Aus dem Institut für Sozialmedizin, Epidemiologie und
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DISSERTATION

Stakeholder Engagement als Optimierungsmöglichkeit
klinischer Studien

Stakeholder engagement for optimization of clinical studies

zur Erlangung des akademischen Grades
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Preface

The present work is based on data previously published in: Heiß et al., "Current practice of stakeholder engagement: researchers' experiences in North America, DACH countries and China. Journal of Comparative Effectiveness Research / 7th May 2020. For a detailed description of my participation see page 39 (Anteilserklärung).

Tables

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Abbreviation

ANOVA	Analysis of variance
BIH	Berlin Institute of Health
CER	Comparative effectiveness research
CHERRIES	Checklist for Reporting Results of Internet E-Surveys
CROSS	Checklist for Reporting Survey Studies
D&I	Dissemination and Implementation
DACH	Germany (D), Austria (A), Switzerland (CH)
MeSH	Medical Subject Headings
NIHR	National Institute for Health research
NLM	National library of medicine
PCORI	Patient-Centered Outcomes Research Institute
UK	United Kingdom

Zusammenfassung

Hintergrund: Stakeholder Engagement steht für die aktive Einbeziehung verschiedener betroffener Gruppen in die Forschung. Diese Methode kann die Relevanz von Forschungsfragen und -ergebnissen erhöhen und die Transparenz und Rekrutierung in einer Studie erleichtern. Das Thema der Einbindung verschiedener Akteure in der klinischen Forschung gewinnt zunehmend an Aufmerksamkeit. Die aktuelle Praxis der Einbeziehung von Interessengruppen durch Forschende in Deutschland ist jedoch unbekannt. In dieser Studie untersuchten wir die Einbeziehung von Stakeholdern in der klinischen Forschung in DACH Ländern (Deutschland, Österreich, Schweiz), sowie in Nordamerika und China. Unser Ziel war es, die Erfahrungen von Forschenden mit der Einbeziehung von Stakeholdern und ihre Wahrnehmung dieser Methode für die zukünftige Forschung zu bewerten.

Methoden: Wir führten eine Querschnittsstudie mittels einer internationalen Online-Umfrage durch. Die von den Forschenden ausgefüllten Fragenkomplexe umfassten soziodemographische Daten sowie zukünftige Prognosen, Herausforderungen und Potenziale der Einbindung von Stakeholdern in die klinische Forschung. Die Daten wurden deskriptiv ausgewertet. Zusätzlich testeten wir auf Unterschiede zwischen den Mittelwerten und kontrollierten für eine Kovariate.

Ergebnisse: Wir erhielten 245 ausgefüllte Fragebögen und gruppierten die Teilnehmenden nach den drei zuvor festgelegten Weltregionen. Von allen Teilnehmenden gaben 11,02 % (27/245) Nordamerika, 22,45 % (55/245) DACH und 51,84 % (127/245) China als Wohnort an. Teilnehmende, die ein „anderes" oder „kein" Land als Wohnsitz angaben (14,69 %, 36/245) wurden von den statistischen Analysen ausgeschlossen. Forschende aus Nordamerika stimmten auf einer Skala von 0 bis 10 mit 8,41 ± 2,3 Punkten (Mittelwert ± sd) überein, dass die Einbindung von Stakeholdern in der klinischen Forschung essentiell ist. Teilnehmende aus China bewerteten dies ähnlich (8,12 ± 2,1), Teilnehmende aus DACH mit deutlich niedrigeren Werten (4,23 ± 2,9, p < 0,001). Unter anderem unterschieden sich die Meinungen darüber, ob die Einbeziehung von Interessengruppen die Relevanz von Forschungsfragen und -ergebnissen erhöht, in den Weltregionen signifikant (DACH: 6,95 ± 2,8, Nordamerika: 8,05 ± 2,3, China: 8,37 ± 1,8, p = 0,009). Der Einsatz digitaler Methoden bei der Einbindung von Stakeholdern wurde von Teilnehmenden aus

DACH am niedrigsten bewertet, z.B. Smartphone Applikation mit einem Mittelwert von 5.04 ± 2.4 (Nordamerika: 6.59 ± 1.9, China 8.28 ± 2.5, $p < 0.001$).

Schlussfolgerung: Wir stellten fest, dass Forschende aus verschiedenen Weltregionen die Einbeziehung von Stakeholdern sehr unterschiedlich beurteilen. Um das Wissen und die Möglichkeiten zur Umsetzung von Stakeholder Engagement zu verbessern, empfehlen wir einen verstärkten internationalen Austausch und spezifische Schulungen für Forschende in DACH.

Abstract

Background: Stakeholder engagement stands for the active involvement of diverse concerned groups in research. It is expected to increase the relevance of research questions and outcomes and facilitate transparency and recruitment. The topic of engaging multiple actors in clinical research is rapidly gaining attention. The use of stakeholder engagement by researchers in Germany is unknown. We investigated the current practice of stakeholder engagement in clinical research in DACH countries (Germany, Austria, and Switzerland), as well as North America and China. We aimed to evaluate researchers' experience with stakeholder engagement and their perception of this method for future research.

Methods: We conducted a cross-sectional study using an international online survey. Researchers completed questions covering sociodemographic information, professional experience, and details about stakeholder engagement in clinical research, such as former practice, future predictions, challenges, and potential. Data were analyzed descriptively. Additionally, we tested for differences among means and controlled for a covariate.

Results: We received 245 filled questionnaires and grouped the participants by the three predetermined world regions. Out of all participants, 11.02 % (27/245) named North America, 22.45 % (55/245) DACH, and 51.84 % (127/245) China as their country of residence. We excluded participants who marked another or 'none' as state of residence (14.69 %, 36/245) from the statistical analyses. Researchers from North America agreed on a scale from 0 to 10 with 8.41 ± 2.3 points (mean ± sd) about the essentiality of stakeholder engagement in clinical research. Participants from China rated similar (8.12 ± 2.1) and those from DACH significantly lower (4.23 ± 2.9, $p < 0.001$). Amongst other aspects, the opinion about stakeholder engagement increasing the relevance of research questions and outcomes differed significantly between regions (DACH: 6.95 ± 2.8, North America: 8.05 ± 2.3, China: 8.37 ± 1.8, $p = 0.009$). The use of digital methods in stakeholder engagement was rated lowest by DACH respondents, e.g., Smartphone Application, with a mean of 5.04 ± 2.4 (North America: 6.59 ± 1.9, China 8.28 ± 2.5, $p < 0.001$).

Conclusion: We found a heterogeneous perception of stakeholder engagement among researchers from the three different world regions. To improve the knowledge and possibility of implementing stakeholder engagement, we recommend increased international exchange and specific training for researchers in DACH.

1. Introduction

1.1 Definition of Stakeholder engagement

With increased focus on translation into practice and patient participation in research, stakeholder engagement gains more and more attention within the medical field. The stakeholder approach originally emerged from the field of business administration and was mainly shaped by Freeman in the 1980s (1). A designated aim was to add value to business and achieve sustained success by engaging different interest groups (2). In the context of clinical research, Concannon et al. define a stakeholder as "an individual or group who is responsible for or affected by health- and healthcare-related decisions that can be informed by research evidence"(3). Engagement is characterized as "a bi-directional relationship between the stakeholder and researcher that results in informed decision-making about the selection, conduct, and use of research" (3).

1.2 Who, how, and when to engage in a research project?

The first step in practicing stakeholder engagement is the identification of relevant stakeholders. There are several descriptions of possible stakeholders in literature, including patients or consumers, clinicians, researchers, and healthcare providers (4, 5). Concannon et al. offer the "7P Framework" naming seven stakeholder categories: "patients and the public, providers, purchasers, payers, policymakers, product makers, principal investigators" (3). A systematic approach using stakeholder categories and techniques like brainstorming and snowball sampling is recommended for meaningful stakeholder identification (6). In current literature, the inclusion of patients and providers is found frequently, but other groups are rarely engaged (7).

The next step is to get in touch with the specific stakeholders and establish a trustful, lasting relationship. Methods of engagement can be divided into two main categories: "high touch approaches" and "high-tech approaches" (8). The former includes more traditional methods such as in person focus groups, advisory boards, community or one-on-one meetings and interviews. They are defined by direct contact with stakeholders. The second involves digital methods, for example online campaigns, social media, ehealth and email communication. They offer the possibility to engage a larger number of stakeholders simultaneously (9) and disseminate information (10).

Another essential aspect is the point in time in which stakeholders are getting engaged and their level of involvement. Stakeholders can be engaged in very early stages of a research project, such as in prioritizing research questions (11). They can serve as consultants or decision makers in the project. A purely advisory ("passive") role is not recognized as proper stakeholder engagement by most authors (12-14).

1.3   Stakeholder impact

Current research shows that stakeholder engagement enhances research quality and increases relevance (15). Furthermore, stakeholders can change project objectives, contribute to study design, interventions or chosen methods, and improve contact with the study population (16-18). In guideline development, stakeholder engagement can increase the acceptance and feasibility of guidelines as well as the subsequent adherence (19). Overall, engagement leads to more meaningful, user-focused research outcomes (14). From an ethical point of view stakeholder, engagement allows participation of affected groups in clinical research and offers an approach to an open ethical discourse (20). Thus, it adds social value to research (11) and follows the idea of democratization and shared decision making (21, 22). Stakeholder engagement requires "effort, attention, resources and flexibility" (16). Most notably, time is a challenge for resources both on the part of researchers and stakeholders (14, 16).

At the time of our study, neither a uniform international definition on stakeholder engagement in medical research nor clear guidelines on how to perform or report about stakeholder engagement were present. However, several studies displayed first frameworks and demanded further investigation about stakeholder engagement (4, 7, 23, 24).

1.4   Institutional landscape

On an international level, the importance of stakeholder engagement in medical research is reflected by multiple institutions which foster stakeholder engagement (25-27). The Patient-Centered Outcomes Research Institute (PCORI), founded in Washington DC in 2010, provides an institutional framework for researchers who plan to engage stakeholders. PCORI focuses on funding studies that include stakeholders and aims for research where "patients and other healthcare stakeholders are equitable partners" (28). In the United Kingdom (UK), the UK National Advisory group INVOLVE was founded in 1996 by the National Institute for Health Research (NIHR) to foster public involvement in medical

research (26). In 2013 the Berlin Institute of Health (BIH) emerged from a cooperation of Charité – Universitätsmedizin Berlin and Max-Delbrück-Centrum as a research center with a focus on medical translation. Recently the BIH started emphasizing stakeholder engagement and is offering an award for Charité-affiliated authors of studies involving stakeholders (29).

1.5   Research question

At the beginning of our research, the topic of stakeholder engagement was mainly neglected in the German-speaking research landscape. Only a few studies reported stakeholder engagement (18, 30). No data was available from DACH about further application and practice of stakeholder engagement in clinical research. Simultaneously, app-studies were an emerging field and brought new dimensions and challenges to the developing team. Particularly in these studies, the involvement of end-users and other stakeholders can be helpful in every study phase.

The aim of our study was first to identify knowledge and use of stakeholder engagement among researchers in DACH. Second, we wanted to systematically assess the perception of this method as a component of clinical research. To place the acquired data in an international context, we conducted the study in an international setting and defined three study groups by residency (North America, DACH, and China). We hypothesized that researchers in DACH have differing knowledge and opinion about stakeholder engagement from researchers in North America or China.

Secondary, we gathered data about the challenges and needs of researchers when engaging stakeholders. We also observed if researchers are willing to include new digital technologies in their projects.

2. Methods

2.1 Online survey

A survey is a systematic research method that collects information by asking specific questions. Especially suitable for descriptive and exploratory cross-sectional studies, the method serves to collect self-disclosures of respondents, e.g. opinions, experiences and beliefs. The aim is to transfer the results from an interviewing subgroup of people to a larger population (31). We selected the method of an online survey to meet the requirements of our research question.

The method of an online survey allows a geographically flexible data collection with relatively low financial outlay (32). Most web-based surveys use non-random sampling rather than random sampling (33). There are two common types of bias to be expected in an online survey. First, participation is limited to people having access to and knowledge of using the Internet and receiving the invitation of the researcher (selection bias). Second, the sample includes solely individuals who voluntarily choose to participate (volunteer bias).

For the implementation of an online survey, various software products are offered. Most providers sell a time-limited license for use. In this project, we worked with SoSci-Survey, a professional non-commercial provider, offering free use for surveys in the academic field (34). The founder and communication scientist Dominik Leiner carries out research, publishes about online surveys, and offers SoSci-Survey users immediate support in an associated forum. Particularly convincing is the fact that the provider hosts its servers in Germany or allows hosting on its own server and thus is compatible with the applicable data protection regulations.

2.2 Development

The survey was developed based on a broad literature research on current aspects of stakeholder engagement. We followed the existing guidelines for survey conduct and report (35, 36). The first draft was on paper and subsequently transferred into the online format. In terms of content, the questionnaire was divided into six sections integrating different aspects of stakeholder engagement (Figure 1). Every section contained an individual number of questions. The first section introduced the definition of stakeholder engagement to build a common ground for the survey (Figure 2). The six main sections

were framed by a sociodemographic and a commentary part. Since the questions build on each other in terms of content, we did not randomize items.

