-services as a research field: past, present and future. Reflections from a decade of research, *J. Clean. Prod.* **14** (2006) 1552–1556.
- [76] Tushman, M., Technical communication in R & D laboratories: The impact of project work characteristics, *Acad. Manag. J.* **21** (1978) 624–645.
- [77] Tushman, M. L., and Nadler, D. A., Information Processing as an Integrating Concept in Organizational Design., *Acad. Manag. Rev.* **3** (1978) 613–624.
- [78] Urde, M., Brand orientation—a strategy for survival, *J. Consum. Mark.* **11** (1994).

- [79] Wedel, M. and Kamakura, W. A., *Market Segmentation - Conceptual and Methodological Foundations*, (Kluwer., Boston, MA, 1998).
- [80] Wynia, M., and Boren, D., Better Regulation of Industry- Sponsored Clinical Trials Is Long Overdue, *J. Law, Med. Ethics* (2009).
- [81] Zaheer, A., and Bell, G. G., Benefiting from network position: Firm capabilities, structural holes, and performance, *Strateg. Manag. J.* **26** (2005) 809–825.
- [82] Zander, U., and Kogut, B., Knowledge and the speed of the transfer and imitation of organizational capabilities: An empirical test, *Organ. Sci.* **6** (1995).