Numerical and categorial variables and various question types were represented in the survey. The selection type allowed respondents to choose one of the shown answers. The dropdown selection was suited for a question with a high number of possible answers. We used a 10-point Likert scale (extremes labeled or fully labeled) to measure the attitude of respondents. A set of questions was designed to assess future expectations of researchers on certain aspects of stakeholder engagement. For this purpose, we formulated three consecutive questions on the same topic (37). The first question refers to the current state, the second to the recommendation for future practice, and the third to the actual anticipated development.
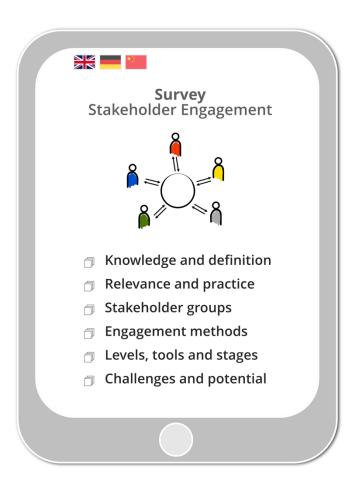
Figure 1: Outline of the survey (own illustration)

Stakeholder engagement is the active inclusion and participation of different individuals or groups in a research process. Stakeholders are characterized by holding an interest in or being affected by the conducted research.
(According to Concannon et al. J Gen Intern Med 2012)

Figure 2: The definition of stakeholder engagement how presented in the survey (38)

2.2.1 Iterative testing

The questionnaire was tested successively by two independent groups to avoid concentration mistakes. Comments from round 1 were integrated (gross errors, layout, technical deficiencies, comprehension questions) for round 2. After these two independent tests, the final version was created, which was then once again tested by both groups. In the third phase, an independent tester and the project manager approved the version (Figure 3). The main objective of this iterative pretest was to uncover content-related or technical deficiencies.

Moreover, we aspired to make the completion of the survey as pleasant and clear as possible for all potential respondents and improve the study's adherence. To this end, we included people of different genders, educational backgrounds, and professions in the pretest. The final version consisted of 18 pages with 29 questions and 13 free text fields, see (38) Supplementary file 1. It was translated into English and Chinese, each reviewed by native speakers.
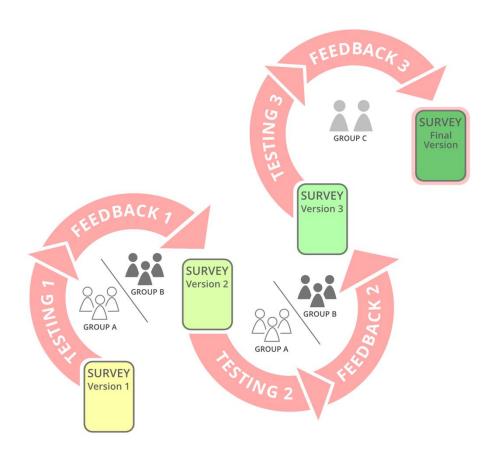
Figure 3: Iterative pretesting of the questionnaire (own illustration)

2.2.2 Handling of completeness

It is possible to check for completeness in an online survey before the participants submit. The software SoSci-Survey provides two options for checking whether the questionnaire has been answered completely.

When checking for completeness at the end of each page, the participant will be obliged to answer every question before continuing the survey. Often respondents consciously decide not to answer a question, so the option "do not specify" must be added to every question. When checking for completeness at the end of the questionnaire, all questions that have not been answered during the survey are collected and displayed at the end. The first option can confuse the design because of an additional number of possible answers on the pages. Besides, a forced response can produce invalid data. With the second option, questions are taken out of context, and the data is not comparable with the regularly collected answers.

In our study, a completeness check was dispensed in favor of usability. We evaluated non-answered items as intentionally not selected. A "back" button allowed the respondents to review their answers.

2.2.3 Technical function test

The technical function test was performed in the German and English versions. The test duration was 3 hours, all variables and their representation were checked. The survey was editable on PC, tablet, and smartphone.

2.3   Consent

The Ethical Board of Charité has approved the study on 3rd May 2016 (Approval Number EA1/128/16). Data was solely stored on an Institute's owned server where only the project's researchers had password-protected access. The data protection vote was positive on 15th June 2016 (AZ 293/16).

On the first page of the survey, we informed participants about the purpose, risks, benefits, compensation, and survey length. Information on data confidentiality and contact data of the investigator was given. Participants could give their consent for the study by pressing a button on the start page of the survey. No one could participate without giving consent to the study, and participants were acquainted with their right to withdraw consent at any time.

2.4   Data collection and sample

Data were collected from 12th September 2016 to 31st October 2017 in an open survey. Initial contact with potential participants was made via email. Recruitment was managed by sending the link to the electronic web survey via international researcher mailing lists and WeChat Groups in China. Access was gained indirectly through the administrators of those lists who had their contact data available online. The exact number of invitees was not possible to calculate because not all administrators provided the numbers of list members, and snowball sampling was nonavoidable. Additionally, outdated or incorrect email addresses could not be subtracted from the known population. The survey mode was open and not password protected. No online or offline advertisement was made, and the survey was voluntary. It was administered through the software SoSci Survey, and no cookies were used. We did not offer specific incentives for participation.

2.5   Statistical analysis

We determined to analyze all questionnaires that completed the 7th page (full sociodemographic data). The data were analyzed with the statistical program R (39) and the additional packages tidyverse, car, emmeans and tableone (40-43). The software SoSci Survey provided the raw data as .csv and a particular script to manage the import into R. Cleaning included the in-depth inspection of raw data and re-coding of single variables to ensure compatibility of the questionnaires in different languages. The differentiation between missing values as "no answer given" and marked as "prefer not to say" was performed. Scripts for cleaning and data analysis were sourced and executed from the Main script of the Project in R (Figure 4).
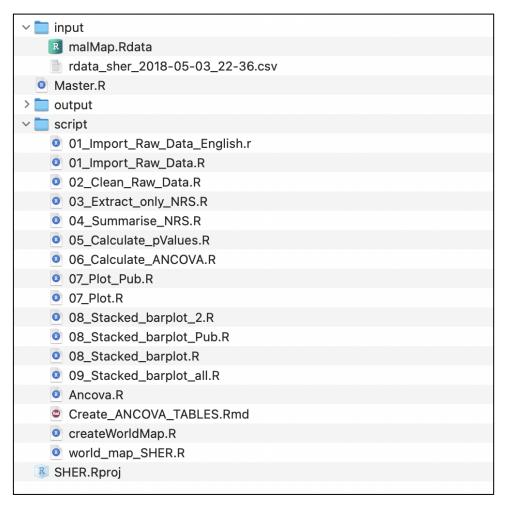
Figure 4: Structure of the Project for data analysis (own illustration)

2.5.1   Descriptive analysis

Descriptive analysis was performed separately for the three subgroups (DACH, North America, China). Sociodemographic variables were summarized in rates for categorial

variables (e.g. gender) and mean with standard deviation as a measure of dispersion for numerical variables (e.g., age in years). The population's characteristics were depicted in one table. The descriptive analysis of numerical variables from sections 1-6 was summarized in tables, including mean, standard deviation, median, interquartile range (q25, q75), minimum and maximum.

2.5.2 Explorative Analysis of Variance

For the statistical assessment of mean differences between more than two groups, a one-way Analysis of variance (ANOVA) was performed.

The null hypothesis was that all groups are equal. We set a significance level of 5%, meaning if the p-value is below the significance level, we can conclude with a 5% probability of error that at least two groups differ. The independent variable was categorial (RESIDENT).

An R script for performing ANOVA across the three groups for all dependent numeric variables was written (using function aov ()). Additional Analysis of Co-Variance with the co-variate age was conducted to reduce the variance of error in a separate script.

3.   Results

3.1   Respondent characteristics

In survey research, we find different kinds of response metrics (35). We defined unique site visitors as persons who visited the first page of the questionnaire but did not consent to participate. We estimated a total of 7000 survey recipients and the software recorded 842 unique site visitors. The participation rate is the percentage of persons who agreed to participate based on unique site visitors. With 311 participants checking the consent box on the first page, the participation rate was 36,9% (311/842). The completion rate, in this context the number of respondents submitting the last page of the questionnaire divided by the number of persons who agreed to participate, was 49,5% (154/311).

In total, we obtained 311 filled-in surveys. Of these, 78,8% (245/311) met our inclusion criteria by having completed the 7th page of the survey as a minimum. Fifty-five participants named a DACH country as their place of residence; 27 lived in North America and 127 in China at the time of the survey. Thirty-six participants named another or no country of residence.

Participants from DACH had a mean age of 48.35±11.8 years, from North America 53.78±10.3 years, and from China 37.47±8.8 years. In self-ascription of gender, female participants were represented in the majority across all three groups (51% in DACH, 52% in North America, and 63% in China). Regarding the professional context, 61,8% of respondents from DACH worked at a university, and 21.8% in other research institutions. Of those participating from North America, 63% were employed at a university and 33% at a hospital or clinic. 33% of the respondents from China had a job at a university and 54% at a hospital or clinic. 49% from DACH, 63% from North America, and 40% from China described their position as principal investigator. Of the respondents from DACH, 38% were research assistants, from North America 7.4%, and from China 28%. The mean work experience in years was 12.7±7.9 in DACH, 18.7±9,4 in North America, and 9.9±8.1 in China. For the complete sample characteristics by group, see Table 1 (38).

Table 1: Sample characteristics as reported in the online survey

Characteristic	DACH n = 55	North America n = 27	China n = 127
Age in years, mean (sd)	48.35 (11.77)	53.78 (10.27)	37.47 (8.84)
Gender, n (%)			
Male	23 (41.8)	12 (44.4)	44 (34.6)
Female	28 (50.9)	14 (51.9)	80 (63.0)
Other	0 (0.0)	0 (0.0)	1 (0.8)
Prefer not to say	2 (3.6)	0 (0.0)	2 (1.6)
[NA] not available	2 (3.6)	1 (3.7)	0 (0.0)
First language, n (%)			
German	50 (90.9)	2 (7.4)	0 (0.0)
English	0 (0.0)	23 (85.2)	1 (0.8)
Chinese	0 (0.0)	0 (0.0)	125 (98.4)
Other	3 (5.5)	2 (7.4)	0 (0.0)
[NA] not available	2 (3.6)	0 (0.0)	1 (0.8)
Professional context, n (%)			
Industry	4 (7.3)	0 (0.0)	7 (5.5)
University	34 (61.8)	17 (63.0)	42 (33.1)
Hospital or Clinic	4 (7.3)	9 (33.3)	69 (54.3)
Other research institution	12 (21.8)	1 (3.7)	9 (7.1)
[NA] not available	1 (1.8)	0 (0.0)	0 (0.0)
Position, n (%)			
Principal investigator	27 (49.1)	17 (63.0)	51 (40.2)
Research assistant	21 (38.2)	2 (7.4)	35 (27.6)
PhD student	1 (1.8)	0 (0.0)	10 (7.9)
Master student	1 (1.8)	0 (0.0)	16 (12.6)
Other	4 (7.3)	8 (29.6)	14 (11.0)
[NA] not available	1 (1.8)	0 (0.0)	1 (0.8)
Main working field, n (%)			
Basic research	8 (14.5)	2 (7.4)	13 (10.2)
Clinical and/or health service research	29 (52.7)	15 (55.6)	54 (42.5)
Teaching	2 (3.6)	1 (3.7)	10 (7.9)
Patient care	6 (10.9)	6 (22.2)	38 (29.9)
Other	9 (16.4)	3 (11.1)	12 (9.4)
[NA] not available	1 (1.8)	0 (0.0)	0 (0.0)
Work experience in years, mean (sd)	12.74 (7.86)	18.74 (9.43)	9.85 (8.10)

All characteristics were self-reported by the study participants. Percentages may not sum up to 100% because of rounding. DACH: Germany (D), Austria (A), and Switzerland (CH); North America: USA and Canada. SD: Standard deviation. Modified after (38)

3.2   Section 1: Knowledge and definition

Of the participants from DACH, 65.45% (36/55) confirmed to know the term stakeholder engagement, 32.73% (18/55) did not know the term, and 1.82% (1/55) chose not to answer the question. In the group from North America, 96.3% (26/27) stated to be familiar with the term stakeholder engagement, and 3.7% (1/27) denied knowing the term. Of all participants from China, 56.69% (72/127) knew the term, and 43.31% (55/127) did not recognize the term, see Figure 5.
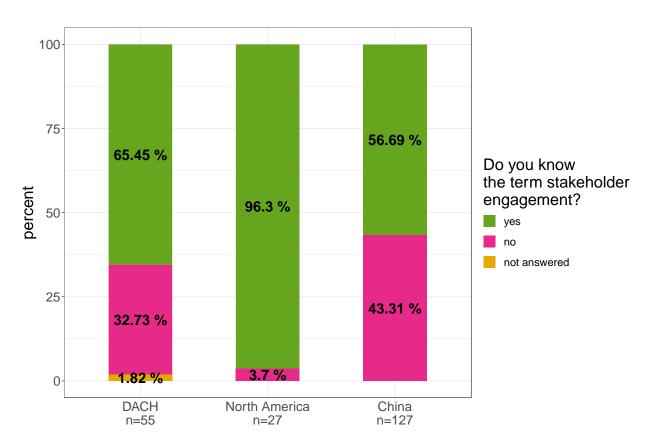
Figure 5: Participant's knowledge of the term stakeholder engagement by country of residence.
DACH: Germany (D), Austria (A) and Switzerland (CH); North America: USA and Canada. Modified after (38)

Several questions addressed the stakeholder definition we introduced in the survey. Comprehensibility of the definition was rated with high means among all groups (DACH 8.19±2.1, North America 9.20±1.1, and China 8.18±2.1). Researchers from DACH agreed with a mean of 7.12±2.8 that the definition was informative, researchers from North America with a mean of 8.70±1.5 and from China with a mean of 7.42±2.8. Asked if the definition mirrors one own opinion, researchers from DACH agreed with the lowest mean (6.81±2.8, North America 8.58±2.3, China 7.21±2.8), see Figure 6.
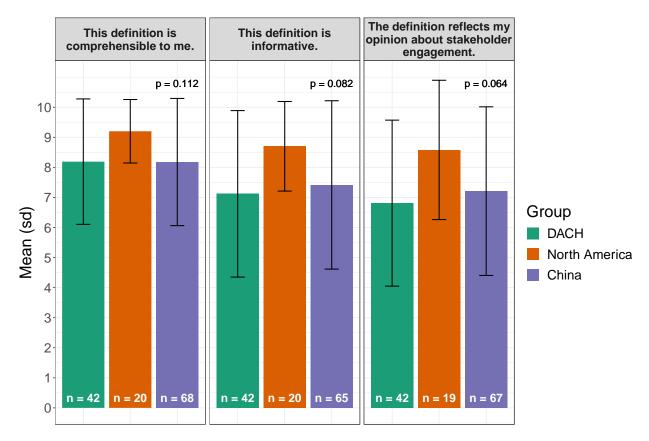
Figure 6: Reception of stakeholder definition
Shown values are the means of the response by group on a scale from 0 to 10 with 0 = do not agree at all and 10 = agree completely; error bars indicate the standard deviation, p-values are from a one-way ANOVA. DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; SD: Standard deviation. Modified after (38)

3.3   Section 2: Relevance and Practice

Participants were asked if they had "already engaged stakeholders" in their research (38). Researchers from DACH showed the lowest agreement with a mean of 5.53±4.1, researchers from North America the highest with a mean of 8.84±2.0 Researchers from China rated intermediately with a mean of 6.22±2.7. When asked about the likelihood of applying stakeholder engagement in the future, researchers from DACH rated with a mean of 7.42±2.9, from North America with a mean of 9.38±1.0, and from China with a mean of 7.61±2.4 (Figure 7).
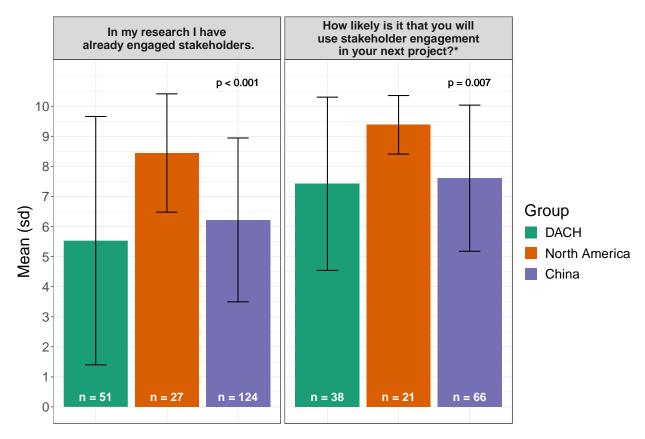
Figure 7: Reported practice of stakeholder engagement
Shown values are the means of the response by group on a scale from 0 to 10 with 0 = do not agree at all and 10 = agree completely; error bars indicate the standard deviation, p-values are from a one-way ANOVA.
*This item was rated on a scale from 0 to 10 with 0 = very unlikely and 10 = very likely.
DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; SD: Standard deviation Modified after (38)

Participants were asked to rate on a scale from 0 (do not agree at all) to 10 (agree completely) if stakeholder engagement plays an important role in clinical research. Researchers from DACH agreed with a mean of 4.23±2.9, from North America with a mean of 8.41±2.2, and from China with a mean of 8.12±2.1. The statement that stakeholder engagement should play a central role in research was evaluated with a mean of 8.33±1.6 by researchers from North America, and with a mean of 7.51±2.4 from DACH and 6.74±2.5 from China. In the estimation, if stakeholder engagement will be important in the future, participants from DACH reached a mean of 6.50±2.3, from North America 8.52±1.6, and from China 7.81±2.1 (Figure 8). Differences between groups were statistically significant (p < 0.05).

Figure 8: Reported relevance of stakeholder engagement in three dimensions
*Shown values are the means of the response by group on a scale from 0 to 10 with 0 = do not agree at all and 10 = agree completely; error bars indicate the standard deviation, p-values are from a one-way ANOVA. DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; SD: Standard deviation. Modified after (38)*

3.4   Section 3: Stakeholder groups

Respondents from DACH rated the engagement of the group 'payers' with a higher mean than researchers from North America and China. The other stakeholder groups were rated with a lower mean by DACH respondents compared to North America and China (Table 2). Across all groups, the frequency of engaging patients, clinicians, and researchers reached higher means than the engagement of stakeholders outside the common scope, like payers, industry, and policymakers.

Table 2: Respondent's ratings of "Which of the following stakeholder groups have you already engaged in research?"

Item/ Group	DACH mean (sd)	North America mean (sd)	China mean (sd)	p-value
Patients	5.48 (3.35)	7.38 (2.41)	7.45 (3.34)	0.004
Clinicians	6.33 (3.0)	8.31 (1.78)	8.33 (2.40)	< 0.001
Researchers	7.7 (2.60)	9.15 (1.67)	8.42 (2.38)	0.038
Payers	4.29 (3.58)	3.46 (3.49)	3.88 (3.47)	0.62
Industry	2.51 (3.09)	3.04 (2.91)	3.92 (3.36)	0.057
Hospitals and Health Systems	3.93 (3.62)	4.23 (3.35)	7.49 (3.02)	< 0.001
Policy makers	2.72 (3.22)	4.0 (3.38)	3.82 (3.34)	0.142
Training institutions	3.02 (3.37)	6.11 (4.04)	3.08 (3.15)	< 0.001

Shown values are the means of the response by group on a scale from 0 to 10 with 0 = never and 10 = always; p-values are from a one-way ANOVA. DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; sd: Standard deviation.

Regarding recommendations for the future engagement of stakeholders, we found differing ratings within the groups. Respondents from DACH rated patients, clinicians, researchers, and hospitals & health systems slightly lower than respondents from North America and China. To engage industry stakeholders was rated with the lowest mean (3.12 ± 2.1) by DACH respondents (North America 5.12 ± 2.7 and China 5.9 ± 3.5). Likewise, policymakers got lower ratings from DACH respondents with a mean of 4.8 ± 3.0 compared to North America (7.31 ± 2.7) and China (7.15 ± 3.2). Payers were rated quite low across all groups but relatively higher in DACH with a mean of 6.61 ± 3.1 (Table 3).

Table 3: Respondent's ratings of "Which stakeholder groups should be engaged in future clinical research?"

Item/ Group	DACH mean (sd)	North America mean (sd)	China mean (sd)	p-value
Patients	7.98 (2.37)	8.64 (1.63)	8.45 (2.51)	0.439
Clinicians	7.78 (2.44)	8.77 (1.53)	8.89 (2.20)	0.018
Researchers	8.47 (2.48)	9.08 (1.60)	8.94 (2.04)	0.383
Payers	6.61 (3.06)	5.62 (3.20)	5.80 (3.77)	0.379
Industry	3.12 (2.13)	5.12 (2.74)	5.90 (3.48)	< 0.001
Hospitals and Health Systems	6.71 (2.37)	7.16 (2.69)	8.60 (2.08)	< 0.001
Policy makers	4.80 (2.98)	7.31 (2.70)	7.15 (3.23)	< 0.001
Training institutions	5.56 (2.58)	8.04 (2.19)	5.80 (3.52)	0.002

Shown values are the means of the response by group on a scale from 0 to 10 with 0 = never and 10 = always; p-values are from a one-way ANOVA. DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; sd: Standard deviation. Modified after (38)

3.5 Section 4: Engagement methods

Participants rated the desirable frequency of a given method to be used for stakeholder engagement. Among DACH respondents, the Nominal Group Technique, Smartphone Application, Webinar, and (Online) Survey were items with the lowest ratings (Table 4). Especially ratings for digital methods differed between groups and were rated lowest by DACH respondents. For example, smartphone application use reached a mean of 5.04±2.4 in DACH, while respondents from North America rated it with a mean of 6.59±1.9 and from China with 8.28±2.5 (p < 0.001). The Webinar was rated with a mean of 5.07±2.9 in DACH, 7.11±2.3 in North America, and 8.09±2.6 in China (p < 0.001).

The analog method of personal meeting reached higher means in respondents from DACH with 7.85±2.4, from North America with 7.2±2.3, and China with 7.49±2.8 (p = 0.631). The item 'focus group' was rated with a mean of 6.36±2.2 in respondents from DACH, 7.05±1.9 from North America and 7.63±2.7 from China (p = 0.043).

Table 4: Participant's ratings of "Which methods of stakeholder engagement should be used?"

Item/Group	DACH mean (sd)	North Amercia mean (sd)	China mean (sd)	p-value
Advisory group	6.84 (2.46)	7.44 (2.01)	8.48 (2.18)	0.002
DELPHI method	5.62 (2.54)	6.40 (1.84)	7.86 (2.91)	0.001
Expert panel	7.41 (2.04)	7.16 (1.57)	8.60 (1.99)	0.001
Focus group	6.36 (2.23)	7.05 (1.87)	7.62 (2.67)	0.043
Interviews	6.53 (2.26)	7.16 (1.89)	8.00 (2.30)	0.004
Nominal group Technique	5.00 (2.49)	6.00 (1.34)	7.04 (3.03)	0.076
(Online) survey	5.22 (2.55)	6.11 (2.11)	8.60 (1.92)	< 0.001
Personal meeting	7.85 (2.42)	7.20 (2.26)	7.49 (2.78)	0.631
Written information	7.11 (2.66)	7.40 (2.06)	7.98 (2.60)	0.200
Smartphone application	5.04 (2.43)	6.59 (1.87)	8.28 (2.51)	< 0.001
Stakeholder mapping	6.75 (2.34)	6.79 (1.93)	7.47 (3.04)	0.556
ResearchKit (Apple)	5.40 (2.22)	5.70 (1.70)	6.52 (3.65)	0.517
Telephone conference	5.93 (2.59)	7.80 (1.94)	7.25 (3.23)	0.026
Webinar	5.07 (2.86)	7.11 (2.33)	8.09 (2.62)	< 0.001
Workshop	6.76 (2.20)	7.30 (2.39)	8.53 (2.28)	< 0.001

Shown values are the means of the response by group on a scale from 0 to 10 with 0 = never and 10 = always; p-values are from a one-way ANOVA. DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; sd: Standard deviation. Modified after (38)

3.6 Section 5: Levels, tools, and stages of engagement

We asked participants about their preferred quality of stakeholder engagement in the research process. Should the engagement be a consulting partnership, have the nature of a collaboration, or should stakeholders be assigned a leading role in the research process? Respondents from DACH agreed to the consulting partnership with the highest mean (DACH 8.11±2.6, North America 7.90±2.4, China 7.91±2.6), to the collaborative relationship with a lower one (DACH 7.05±2.8, North America 8.20±2.1, China 8.07±2.5). Agreement to a leading stakeholder role was the lowest with a mean of 4.45±3.3 in respondents from DACH, 5.50±2.6 in North America, and 6.55±3.2 in those from China (see Table 5).

Table 5: Opinion on levels of stakeholder engagement as reported in the survey

Item/ Group	DACH mean (sd)	North America mean (sd)	China mean (sd)	p-value
Stakeholders should be engaged in clinical research as consulting partners	8.11 (2.58)	7.90 (2.40)	7.91 (2.62)	0.924
Stakeholders should be engaged in clinical research as collaborative partners	7.05 (2.78)	8.20 (2.14)	8.07 (2.52)	0.112
Stakeholders should have a leading role in the research process	4.45 (3.28)	5.50 (2.59)	6.55 (3.16)	0.005

Shown values are the means of the response by group on a scale from 0 to 10 with 0 = do not agree at all and 10 = agree completely; p-values are from a one-way ANOVA. DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; sd: Standard deviation. Modified after (38)

In addition, participants were asked for their recommendation of communication tools for future stakeholder engagement. In this question, technology (email, instant messaging, online blog, online forum, smartphone application, SMS, social network, website) and person-based methods (personal meeting, mail, phone call) were represented. 'Email' as communication tool was rated with very similar means in all groups (DACH 8.89±2.0, North America 8.17±2.4, China 8.99±1.9, p = 0.293). 'Instant messaging' resulted in highly differing means (DACH 3.73±3.6, North America 5.06±3.1 and China 9.26±1.4, p < 0.001), as well as 'Smartphone application' (DACH 4.67±2.6, North America 5.94±2.7, China 8.79±2.3, p < 0.001) (38). The item 'personal meeting' got the highest mean amongst respondents from DACH with 8.79±1.9 when compared to North America (8.11±2.2) and China (7.49±3.1, see Table 6).

Table 6: Respondent's ratings of "Which communication tools should be used?"

Item/Group	DACH mean (sd)	North America mean (sd)	China mean (sd)	p-value
Email	8.89 (2.01)	8.17 (2.36)	8.99 (1.92)	0.293
Instant messaging	3.73 (3.63)	5.06 (3.12)	9.26 (1.37)	< 0.001
Online blog	3.43 (3.01)	4.75 (2.57)	6.00 (3.93)	0.004
Online forum	5.46 (2.84)	6.06 (2.32)	7.15 (3.44)	0.028
Personal meeting	8.79 (1.87)	8.11 (2.18)	7.49 (3.07)	0.045
Mail	4.46 (3.32)	4.06 (3.24)	4.51 (3.90)	0.894
Smartphone application	4.67 (2.58)	5.94 (2.72)	8.79 (2.25)	< 0.001
SMS (text message)	2.82 (2.53)	5.89 (2.87)	7.14 (3.41)	< 0.001
Social network	4.34 (3.33)	5.72 (2.59)	6.08 (3.87)	0.075
Phone call	8.29 (1.96)	7.00 (3.36)	8.44 (2.26)	0.065
Website	7.06 (2.73)	6.88 (2.09)	8.30 (2.67)	0.024

Shown values are the means of the response by group on a scale from 0 to 10 with 0 = never and 10 = always; p-values are from a one-way ANOVA. DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; sd: Standard deviation. Modified after (38)

We also addressed the question in which research stages stakeholders should be engaged. Analysis showed that participants from DACH compared to North America and China rated with lower means across all items other than 'implementation of results'. The frequency of stakeholder engagement in the implementation phase (0 = never, 10 = always) was rated with a mean of 8.50±2.2 by respondents from DACH, with 7.90±2.6 from America and with 8.72±2.1 from China (p = 0.0357). Engagement in the study design phase was assessed by respondents from DACH with a mean of 6.38±2.9, from North America with 7.26±2.8, and from China with 8.54±2.3 (p < 0.001). For detailed results, see Table 7.

Table 7: Opinion on research stage in which stakeholders should be engaged

Item/Group	DACH mean (sd)	North America mean (sd)	China mean (sd)	p-value
Selection and prioritizing of research topics	7.21 (2.99)	8.10 (2.34)	8.91 (1.71)	0.002
Development of the research question	7.61 (2.41)	7.95 (2.40)	8.90 (2.02)	0.012
Outcome definition	6.71 (3.08)	8.10 (2.43)	8.19 (2.76)	0.031
Study design	6.38 (2.88)	7.26 (2.79)	8.54 (2.25)	< 0.001
Pretest	7.19 (2.58)	8.11 (2.32)	8.46 (2.19)	0.035
Analysis of results	5.53 (3.50)	6.68 (2.89)	8.13 (2.71)	< 0.001
Publication of results	6.68 (3.16)	7.05 (2.74)	8.57 (2.28)	0.001
Implementation of results	8.50 (2.23)	7.90 (2.65)	8.72 (2.07)	0.0357

Shown values are the means of the response by group on a scale from 0 to 10 with 0 = never and 10 = always; p-values are from a one-way ANOVA. DACH: Germany (D), Austria (A), Switzerland (CH); North America: USA and Canada; sd: Standard deviation. Modified after (38)

3.7 Section 6: Challenges and Potential

First, we assessed which general framework is necessary for researchers to implement stakeholder engagement. The need for a standardized definition was rated low in DACH and North America (5.84±2.9; 6.26±2.8) and higher in China (9.19±1.4, p < 0.001). Similarly, the need for guidelines was scored low in DACH (5.69±3.2) and higher in North America (8.47±1.8) and China 8.95±1.8, p < 0.001) (38). Existing interest on the part of stakeholders as a requirement was rated high among all three groups with 8.73±1.7 in DACH, 9.05±2.2 in North America, and 8.72±1.7 in China (p = 0.754). Each of the other items was considered less necessary from the DACH group compared to higher ratings by North America and China (see Table 8). For example, the necessity of funding programs for studies using stakeholder engagement was rated with 6.74±3.1 in DACH, 8.37±2.3 in North America, and 8.74±1.8 in China.

Regarding potential benefits and downsides of stakeholder engagement, participants were asked to express their agreement to a set of statements. Participants agreed to a low extent on stakeholder engagement leading to additional financial costs (DACH 3.08±3.2, North America 2.74±2.5, China 3.48±2.8, p = 0.572). They instead see a high burden on human resources (DACH 8.0±3.2, North America 6.42±3.0, China 5.44±3.1, p = 0.049) and workload for researchers and stakeholders (see Table 8). The pitfall of lobbyism was considered slightly different between groups with 6.33±2.8 in DACH, 5.05±2.6

in North America, and 7.05±2.9 in China (p = 0.026). Participants agreed with a high mean that stakeholder engagement might lead to more relevant research (DACH 8.05±2.4, North America 8.75±1.7, China 7.71±2.3, p = 0.200). The impact on transparency and recruitment facilitation was evaluated differently among the three groups (see Table 8).

Table 8: Participant's opinion about necessary factors, advantages, and disadvantages of stakeholder engagement (38)

Question/ Group	DACH mean (sd)	North America mean (sd)	China mean (sd)	p-value$
Which of the following factors are necessary to foster stakeholder engagement in research?#				
Standardized definition of stakeholder engagement	5.84 (2.91)	6.26 (2.75)	9.19 (1.40)	< 0.001
Stakeholders interest in participation	8.73 (1.71)	9.05 (2.16)	8.72 (1.71)	0.754
Publication of guidelines for stakeholder engagement	5.69 (3.20)	8.47 (1.78)	8.95 (1.77)	< 0.001
Institutional infrastructure	6.55 (2.55)	8.33 (1.78)	8.72 (1.79)	< 0.001
Funding programs to support researchers adopt stakeholder engagement	6.74 (3.08)	8.37 (2.27)	8.74 (1.78)	< 0.001
Funding to do research about stakeholder engagement	6.45 (2.84)	7.16 (2.57)	8.55 (1.81)	< 0.001
Stakeholder engagement…*				
Leads to additional financial costs	3.08 (3.18)	2.74 (2.49)	3.48 (2.76)	0.572
Places a high burden on the human resources of a research team	8.00 (3.24)	6.42 (2.99)	5.44 (3.14)	0.049
Will not lead to widely applicable study results because it only takes individual perspectives into consideration	3.87 (3.25)	2.28 (2.24)	4.29 (3.24)	0.060
Leads to lobbyism, meaning the organized influence of particular groups on clinical research	6.33 (2.76)	5.05 (2.55)	7.05 (2.91)	0.026
Implies higher workload for researchers	7.38 (2.98)	7.00 (2.91)	6.46 (2.88)	0.300
Constitutes a higher workload for potential stakeholders	7.58 (2.33)	7.00 (2.52)	6.28 (2.87)	0.058
Enables external persons to participate in a research project	7.36 (2.43)	8.37 (1.61)	8.17 (1.90)	0.100
Integrates individual perspectives of decision makers into the research process, which may lead to more relevant research	8.05 (2.42)	8.75 (1.74)	7.71 (2.29)	0.200
Includes empirical values/data in the research process	8.05 (2.70)	7.11 (1.78)	7.35 (2.28)	0.247
Strengthens patients' rights to participate in health care decision-making	6.42 (3.19)	7.32 (2.52)	8.30 (1.85)	0.001
Increases the relevance of research questions and outcomes	6.95 (2.80)	8.05 (2.33)	8.37 (1.79)	0.009
Leads to implementable research results	6.25 (2.71)	6.95 (2.57)	8.39 (1.68)	< 0.001
Has a positive impact on the transparency of research institutions	5.13 (2.68)	7.56 (1.62)	8.42 (1.43)	< 0.001
Strengthens the trust in research results of all persons involved	7.43 (2.67)	8.15 (2.28)	8.31 (1.77)	0.141
Enhances the adherence of study participants	6.05 (2.86)	6.32 (2.69)	8.23 (1.91)	< 0.001
Facilitates recruitment	4.69 (2.73)	6.74 (2.96)	7.72 (2.07)	< 0.001

This item was scaled from 0 to 10 with 0 = not necessary at all and 10 = very necessary.
* This item was scaled from 0 to 10 with 0 = do not agree at all and 10 = agree completely.
$ P-value from a one-way ANOVA.
DACH: Germany (D), Austria (A) and Switzerland (CH); North America: USA and Canada

4.   Discussion

4.1   Summary of the results

We found relevant differences in knowledge about stakeholder engagement across the three groups. One third of the participants from DACH did not know the term stakeholder engagement, whereas in North America, almost all the participants knew the term. Researchers from North America and China agreed that stakeholder engagement is important in current research. In contrast, researchers from DACH consider its role as low in contemporary - but impute high importance in future research. They have little experience with engaging stakeholders who are not clinicians or researchers. Nevertheless, they aim to engage different groups of stakeholders in future research. The disposition of using digital methods is lower among DACH researchers compared to researchers from North America and China.

The benefits of stakeholder engagement are perceived divergently. Researchers from DACH do not accredit stakeholder engagement a great effect on the facilitation of recruitment or the transparency of research institutions. On the other hand, they agree on stakeholder engagement leading to more relevant research, strengthening patients' rights, and the general trust in study results. Researchers from North America and China agree to a higher level on these potential advantages of stakeholder engagement.

Researchers from all groups do not see financial costs as a great challenge. Compared to the researchers from North America and China, researchers from DACH consider guidelines, definitions, funding, and institutional infrastructure as less critical.

4.2   What you don't know won't hurt you?

Our data shows that the concept of stakeholder engagement is neither well known nor well established in researchers' practice in German-speaking countries. This is contrasted by the fact that researchers emphasize stakeholder engagement for future research. But what keeps researchers from implementing stakeholder engagement? We cannot answer this question conclusively. However, our research results give valuable insights. Participants from DACH, having little knowledge about stakeholder engagement, do not state a high need for stakeholder engagement guidelines, whereas participants from North America and China put a higher emphasis on the organizational frame. It is conceivable that researchers with less practical experiences underestimate the need for

institutional and funding structures. Instead, they put high responsibility on stakeholders who should show interest in research to allow engagement.

Unexpectedly, researchers from DACH did not think of stakeholder engagement as a cause of additional financial costs but as an extra burden on human resources. This is indicative of researchers not considering stakeholder engagement as a part of the declared costs in their initial research plan but as an "add-on" later in the process.

4.3   Comparison with the current state of research

This study is, to our knowledge, the first to assess the awareness about stakeholder engagement in DACH. Concannon et al. have reviewed stakeholder engagement reported by US researchers in PCORI and Comparative effectiveness research (CER) between 2003-2012. Their data shows "frequent engagement with patients, modestly frequent engagement with clinicians and infrequent engagement with stakeholders representing other key decision-makers across the healthcare system" (7). This is equally reflected in our results. We found a higher frequency in including patients, clinicians, and researchers as stakeholders among participants from North America. Payers, Industry, Hospitals, and policymakers were engaged less frequently.

A study by Knoepke et al. examines the dissemination practices and use of engagement by Dissemination and Implementation (D&I) researchers from the United States and Canada in reference to a survey conducted by Brownson et al. in 2012. The authors performed a similar survey in 2018, focusing on the aspect of stakeholder engagement (44), and compared the results to a study from 2012 (45). Asked in 2012 how often stakeholders are involved, 34% of survey respondents answered always/usually, 49% sometimes/rarely, and 17% never. 72% of respondents reported using stakeholder engagement in an advisory role, 62% worked with stakeholders to make their research relevant to the stakeholders setting, 59% aimed to understand how to enhance the relevance of their study to stakeholders (45). In 2018 participants were asked how often they meet with stakeholders during a research project. 7% stated not to involve stakeholders, 55% reported meeting "four or more times" with stakeholders, and 35% "two or three times" (44). These numbers correspond to our results, with 96% of participants from North America who know about stakeholder engagement and stated to have already engaged stakeholders. Knoepke et al. looked at methods to engage stakeholders by stakeholder type,

whereas we considered these aspects separately. This circumstance does not allow a direct comparison of numbers.

Nonetheless, in 2018 "focus groups" and "advisory committees" were the most used methods among respondents from the United States and Canada (44). Accordantly in our study, these items were rated highly by respondents from North America. Knoepke et al. found that researchers with D&I Training "were more likely to use a variety of stakeholder engagement in a number of ways" and "more likely to engage organizational and policy-level decision makers" (44). In our study, the engagement of policymakers was very low among all groups.

While conducting our research, the number of studies involving stakeholders and the recognition of the importance of stakeholder engagement increased (46-48). First guidance for reporting stakeholder engagement was published (49, 50), and an international research group is currently aiming to compile a comprehensive guide for stakeholder engagement in guideline developement (19). In 2018 the term "stakeholder participation" was introduced into the Medical Subject Headings (MeSH) database of the National Library of Medicine (NLM). However, it has been assigned to the anthropology and sociology section and is not yet included in the health care or methods section (51).

Recent studies have shown a more frequent application of digital technologies in the health system during the pandemic. In the United States, health technologies were used more extensively, especially in mental health, despite a lack of evidence-based evaluation of health apps (52). The NHS in the United Kingdom reported an accelerated use of digital technologies in patient care (53). Many methods or strategies were born out of necessity and have been rapidly implemented without being properly reviewed or tested (54). In our opinion, this rapidly evolving area stresses the need for the engagement of stakeholders from different fields, like end-users, designers, and developers.

4.4 Strengths of the study

This study is based on a broad literature review and performed in an international setting. The content has a clear outline focusing on the research question. We carefully selected the definition for stakeholder engagement and stakeholder groups from previous publications. The questionnaire was designed thoughtfully and ran through iterative pretesting

following the current guidelines for online surveys to ensure high quality and comparability.

The method of online survey is resource-efficient and user-centered. It allows to join information from different continents and research settings and expand the horizon beyond the national stakeholder engagement practices. The advantages of an online survey are the low demands on the IT skills of the participants and the fast feasibility. Leveraging a digital method and warranting data security, we reached a global sample. With the use of R, we performed a transparent and reproducible data analysis. Our findings are highly relevant in shaping the future of stakeholder engagement in DACH by providing the first systematically assessed information about researchers' experience with and positions towards stakeholder engagement.

4.5 Limitations of the study

A few issues may have led to a low response rate and thus limited the representativity of our sample. First, we decided on a detailed survey to cover the initially described aspects of stakeholder engagement. It could have exceeded participants' knowledge and capacities and led to dropouts. Second, double entries could not be prevented due to the anonymity of our survey (no IP address was collected); hence it was possible that the invitation was sent out repeatedly to the same person. For privacy reasons we did not list the recipients of the survey invitation and thus could not send out personal reminders. Outdated email addresses without reach or double entries on mailing lists were possible. Additionally, the technique of convenience sampling limits the generalizability of our results.

Using different languages, we opened the stage for linguistic and cultural bias. We did not conduct a separate iterative pretest per language and recognize that the wording and perspective of research structures and health systems are Eurocentric.

In 2021 an upgraded Checklist for Reporting Survey Studies (CROSS) was published to improve the quality of (online-) surveys (55). As our study followed the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) guidelines that the Equator Network recommended at the time of our study, we did not include all points of the latest checklist.

We decided to group our study participants by world regions, assuming each region has a particular research culture. Global mobility could soften this categorization. A researcher's knowledge and possibilities are determined not simply by her place of residence but depend on education and training. Consequently, it could be interesting to investigate another crucial factor like the specific area of research.

4.6   Implications for practice and future research

Our data shows the need for international exchange on an institutional level regarding stakeholder engagement implementation. A re-evaluation of the stakeholder practice using a condensed version of our questionnaire could allow longitudinal monitoring and comparison of stakeholder practice. We propose the development of training programs and workshops for researchers on how to engage stakeholders in DACH.

Researchers are not currently exploiting digital methods for building relationships with stakeholders. We see a great need for equipping researchers with digital skills. Another aspect the pandemic unveils is the relevance of building trust and collaborating with multi-stakeholders in health research. Stakeholder engagement is a chance to recognize relevant outcomes and strengthen societal backing and implementation of new research findings.

5. Conclusion

We see differing experiences and practices of stakeholder engagement in North America, China and DACH. At the time of our study, researchers from DACH showed a low level of knowledge about stakeholder engagement but assigned an essential role to stakeholder engagement in future research. The presumption that high financial costs would discourage researchers from applying stakeholder engagement was not confirmed.

To close the gap between current practice and future expectations, we suggest providing stakeholder engagement funding, albeit not merely in monetary form but rather equipping researchers with the necessary knowledge and the tools to apply stakeholder engagement in the field. Motivation for stakeholder engagement should be a well-formulated aim, not only a checkmark for funding purposes. To assess the fast changes in the research environment, we propose to conduct a condensed version of the survey and monitor researchers' approaches to stakeholder engagement.

Literaturverzeichnis

1. Freeman RE, McVea J. A Stakeholder Approach to Strategic Management. Oxford. 2001; https://ssrn.com/abstract=263511. Accessed June 9, 2021.

2. Freeman RE. Managing for Stakeholders. 2007; https://ssrn.com/abstract=1186402. Accessed June 9, 2021.

3. Concannon TW, Meissner P, Grunbaum JA, McElwee N, Guise JM, Santa J, Conway PH, Daudelin D, Morrato EH, Leslie LK. A new taxonomy for stakeholder engagement in patient-centered outcomes research. J Gen Intern Med. 2012;27(8):985-91.

4. Deverka PA, Lavallee DC, Desai PJ, Esmail LC, Ramsey SD, Veenstra DL, Tunis SR. Stakeholder participation in comparative effectiveness research: defining a framework for effective engagement. J Comp Eff Res. 2012;1(2):181-94.

5. Guise JM, O'Haire C, McPheeters M, Most C, Labrant L, Lee K, Barth Cottrell EK, Graham E. A practice-based tool for engaging stakeholders in future research: a synthesis of current practices. J Clin Epidemiol. 2013;66(6):666-74.

6. Schiller C, Winters M, Hanson HM, Ashe MC. A framework for stakeholder identification in concept mapping and health research: a novel process and its application to older adult mobility and the built environment. BMC Public Health. 2013;13:428.

7. Concannon TW, Fuster M, Saunders T, Patel K, Wong JB, Leslie LK, Lau J. A systematic review of stakeholder engagement in comparative effectiveness and patient-centered outcomes research. J Gen Intern Med. 2014;29(12):1692-701.

8. Lavallee DC, Wicks P, Alfonso Cristancho R, Mullins CD. Stakeholder engagement in patient-centered outcomes research: high-touch or high-tech? Expert Rev Pharmacoecon Outcomes Res. 2014;14(3):335-44.

9. Kim KK, Khodyakov D, Marie K, Taras H, Meeker D, Campos HO, Ohno-Machado L. A Novel Stakeholder Engagement Approach for Patient-centered Outcomes Research. Med Care. 2018;56 Suppl 10 Suppl 1:S41-S7.

10. Mallery C, Ganachari D, Fernandez J, Smeeding L, Robinson S, Moon M, Lavallee D, Siegel J. Innovative Methods in Stakeholder Engagement: An Environmental Scan. AHRQ Publication NO. 12-EHC097-EF. Rockville, MD: Agency for Healthcare Research and Quality. May 2012. http://www.effectivehealthcare.ahrq.gov/index.cfm/tools-and-resources/how-to-get-involved-in-the-effective-health-care-program/. Accessed June 9 2021.

11. DuBois JM, Antes AL. Five Dimensions of Research Ethics: A Stakeholder Framework for Creating a Climate of Research Integrity. Acad Med. 2018;93(4):550-5.

12. Goodman MS, Sanders Thompson VL. The science of stakeholder engagement in research: classification, implementation, and evaluation. Transl Behav Med. 2017;7(3):486-91.

13. Concannon TW, Grant S, Welch V, Petkovic J, Selby J, Crowe S, Synnot A, Greer-Smith R, Mayo-Wilson E, Tambor E, Tugwell P, Multi Stakeholder Engagement C. Practical Guidance for Involving Stakeholders in Health Research. J Gen Intern Med. 2019;34(3):458-63.

14. Woolf SH, Zimmerman E, Haley A, Krist AH. Authentic Engagement Of Patients And Communities Can Transform Research, Practice, And Policy. Health Aff (Millwood). 2016;35(4):590-4.

15. Brett J, Staniszewska S, Mockford C, Herron-Marx S, Hughes J, Tysall C, Suleman R. Mapping the impact of patient and public involvement on health and social care research: a systematic review. Health Expect. 2014;17(5):637-50.

16. Forsythe LP, Ellis LE, Edmundson L, Sabharwal R, Rein A, Konopka K, Frank L. Patient and Stakeholder Engagement in the PCORI Pilot Projects: Description and Lessons Learned. J Gen Intern Med. 2016;31(1):13-21.

17. Selby JV, Forsythe L, Sox HC. Stakeholder-Driven Comparative Effectiveness Research: An Update From PCORI. JAMA. 2015;314(21):2235-6.

18. Blödt S, Schützler L, Huang W, Pach D, Brinkhaus B, Hummelsberger J, Kirschbaum B, Kuhlmann K, Lao L, Liang F, Mietzner A, Mittring N, Müller S, Paul A, Pimpao-Niederle C, Roll S, Wu H, Zhu J, Witt CM. Effectiveness of additional self-care acupressure for women with menstrual pain compared to usual care alone: using stakeholder engagement to design a pragmatic randomized trial and study protocol. Trials. 2013;14(1):99.

19. Petkovic J, Riddle A, Akl EA, Khabsa J, Lytvyn L, Atwere P, Campbell P, Chalkidou K, Chang SM, Crowe S, Dans L, Jardali FE, Ghersi D, Graham ID, Grant S, Greer-Smith R, Guise JM, Hazlewood G, Jull J, Katikireddi SV, Langlois EV, Lyddiatt A, Maxwell L, Morley R, Mustafa RA, Nonino F, Pardo JP, Pollock A, Pottie K, Riva J, Schünemann H, Simeon R, Smith M, Stein AT, Synnot A, Tufte J, White H, Welch V, Concannon TW, Tugwell P. Protocol for the development of guidance for stakeholder engagement in health and healthcare guideline development and implementation. Syst Rev. 2020;9(1):21.

20. Hansen SL, Holetzek T, Heyder C, Wiesemann C. Stakeholder-Beteiligung in der klinischen Forschung: eine ethische Analyse. Ethik in der Medizin. 2018;30(4):289-305.

21. Esmail L, Moore E, Rein A. Evaluating patient and stakeholder engagement in research: moving from theory to practice. J Comp Eff Res. 2015;4(2):133-45.

22. Morain SR, Concannon TW, Wittenberg E. HIV, breast cancer and vaccines: what do high-profile cases reveal about stakeholder engagement in research? J Comp Eff Res. 2017;6(1):43-9.

23. Brereton L, Ingleton C, Gardiner C, Goyder E, Mozygemba K, Lysdahl KB, Tummers M, Sacchini D, Leppert W, Blaževičienė A, van der Wilt GJ, Refolo P, De Nicola M, Chilcott J, Oortwijn W. Lay and professional stakeholder involvement in scoping palliative care issues: Methods used in seven European countries. Palliat Med. 2017;31(2):181-92.

24. Lavery JV. Building an evidence base for stakeholder engagement. Science. 2018;361(6402):554-6.

25. PCORI. Our Story. 2014. Patient-Centered Outcomes Research Institute. Available from: https://www.pcori.org/about-us/our-story. Accessed June 9, 2021.

26. NIHR. About INVOLVE. 2021. National Institute for Health Research. . Available from: https://www.invo.org.uk/about-involve/. Accessed June 9, 2021.

27. SPOR. Strategy for Patient-Oriented Research. 2021. Canadian Institutes of Health Research. Available from: https://cihr-irsc.gc.ca/e/41204.html. Accessed June 8, 2021.

28. PCORI. The Value of Engagement. 2018. Patient-Centered Outcomes Research Institute. Available from: https://www.pcori.org/engagement/value-engagement. Accessed June 9, 2021.

29. BIH. Patient & Stakeholder Engagement 2021. Berlin Institute of Health at Charite. Available from: https://www.bihealth.org/en/translation/innovation-enabler/quest-center/service/stakeholder-engagement. Accessed June 8, 2021.

30. Blödt S, Pach D, Roll S, Witt CM. Effectiveness of app-based relaxation for patients with chronic low back pain (Relaxback) and chronic neck pain (Relaxneck): study protocol for two randomized pragmatic trials. Trials. 2014;15:490.

31. Groves RM, Fowler Jr. FJ, Couper MP, Lepkowski JM, Singer E, Tourangeau R. Survey methodology. 2. ed. ed. Hoboken, NJ: Wiley; 2009.

32. Ritter P, Lorig K, Laurent D, Matthews K. Internet versus mailed questionnaires: a randomized comparison. J Med Internet Res. 2004;6(3):e29.

33. Schonlau M. Will web surveys ever become part of mainstream research? J Med Internet Res. 2004;6(3):e31.

34. Leiner DJ. SoSci Survey 2016. Available from: https://www.soscisurvey.de/. Accessed 2016.

35. Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). J Med Internet Res. 2004;6(3):e34.

36. Kelley K, Clark B, Brown V, Sitzia J. Good practice in the conduct and reporting of survey research. Int J Qual Health Care. 2003;15(3):261-6.

37. Allmendinger J. Das Land, in dem wir leben wollen: wie die Deutschen sich ihre Zukunft vorstellen / Jutta Allmendinger. Erste Auflage ed. München: Pantheon; 2017.

38. Heiß A, Wang J, Fei Y, Xia R, Icke K, Pach D, Witt CM. Current practice of stakeholder engagement: researchers' experiences in North America, DACH countries and China. J Comp Eff Res. 2021;10(9):751-61.

39. R Developement Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statsitical Computing; 2017.

40. Yoshida K, Bartel A. tableone: Create ‚Table 1' to Describe Baseline CHaracteristics with or without Prospensity Socre Weights. R package version 0.12.0 ed2020.

41. Wickham H, Averick M, Bryan J, Chang W, D'Agostino McGowan L, François R, Grolemund G, Hayes A, Henry L, Hester J, Kuhn M, Lin Pedersen T, Miller E, Bache S, Müller K, Ooms J, Robinson D, Paige Seidel D, Spinu V, Takahashi K, Vaughan

D, Wilke C, Woo K, Yutani H. Welcome to the tidyverse. Journal of Open Source Software. 2019;4(43):1686.

42. Fox J, Weisberg S. An R companion to applied regression / John Fox, Sanford Weisberg. 3rd edition ed. Los Angeles: Sage; 2019.

43. Lenth R. emmeans: Estimated Marginal Means, aka Least-Squares Means. R package version 1.5.4 ed2021.

44. Knoepke CE, Ingle MP, Matlock DD, Brownson RC, Glasgow RE. Dissemination and stakeholder engagement practices among dissemination & implementation scientists: Results from an online survey. PLoS One. 2019;14(11):e0216971.

45. Brownson RC, Jacobs JA, Tabak RG, Hoehner CM, Stamatakis KA. Designing for Dissemination Among Public Health Researchers: Findings From a National Survey in the United States. American Journal of Public Health. 2013;103(9):1693-9.

46. Beneciuk JM, Verstandig D, Taylor C, Scott D, Levin J, Osborne R, Bialosky JE, Lentz TA, Buck T, Davis AL, Harder C, Beneciuk MB, Wittmer V, Sylvester J, Rowe R, McInnes D, Fisher TP, McGarrie L. Musculoskeletal pain stakeholder engagement and partnership development: determining patient-centered research priorities. Res Involv Engagem. 2020;6:28.

47. Schleimer E, Pearce J, Barnecut A, Rowles W, Lizee A, Klein A, Block VJ, Santaniello A, Renschen A, Gomez R, Keshavan A, Gelfand JM, Henry RG, Hauser SL, Bove R. A Precision Medicine Tool for Patients With Multiple Sclerosis (the Open MS BioScreen): Human-Centered Design and Development. J Med Internet Res. 2020;22(7):e15605.

48. Mathioudakis AG, Abroug F, Agusti A, Bakke P, Bartziokas K, Beghe B, Bikov A, Bradbury T, Brusselle G, Cadus C, Coleman C, Contoli M, Corlateanu A, Corlateanu O, Criner G, Csoma B, Emelyanov A, Faner R, Romero GF, Hammouda Z, Horváth P, Huerta AG, Jacobs M, Jenkins C, Joos G, Kharevich O, Kostikas K, Lapteva E, Lazar Z, Leuppi JD, Liddle C, López-Giraldo A, McDonald VM, Nielsen R, Papi A, Saraiva I, Sergeeva G, Sioutkou A, Sivapalan P, Stovold E, Wang H, Wen F, Yorke J, Williamson PR, Vestbo J, Jensen JU. Core outcome set for the management of acute exacerbations of chronic obstructive pulmonary disease: the COS-AECOPD ERS Task Force study protocol. ERJ Open Res. 2020;6(3).

49. Staniszewska S, Brett J, Simera I, Seers K, Mockford C, Goodlad S, Altman DG, Moher D, Barber R, Denegri S, Entwistle A, Littlejohns P, Morris C, Suleman R, Thomas V, Tysall C. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. BMJ. 2017;358:j3453.

50. Pollock A, Campbell P, Struthers C, Synnot A, Nunn J, Hill S, Goodare H, Morris J, Watts C, Morley R. Development of the ACTIVE framework to describe stakeholder involvement in systematic reviews. J Health Serv Res Policy. 2019;24(4):245-55.

51. National Center for Biotechnology Information, U.S. National Library of Medicine. MeSH Stakeholder Participation. 2018. Available from: https://www.ncbi.nlm.nih.gov/mesh/2023140. Accessed June 9, 2021.

52. Sorkin D, Janio E, Eikey E, Schneider M, Davis K, Schueller S, Stadnick N, Zheng K, Neary M, Safani D, D M. Rise in Use of Digital Mental Health Tools and

Technologies in the United States During the COVID-19 Pandemic: Survey Study. J Med Internet Res. 2021;23((4)).

53. Hutchings R. The impact of Covid-19 on the use of digital technology in the NHS. London, UK; 2020. https://www.nuffieldtrust.org.uk/research/the-impact-of-covid-19-on-the-use-of-digital-technology-in-the-nhs Accessed October 7, 2021.

54. Budd J, Miller BS, Manning EM, Lampos V, Zhuang M, Edelstein M, Rees G, Emery VC, Stevens MM, Keegan N, Short MJ, Pillay D, Manley E, Cox IJ, Heymann D, Johnson AM, McKendry RA. Digital technologies in the public-health response to COVID-19. Nature Medicine. 2020;26(8):1183-92.

55. Sharma A, Minh Duc NT, Luu Lam Thang T, Nam NH, Ng SJ, Abbas KS, Huy NT, Marusic A, Paul CL, Kwok J, Karbwang J, de Waure C, Drummond FJ, Kizawa Y, Taal E, Vermeulen J, Lee GHM, Gyedu A, To KG, Verra ML, Jacqz-Aigrain EM, Leclercq WKG, Salminen ST, Sherbourne CD, Mintzes B, Lozano S, Tran US, Matsui M, Karamouzian M. A Consensus-Based Checklist for Reporting of Survey Studies (CROSS). J Gen Intern Med. 2021;36(10):3179-87.

Eidesstattliche Versicherung

„Ich, Anna Jana Lisa Heiß, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: „Stakeholder Engagement als Optimierungsmöglichkeit klinischer Studien" (Stakeholder engagement for optimization of clinical studies) selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe. Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren/innen beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) werden von mir verantwortet.

Ich versichere ferner, dass ich die in Zusammenarbeit mit anderen Personen generierten Daten, Datenauswertungen und Schlussfolgerungen korrekt gekennzeichnet und meinen eigenen Beitrag sowie die Beiträge anderer Personen korrekt kenntlich gemacht habe (siehe Anteilserklärung). Texte oder Textteile, die gemeinsam mit anderen erstellt oder verwendet wurden, habe ich korrekt kenntlich gemacht.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit der Erstbetreuerin, angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.og) zur Autorenschaft eingehalten. Ich erkläre ferner, dass ich mich zur Einhaltung der Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis verpflichte.

Weiterhin versichere ich, dass ich diese Dissertation weder in gleicher noch in ähnlicher Form bereits an einer anderen Fakultät eingereicht habe.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§§156, 161 des Strafgesetzbuches) sind mir bekannt und bewusst."

Datum   Unterschrift

Anteilserklärung an den erfolgten Publikationen

Anna Jana Lisa Heiß hatte folgenden Anteil an der folgenden Publikation:

Publikation 1: Heiß, A., Wang, J., Fei, Y., Xia, R., Icke, K., Pach, D., Witt, C. M. Current practice of stakeholder engagement: researchers' experiences in North America, DACH countries and China. J Comp Efff Res. 2021.

Thema: Das Thema ist eingebettet in die Forschungstätigkeit der Arbeitsgruppe Integrative Medizin und Digitale Gesundheit des Institutes für Sozialmedizin, Epidemiologie und Gesundheitsökonomie unter der Leitung von Frau Prof. C. Witt.

Literaturrecherche: Die Auswahl der Literatur erfolgte eigenständig durch die Promovierende AH.

Studiendesign und Genehmigung: Die Literaturrecherche zur Forschungsfrage und Methodik erfolgte eigenständig durch die Promovendin. Die erste Version des Fragebogens sowie des Ethikantrages für die Studie wurde von der Promovendin verfasst. Hierzu wandte AH die im Rahmen der Design Thinking Basic Tracks an der School of Design Thinking, HPI Potsdam erworbenen Fertigkeiten an. Die online Version des Fragebogens wurde von AH eigenständig erstellt.

Durchführung: Die Erhebung der Daten erfolgte im Verbund mit den internationalen Kooperationspartner*innen. AH beteiligte sich an der Kontaktaufnahme zu Studienteilnehmer*innen und dokumentierte das Studienprotokoll.

Auswertung: Die Aufbereitung, statistischen Auswertungen und graphische Darstellung der Daten erfolgten durch AH. Zur Erlangung der notwendigen Qualifikation besuchte AH Kurse zur Guten Wissenschaftlichen Praxis, ein Dokorandenkolloquium sowie die Workshops „Introduction to Reproducible Research with R" und „Advanced Reproducible Research with R". Dabei wurde die Promovierende von Dr. D. Pach supervidiert, mit ihm wurden Fragen und Unklarheiten in regelmäßigen gemeinsamen Sitzungen diskutiert.

Publikation: Die erste Version des Artikels wurde maßgeblich durch AH verfasst. Insbesondere an der Einleitung und Gliederung hatte AH Anteil. Anmerkungen aus den Diskussionen mit den Co-Autor*innen wurden von AH eingearbeitet. Im Peer-Review-Prozess führte AH inhaltliche Ergänzungen und formelle Korrekturen durch. Tabelle 1 und 2 sowie Graphik 2 und 3 der Publikation entstanden aus der statistischen Auswertung von AH und wurden von AH eigenständig entworfen. Zur Präsentation der Ergebnisse wurde ein Poster von AH vorbereitet.

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Unterschrift, Datum und Stempel des/der erstbetreuenden Hochschullehrers/in

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Unterschrift des Doktoranden/der Doktorandin

Auszug aus der Journal Summary List

Journal Data Filtered By: **Selected JCR Year: 2019** Selected Editions: SCIE,SSCI
Selected Categories: **"HEALTH CARE SCIENCES and SERVICES"**
Selected Category Scheme: WoS
Gesamtanzahl: 102 Journale

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	BMJ Quality & Safety	5,825	6.084	0.015370
2	Implementation Science	10,777	5.531	0.020190
3	ACADEMIC MEDICINE	17,605	5.354	0.028860
4	HEALTH AFFAIRS	17,516	5.331	0.047430
5	JOURNAL OF MEDICAL INTERNET RESEARCH	16,349	5.034	0.029410
6	JOURNAL OF CLINICAL EPIDEMIOLOGY	28,878	4.952	0.028410
7	VALUE IN HEALTH	10,040	4.748	0.017370
8	JOURNAL OF GENERAL INTERNAL MEDICINE	20,229	4.597	0.026960
9	MEDICAL EDUCATION	10,598	4.570	0.011180
10	Journal of Personalized Medicine	617	4.433	0.001950
11	JMIR mHealth and uHealth	4,226	4.313	0.010020
12	MILBANK QUARTERLY	3,822	4.195	0.004300
13	JOURNAL OF THE AMERICAN MEDICAL INFORMATICS ASSOCIATION	9,959	4.112	0.017380
14	International Journal of Health Policy and Management	1,463	3.821	0.004860
15	PALLIATIVE MEDICINE	5,413	3.739	0.008460
16	PHARMACOECONOMICS	5,150	3.563	0.009120
17	Internet Interventions-The Application of Information Technology in Mental and Behavioural Health	996	3.513	0.002720
18	HEALTH TECHNOLOGY ASSESSMENT	5,573	3.370	0.009440
19	Patient-Patient Centered Outcomes Research	1,204	3.226	0.003990

Selected JCR Year: 2019; Selected Categories: "HEALTH CARE SCIENCES and SERVICES"

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
20	MEDICAL CARE RESEARCH AND REVIEW	2,459	3.212	0.003300
21	MEDICAL CARE	20,261	3.210	0.019020
22	JOURNAL OF PAIN AND SYMPTOM MANAGEMENT	10,897	3.077	0.014840
23	JOURNAL OF MEDICAL SYSTEMS	5,695	3.058	0.007050
24	BMC Medical Research Methodology	11,581	3.031	0.018590
24	Journal of Patient Safety	1,094	3.031	0.002310
26	INTERNATIONAL JOURNAL OF MEDICAL INFORMATICS	5,368	3.025	0.007110
27	Journal of Managed Care & Specialty Pharmacy	1,667	3.021	0.005780
28	HEALTH EXPECTATIONS	3,600	3.008	0.008230
29	Health Informatics Journal	981	2.932	0.001530
30	JOURNAL OF HEALTH ECONOMICS	7,404	2.827	0.014020
31	QUALITY OF LIFE RESEARCH	14,492	2.773	0.018650
32	International Journal of Integrated Care	1,245	2.753	0.001750
33	HEALTH POLICY AND PLANNING	5,413	2.704	0.010540
34	BMJ Supportive & Palliative Care	1,309	2.681	0.003390
35	JOURNAL OF RURAL HEALTH	2,005	2.667	0.003100
36	MEDICAL TEACHER	8,633	2.654	0.009410
37	SUPPORTIVE CARE IN CANCER	12,842	2.635	0.021660
38	JOURNAL OF TELEMEDICINE AND TELECARE	2,703	2.616	0.003430
39	ADVANCES IN HEALTH SCIENCES EDUCATION	2,696	2.480	0.004210
40	Applied Health Economics and Health Policy	1,234	2.442	0.003140
41	Risk Management and Healthcare Policy	549	2.429	0.001530

Selected JCR Year: 2019; Selected Categories: "HEALTH CARE SCIENCES and SERVICES"

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
42	HEALTH SERVICES RESEARCH	8,160	2.351	0.014390
43	Health and Quality of Life Outcomes	8,924	2.344	0.010980
44	MEDICAL DECISION MAKING	5,291	2.309	0.007670
45	STATISTICAL METHODS IN MEDICAL RESEARCH	4,647	2.291	0.011850
46	HEALTH ECONOMICS	6,113	2.250	0.011200
47	American Health and Drug Benefits	594	2.220	0.001550
48	HEALTH POLICY	7,254	2.212	0.009010
49	EUROPEAN JOURNAL OF CANCER CARE	3,303	2.161	0.005980
50	SCANDINAVIAN JOURNAL OF PRIMARY HEALTH CARE	1,509	2.160	0.001820
51	Population Health Management	901	2.138	0.002570
52	JOURNAL OF PALLIATIVE MEDICINE	5,913	2.085	0.009950
53	Disability and Health Journal	1,446	2.056	0.003510
54	Expert Review of Pharmacoeconomics & Outcomes Research	1,716	2.032	0.003020
55	BMC Palliative Care	1,610	2.015	0.003950
56	BMC HEALTH SERVICES RESEARCH	18,006	1.987	0.037740
57	Informatics for Health & Social Care	396	1.982	0.000680
58	JOURNAL OF MEDICAL ECONOMICS	2,093	1.958	0.004780
59	INTERNATIONAL JOURNAL FOR QUALITY IN HEALTH CARE	5,531	1.957	0.004920
60	Telemedicine and e-Health	3,535	1.931	0.005830
61	International Journal of Evidence-Based Healthcare	1,013	1.930	0.002410
62	Healthcare	1,049	1.916	0.003210
63	Journal of Multidisciplinary Healthcare	1,033	1.913	0.002510

Selected JCR Year: 2019; Selected Categories: "HEALTH CARE SCIENCES and SERVICES"

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
64	Therapeutics and Clinical Risk Management	3,223	1.888	0.006190
65	JOURNAL OF HEALTH POLITICS POLICY AND LAW	1,154	1.878	0.002850
66	TEACHING AND LEARNING IN MEDICINE	1,448	1.848	0.002370
67	Journal of Healthcare Engineering	1,006	1.803	0.001690
68	Simulation in Healthcare-Journal of the Society for Simulation in Healthcare	1,501	1.761	0.002100
69	Journal of Interprofessional Care	2,814	1.726	0.003130
70	Annals of Palliative Medicine	613	1.681	0.001730
70	JOURNAL OF EVALUATION IN CLINICAL PRACTICE	4,009	1.681	0.004990
72	AMERICAN JOURNAL OF MANAGED CARE	4,380	1.679	0.007330
73	JOURNAL OF SCHOOL HEALTH	3,858	1.673	0.003730
74	American Journal of Hospice & Palliative Medicine	2,182	1.638	0.004170
75	Current Opinion in Supportive and Palliative Care	1,133	1.618	0.002350
76	HASTINGS CENTER REPORT	1,530	1.608	0.002170
77	JOURNAL OF BEHAVIORAL HEALTH SERVICES & RESEARCH	1,200	1.590	0.001870
78	EVALUATION & THE HEALTH PROFESSIONS	1,324	1.578	0.001160
79	METHODS OF INFORMATION IN MEDICINE	1,379	1.574	0.001540
80	Gaceta Sanitaria	1,809	1.564	0.001770
81	JOURNAL OF PUBLIC HEALTH POLICY	1,011	1.500	0.001430
82	INTERNATIONAL JOURNAL OF TECHNOLOGY ASSESSMENT IN HEALTH CARE	2,236	1.494	0.002050
83	Journal of Comparative Effectiveness Research	613	1.468	0.001810

Selected JCR Year: 2019; Selected Categories: "HEALTH CARE SCIENCES and SERVICES"

Druckexemplar der Publikation

Current practice of stakeholder engagement: researchers' experiences in North America, DACH countries and China

Journal of **Comparative Effectiveness Research**

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Aim: To explore the current practice of stakeholder engagement in clinical trials and its evaluation in North America (USA and Canada), DACH countries (Germany, Austria and Switzerland) and China. **Participants & methods:** We conducted a web-based, anonymous, international, cross-sectional online survey for clinical researchers. Data were analyzed using descriptive and explorative statistical analysis including analysis of variance and analysis of covariance. **Results:** Stakeholder engagement is more prominent and higher accepted among researchers in North America. Researchers in DACH countries have less knowledge of the stakeholder engagement method and are less likely to apply it. **Conclusion:** Stakeholder engagement is perceived very differently among participants from DACH countries, North America and China. For a broader acceptance and implementation institutional support and motivational conditions might be needed.

Stakeholder engagement is defined as the active involvement of an 'individual or group who is responsible for or affected by health – and healthcare-related decisions' in a research process [1]. Methods of engagement include both in-person meetings (e.g., focus groups, one-on-one-discussions, interviews) and technology-based approaches, such as online surveys, webinars and social media platforms [2,3]. Proponents of stakeholder engagement predict increased quality, translation and implementation of research results, and an empowerment of stakeholders through engagement [4–6]. Furthermore, it is regarded as an important approach to an open ethical discourse, not exclusively led by specialists [7]. Originating in economics [8], stakeholder engagement gains growing attention within the medical field since the establishment of the Patient-Centered Outcomes Research Institute in 2010 [9].

Patient-Centered Outcomes Research Institute offers funding opportunities specifically for studies that engage stakeholders [10]. First reports revealed that stakeholder engagement led to changes in study design, allowed a deeper understanding of end-user needs and facilitated access to study populations [11–13]. Published articles mainly report engagement of patients and clinicians, mostly in early stages of research [14].

Infrastructure for stakeholder engagement and its evaluation is continuously growing in North America (USA and Canada) and the UK [5,15]. We were aware of the advanced progress stakeholder involvement in research in UK [16–18] and assumed that UK is at a similar level as North America. Therefore, we did not specially look into this region. We have no data about practice and reception of stakeholder engagement among researchers in DACH countries (country codes for Germany, Austria and Switzerland). Also, some previous studies reported stakeholder engagement

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in Europe [19], in China [20], or in other world regions, however, very little attention has been paid to understand their specifics and gaps with North America in a worldwide scope.

Our aim was to identify current practices of stakeholder engagement in different world regions and factors that encourage or discourage researchers from its application. We hypothesized that stakeholder engagement is more prominent and higher accepted among researchers in North America.

Materials & methods

We performed a cross-sectional study to assess current practices and opinions about potential advantages and challenges of stakeholder engagement among clinical researchers. We conducted an anonymous web-based survey to reach an international sample and ensure feasible access to the questionnaire in three different languages (English, German and Chinese).

Development

Through a broad literature review, we identified currently discussed aspects of stakeholder engagement in clinical research which formed the six questionnaire sections: knowledge and definition; relevance and practice; potential stakeholder groups; methods for engagement; levels and stages; and perceived challenges and potential of stakeholder engagement. Most questions were designed as three-dimensional sets of questions. These represent the respondent's existing practice, normative beliefs and future expectations on the respective aspect of stakeholder engagement. This method was adopted from existing surveys exploring current state of what is important to respondents and to give perspectives for future generations [21]. Native speakers reviewed English and Chinese translations of the initial German version. After iterative pretesting of four independent testers and a technical function test the final web-version of the questionnaire comprised 18 pages with 29 questions determining participants' opinions on stakeholder engagement as part of clinical research (Supplementary Material 1). For survey administration, we used the noncommercial software SoSci Survey [22]. Data were stored on a secured local German server, accessible only to study team members.

Survey dissemination

Participants were recruited via e-mail and WeChat groups, addressed through lists of national and international researcher associations, among others from the field of epidemiology, public health, integrative medicine and oncology. We approached administrators of mailing lists based on their publicly available contact information or personal contacts. The questionnaire was nonmandatory, without incentive and not available on an open homepage. The study received approval from the Charité – Universitätsmedizin Berlin Ethic Committee on 3 May 2016 (Approval Number EA1/128/16) and data protection committee on 15 June 2016 (AZ 293/16). The survey was available online from 12 September 2016 to 31 October 2017. All participants were informed about the objectives of the study and could provide their informed consent by initiating the online survey. No personal identifying information or IP-addresses were collected.

Data & measurements

In the first part of the survey, sociodemographic data (year of birth, gender, first language and country of residence) and data regarding working context (professional context, position, main working field and years of working experiences) were collected.

Data regarding participants' perspective on stakeholder engagement were collected in the second part of the survey through six questionnaire sections as above mentioned. Various types of questions were implemented, including polar question, dropdown selection, text input and predominantly scales from 0 to 10 (e.g., 0 = "do not agree at all" and 10 = "agree completely" for agreement and 0 = "never" and 10 = "always" for frequency).

Statistical analysis

Statistical analysis was performed with the open source statistical program R and R Studio [23–25]. We chose an 'available-case' analysis approach and included all cases with available data on sociodemographic background and general knowledge of stakeholder engagement (seventh page completed). Descriptive statistics was performed to characterize the sample and analysis of variance to compare the sample subgroups using a significance level of 5%. As different generations of researchers might answer questions differently, we controlled for the possible confounder
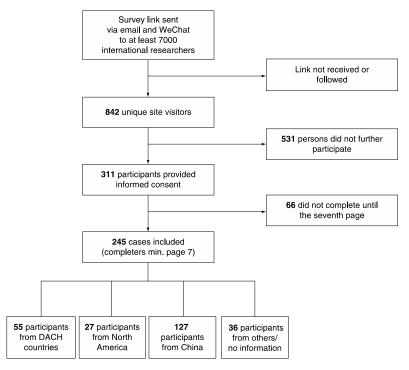
Figure 1. Flowchart of the response to the survey stakeholder engagement in clinical research.
WeChat: Chinese messaging, social media and mobile payment app.
DACH: Germany (D), Austria (A) and Switzerland (CH).
North America: USA and Canada.

'age of participant' by conducting an explorative analysis of covariance (ANCOVA) with the covariate age. Results are reported as descriptive group means plus/minus standard deviation (SD) and p-values for group comparisons.

Results

Response rates

The newsletters and mailing lists reached about 7000 researchers. The survey recorded 842 unique site visitors, 311 respondents agreed to participate (participation rate 36.9%, Figure 1), and 154 participants submitted the last questionnaire page (completion rate 49.5%).

Sample characteristics

From overall 311 survey participants, 245 completed the online survey until at least the seventh page and were included to further analysis.

A total of 27 (11%) participants stated to live in North America, 55 (22%) in DACH countries and 127 (51.84%) in China, whereas 36 (15%) indicated another or no specific country of residence. The mean age of participants from North America was 53.78 ± 10.2 years (mean ± SD), from DACH countries 48.35 ± 11.8 years, and from China 37.47 ± 8.8 years. Among participants from North America, the majority worked as principal investigators (63%). In DACH countries, principal investigators represented 49% of all participants and in China 40%, respectively.

All collected sample characteristics are given in Table 1.

Table 1. Sample characteristics as reported in the online survey.[†]			
Characteristic	DACH n = 55	North America n = 27	China n = 127
Age in years, mean (SD)	48.35 (11.77)	53.78 (10.27)	37.47 (8.84)
Gender, n (%)			
– Male	23 (41.8)	12 (44.4)	44 (34.6)
– Female	28 (50.9)	14 (51.9)	80 (63.0)
– Other	0 (0.0)	0 (0.0)	1 (0.8)
– Prefer not to say	2 (3.6)	0 (0.0)	2 (1.6)
– Not available	2 (3.6)	1 (3.7)	0 (0.0)
First language, n (%)			
– German	50 (90.9)	2 (7.4)	0 (0.0)
– English	0 (0.0)	23 (85.2)	1 (0.8)
– Chinese	0 (0.0)	0 (0.0)	125 (98.4)
– Other	3 (5.5)	2 (7.4)	0 (0.0)
– Not available	2 (3.6)	0 (0.0)	1 (0.8)
Professional context, n (%)			
– Industry	4 (7.3)	0 (0.0)	7 (5.5)
– University	34 (61.8)	17 (63.0)	42 (33.1)
– Hospital or clinic	4 (7.3)	9 (33.3)	69 (54.3)
– Other research institution	12 (21.8)	1 (3.7)	9 (7.1)
– Not available	1 (1.8)	0 (0.0)	0 (0.0)
Position, n (%)			
– Principal investigator	27 (49.1)	17 (63.0)	51 (40.2)
– Research assistant	21 (38.2)	2 (7.4)	35 (27.6)
– PhD student	1 (1.8)	0 (0.0)	10 (7.9)
– Master student	1 (1.8)	0 (0.0)	16 (12.6)
– Other	4 (7.3)	8 (29.6)	14 (11.0)
– Not available	1 (1.8)	0 (0.0)	1 (0.8)
Main working field, n (%)			
– Basic research	8 (14.5)	2 (7.4)	13 (10.2)
– Clinical and/or health service research	29 (52.7)	15 (55.6)	54 (42.5)
– Teaching	2 (3.6)	1 (3.7)	10 (7.9)
– Patient care	6 (10.9)	6 (22.2)	38 (29.9)
– Other	9 (16.4)	3 (11.1)	12 (9.4)
– Not available	1 (1.8)	0 (0.0)	0 (0.0)
Work experience in years, mean (SD)	12.74 (7.86)	18.74 (9.43)	9.85 (8.10)
[†]All characteristics were self-reported by the study participants. Percentages may not sum up to 100% because of rounding. DACH: Germany (D), Austria (A) and Switzerland (CH); North America: USA and Canada. SD: Standard deviation.			

Knowledge & definition

Almost all participants from North America stated knowing the term 'stakeholder engagement' (96.30%), while it were 65% among participants from DACH and 56% among those from China (Figure 2).

In the course of the survey, we introduced a stakeholder engagement definition (Box 1) [1] for which participants from North America showed the highest agreement, however, without a statistically significant difference between groups (Figure 3).

Relevance & practice

The perception of stakeholder engagement as an important matter in contemporary clinical research varied between the groups, measured on a scale from 0 = do not agree at all to 10 = agree completely (North America: 8.41 ± 2.2, DACH: 4.23 ± 2.9, China: 8.12 ± 2.1; $p < .001$). When asked if they had already included stakeholders in research, participants from North America showed the highest and from DACH countries the lowest agreement (North
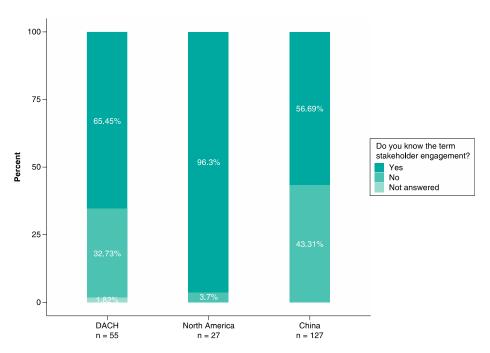
Figure 2.   Participant's knowledge of the term 'stakeholder engagement' by country of residence.
DACH: Germany (D), Austria (A) and Switzerland (CH); North America: USA and Canada.

Box 1. Working definition of stakeholder engagement according to Concannon *et al.* (2012), how presented in the survey.

Stakeholder engagement is the active inclusion and participation of different individuals or groups in a research process. Stakeholders are characterized by holding an interest in or being affected by the conducted research.

America: 8.44 ± 2.0, DACH: 5.53 ± 4.1, China: 6.22 ± 2.7; $p < 0.001$). Concerning the question if stakeholder engagement should form an important part of future clinical research, participants from North America rated with a mean of 8.33 ± 1.6, from DACH countries with 7.51 ± 2.4 and from China with 6.74 ± 2.5 ($p = 0.004$).

The likelihood of engaging stakeholders in an upcoming project was rated on a scale from 0 = very unlikely to 10 = very likely with a high mean in North America (9.38 ± 1.0), while participants from DACH countries (7.42 ± 2.9) and China (7.61 ± 2.4) achieved a comparably lower one ($p = 0.007$).

Perceived challenges & potential contribution of stakeholder engagement

Participants evaluated requirements for successful stakeholder engagement and possible advantages/disadvantages of stakeholder engagement (Table 2). The necessity of 'stakeholders interest in participation' was rated with high means across all groups: 9.05 ± 2.2 for North America, 8.76 ± 1.7 for DACH countries and 8.72 ± 1.7 for China ($p = 0.754$). In contrast, the statement 'stakeholder engagement leads to additional financial costs' was rated relatively low, with a mean of 2.74 ± 2.5 for North America, 3.08 ± 3.2 for DACH countries and 3.48 ± 2.8 for China ($p = 0.572$). Furthermore, the need for a guideline publication to foster stakeholder engagement was rated with a lower mean in DACH countries (5.69 ± 3.2), but a higher one in North America (8.47 ± 1.8) and China (8.95 ± 1.8; $p < 0.001$). Correspondingly, the need for institutional infrastructure was rated lower in DACH countries (6.55 ± 2.55) than in North America (8.33 ± 1.78) and China (8.72 ± 1.79); $p < 0.001$). Asked, if funding programs to support researchers adopting stakeholder engagement are necessary, researchers from DACH
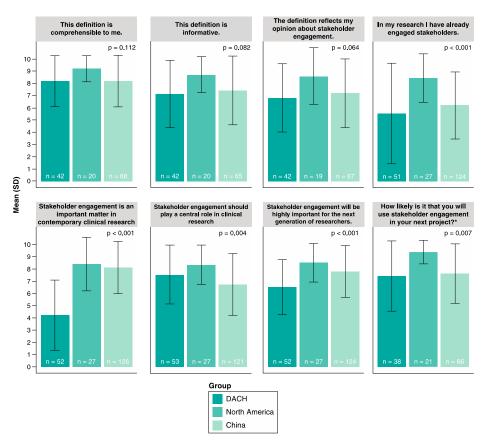
Figure 3.   Opinion on stakeholder definition and relevance reported in the survey. Shown values are the means of the responses by group on a scale from 0 to 10 with 0 = do not agree at all and 10 = agree completely; error bars indicate the standard deviation; p-values are from a one-way ANOVA.
*This item was scaled from 0 to 10 with 0 = very unlikely and 10 = very likely.
DACH: Germany (D), Austria (A) and Switzerland (CH); North America: USA and Canada.
ANOVA: Analysis of variance; SD: Standard deviation.

countries rated with a lower mean (6.74 ± 3.08) than researchers from North America (8.37 ± 2.27) and China (8.74 ± 1.78; p < 0.001). To the potential positive impact of stakeholder engagement on transparency of research institutions, participants agreed in a variable extent, with a lower mean (5.13 ± 2.7) for DACH countries, and higher ones for North America (7.56 ± 1.6) and China (8.42 ± 1.4; p < 0.001). The results for other aspects of stakeholder engagement are given in Table 2.

Levels & stages of engagement

In the evaluation of the question if stakeholders should be engaged as consulting partners in clinical research, means were consistent and relatively high across all groups (North America: 7.90 ± 2.4, DACH: 8.11 ± 2.6, China: 7.91 ± 2.6; p = 0.924). Concerning a collaborative engagement, analysis showed similar results, but with a slightly lower mean in DACH countries (North America: 8.20 ± 2.1, DACH: 7.05 ± 2.8, China: 8.07 ± 2.5; p = 0.112). When asked if stakeholders should have a leading role in research, participants from DACH countries rated with the lowest mean (4.45 ± 3.3) and participants from China with the highest (6.55 ± 3.2; p = 0.005). Regarding stakeholder engagement in different research stages, from topic selection to publication and implementation of

Table 2. Participants opinion about necessary factors and advantages/disadvantages of stakeholder engagement by group.

Question/group	DACH mean (SD)	North America mean (SD)	China mean (SD)	p-value§
Which of the following factors are necessary to foster stakeholder engagement in research?†				
Standardized definition of stakeholder engagement	5.84 (2.91)	6.26 (2.75)	9.19 (1.40)	<0.001
Stakeholders interest in participation	8.73 (1.71)	9.05 (2.16)	8.72 (1.71)	0.754
Publication of guidelines for stakeholder engagement	5.69 (3.20)	8.47 (1.78)	8.95 (1.77)	<0.001
Institutional infrastructure	6.55 (2.55)	8.33 (1.78)	8.72 (1.79)	<0.001
Funding programs to support researchers adopt stakeholder engagement	6.74 (3.08)	8.37 (2.27)	8.74 (1.78)	<0.001
Funding to do research about stakeholder engagement	6.45 (2.84)	7.16 (2.57)	8.55 (1.81)	<0.001
Stakeholder engagement…‡				
Leads to additional financial costs	3.08 (3.18)	2.74 (2.49)	3.48 (2.76)	0.572
Places a high burden on the human resources of a research team	8.00 (3.24)	6.42 (2.99)	5.44 (3.14)	0.049
Will not lead to widely applicable study results because it only takes individual perspectives into consideration	3.87 (3.25)	2.28 (2.24)	4.29 (3.24)	0.060
Leads to lobbyism, meaning the organized influence of particular groups on clinical research	6.33 (2.76)	5.05 (2.55)	7.05 (2.91)	0.026
Implies higher workload for researchers	7.38 (2.98)	7.00 (2.91)	6.46 (2.88)	0.300
Constitutes a higher workload for potential stakeholders	7.58 (2.33)	7.00 (2.52)	6.28 (2.87)	0.058
Enables external persons to participate in a research project	7.36 (2.43)	8.37 (1.61)	8.17 (1.90)	0.100
Integrates individual perspectives of decision makers into the research process, which may lead to more relevant research	8.05 (2.42)	8.75 (1.74)	7.71 (2.29)	0.200
Includes empirical values/data in the research process	8.05 (2.70)	7.11 (1.78)	7.35 (2.28)	0.247
Strengthens patients' rights to participate in healthcare decision-making	6.42 (3.19)	7.32 (2.52)	8.30 (1.85)	0.001
Increases the relevance of research questions and outcomes	6.95 (2.80)	8.05 (2.33)	8.37 (1.79)	0.009
Leads to implementable research results	6.25 (2.71)	6.95 (2.57)	8.39 (1.68)	<0.001
Has a positive impact on the transparency of research institutions	5.13 (2.68)	7.56 (1.62)	8.42 (1.43)	<0.001
Strengthens the trust in research results of all persons involved	7.43 (2.67)	8.15 (2.28)	8.31 (1.77)	0.141
Enhances the adherence of study participants	6.05 (2.86)	6.32 (2.69)	8.23 (1.91)	<0.001
Facilitates recruitment	4.69 (2.73)	6.74 (2.96)	7.72 (2.07)	<0.001

†This item was scaled from 0 to 10 with 0 = not necessary at all and 10 = very necessary.
‡This item was scaled from 0 to 10 with 0 = do not agree at all and 10 = agree completely.
§p-value from a one-way ANOVA.
DACH: Germany (D), Austria (A) and Switzerland (CH); North America: USA and Canada.
ANOVA: Analysis of variance; SD: Standard deviation.

results, participants from DACH countries rated with the lowest means over all items, with an exception of the 'implementation of results' (see Supplementary Material 2).

Stakeholder groups

Participants were asked which groups of stakeholders should be engaged in future clinical research, namely: patients, clinicians, researchers, payers, industry, hospitals & health systems, policy makers and training institutions. With an exception of the item 'payers' (DACH: 6.61 ± 3.1, North America: 5.62 ± 3.2, China: 5.80 ± 3.8, p = 0.379), means in the DACH group were slightly lower over all items (Supplementary Material 2).

Methods for engagement

The study presented 15 methods to engage stakeholders. Participants rated the frequency of how often they should be used. For all digital/technical methods (e.g., webinar, online-survey), means of the DACH-group remained lower than means of the other two groups (e.g., item 'webinar': DACH: 5.07 ± 2.9, North America: 7.11 ± 2.3, China: 8.09 ± 2.6; p < 0.001). In contrast, DACH countries reached the highest mean for the item 'personal meeting' (DACH: 7.85 ± 2.4, North America: 7.20 ± 2.3, China: 7.49 ± 2.8; p = 0.631, Supplementary Material 2).

Communication tools

Participants rated how often specific communication tools should be used to engage stakeholders. In all groups means were high for contacting stakeholders via email. Biggest mean differences were found for the items 'Instant messaging', 'Smartphone Application' and 'SMS (text message)', where participants from China rated the highest and from DACH countries the lowest (e.g., item 'Smartphone Application' DACH: 4.67 ± 2.6, North America: 5.94 ± 2.7, China: 8.79 ± 2.3; $p < 0.001$). Compared with the other groups, DACH countries rated also lower for digital tools like 'Online Blog', 'Online Forum', 'Social network', but higher for the direct contact through 'Personal meeting' (DACH: 8.80 ± 1.9, North America: 8.11 ± 2.2, China: 7.49 ± 3.1; $p = 0.045$, Supplementary Material 2).

We conducted an ANCOVA to adjust for the observed age difference between groups. This analysis showed that group differences did not disappear when controlling for the age of participants.

Discussion

The results of this international, cross-sectional study indicate that the researchers in North America are more familiar with the method and definition of stakeholder engagement. In comparison, among the participating researchers from DACH countries stakeholder engagement is not broadly known and not considered as an important method of existing contemporary clinical research. Nevertheless, they regard it as an important method for future clinical research.

A second finding of our study is a group difference in the perception of advantageous effects of stakeholder engagement in clinical research. Participants from DACH countries rated the beneficial effects of stakeholder engagement like increased transparency, patient empowerment, or facilitation of recruitment and implementation, lower when compared with participants from North America and China.

Overall, researchers from the DACH countries use stakeholder engagement less than researchers from the comparison regions. They also indicate less willing to make joint decisions regarding their research. Furthermore, they have lower expectations when it comes to applying technology-based methods for stakeholder engagement than participants from North America and China. Surprisingly, participants across all groups gave low scores for possible high financial cost of the stakeholder engagement process and the overrepresentation of individual stakeholder opinions.

The main strength of this study is its global approach with participants from different world regions. Furthermore, the questionnaire is profound, built on an intensive literature review and hence on previous works and findings [1,11,26–29]. Conceptualization of different sections, extensive discussion and pretesting lead to a well-elaborated survey. We used a modern online survey technique, which is economic, safe, anonymous, user-friendly and allows reaching an international sample without risk of interviewer bias. We aimed to answer a research question that has high relevance for usual care practice and reflects an international setting. Our sample groups showed notable varieties in characteristics. We controlled for the possible confounder age in an ANCOVA and obtained results that were consistent with our primary findings.

Nevertheless, our study has several limitations. The complexity of the survey could have led to frustration and dropout of study participants, reflected in the participation rate of 36.9% and the completion rate of roundly 50%. The overall view rate from links to the survey homepage was <4%. However, these rates are commonly observed in web-based surveys and do not necessarily lead to nonresponse bias [30,31]. More likely, results underly a social desirability bias and nonresponse was caused by the inability to send out personal reminders, due to the anonymity of the study [32]. Additionally, the sample is a convenience sample with volunteer bias, including solely researchers who are member of mailing lists with limited reach [33]. This resulted in a small sample size which limits the representativeness of the data. Future studies should consider using incentives and aim for bigger samples. Low response could also have been affected by noninterest in newsletters content in the first place. We endeavored to address diverse mailing lists, but yet conclusions on the population are only allowed to a limited extent. Furthermore, we were facing the challenge of transferring information between different languages, cultures and systems. First, a certain term or expression may not have the same significance in all languages. Second, addressed health systems, research infrastructures and cultures may vary significantly. Even so, we used the same questionnaire in all target samples, aiming for high comparability.

The grouping of participants intends to recognize possible differences in mindsets by world region, assuming that there exist different research cultures across the world. Nonetheless a categorization by their country of residence does not guarantee relation between world region (or more broadly defined: research culture) and the participants'

opinion. Moreover, a participant residing in China could have been trained in North America, and afterward finding herself applying what she has learned in a Chinese research context. To conclude, in our globalized world clear relationship between place of residence and stakeholder practice is not necessarily given, but could result out of different framework conditions and research cultures. It would also be of great interest to consider the influence of the researcher's particular field of research, as existing experiences and practices differ across research fields. Data on these were not collected in our survey and should be part of future research.

Consistent with previous work, this study points out that researchers are not assigning a leading role to stakeholders, but prefer a consulting or collaborating level of engagement [14]. Our findings show that especially researchers in DACH countries favor to engage patients, clinicians and researchers, although other actors like payers, policy makers and training institutions are also promoted by the stakeholder approach [11].

Conclusion
Clinical researchers in North America are more familiar with the method and definition of stakeholder engagement and regard institutional infrastructure and funding essential to foster stakeholder engagement in clinical research. In comparison, stakeholder engagement is not broadly known among researchers from DACH countries and not considered as an important method of existing contemporary clinical research but of future research. The reasons for lack of implementation of stakeholder engagement remain unclear.

Future perspective
For a broader acceptance and implementation of stakeholder engagement in clinical researches, institutional support and motivational conditions might be needed.

More data are needed to find out what prevents researchers in DACH countries from implementing stakeholder engagement. As a first step, information and training on stakeholder engagement should be provided to inform researchers about the concept.

Summary points

- Stakeholder engagement is defined as the active inclusion and participation of different individuals or groups in a research process. Stakeholders are characterized by holding an interest in or being affected by the conducted research.
- Infrastructure for stakeholder engagement and its evaluation is continuously growing in North America and the UK. However, very little attention has been paid to understand practices in DACH countries (country codes for Germany, Austria and Switzerland) and China in a worldwide scope.
- This well-elaborated survey was built based on intensive literature review and pretesting, and ensured feasible access with three different languages (English, German and Chinese).
- The sample was a convenience sample based on researcher newsletters and mailing lists; the resulted small sample size might limit the representativeness of the data; participants may yield substantial volunteer bias.
- Almost all participants from North America stated knowing the term "stakeholder engagement" (96.30%), while it was 65% among participants from DACH and 56% among those from China.
- For researchers from DACH countries, stakeholder engagement is not broadly known and not considered as an important method of existing contemporary clinical research. However, they regard it important for future clinical research.
- Results should be carefully interpreted, as health systems, research infrastructures, term expressions and cultures may vary significantly.
- Our study results suggested that, for a broader acceptance and implementation of stakeholder engagement in clinical studies, institutional support and motivational conditions might be needed.

Acknowledgments

Financial & competing interests disclosure

Ethical conduct of research

The study received approval from the Charité – Universitätsmedizin Berlin Ethic Committee on 3 May 2016 (Approval Number EA1/128/16) and data protection committee on 15 June 2016 (AZ 293/16).

All participants were informed about the objectives of the study and could provide their informed consent by initiating the online survey.

Data sharing statement

The anonymized survey datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Open access

References
Papers of special note have been highlighted as: ● of interest

1. Concannon TW, Meissner P, Grunbaum JA *et al.* A new taxonomy for stakeholder engagement in patient-centered outcomes research. *J. Gen. Intern. Med.* 27(8), 985–991 (2012).
   ● **Reports the definition, practices and implementations of stakeholder engagement.**
2. Kim KK, Khodyakov D, Marie K *et al.* A novel stakeholder engagement approach for patient-centered outcomes research. *Med. Care* 10(Suppl. 1), S41–S47 (2018).
3. Lavallee DC, Wicks P, Alfonso Cristancho R, Mullins CD. Stakeholder engagement in patient-centered outcomes research: high-touch or high-tech? *Expert Rev. Pharmacoecon. Outcomes Res.* 14(3), 335–344 (2014).
4. Esmail L, Moore E, Rein A. Evaluating patient and stakeholder engagement in research: moving from theory to practice. *J. Comp. Eff. Res.* 4(2), 133–145 (2015).
   ● **Reports the definition, practices and implementations of stakeholder engagement.**
5. Van Der Scheer L, Garcia E, Van Der Laan AL, Van Der Burg S, Boenink M. The benefits of patient involvement for translational research. *Health Care Anal.* 25(3), 225–241 (2017).
6. Goodman MS, Sanders Thompson VL. The science of stakeholder engagement in research: classification, implementation, and evaluation. *Transl. Behav. Med.* 7(3), 486–491 (2017).
   ● **Reports the definition, practices and implementations of stakeholder engagement.**
7. Hansen SL, Holetzek T, Heyder C, Wiesemann C. Stakeholder-Beteiligung in der klinischen Forschung: eine ethische analyse. *Ethik in der Medizin.*30(4), 289–305 (2018).
8. Freeman RE. *Strategic Management: A Stakeholder Approach.* Cambridge University Press, MA, USA (1984).
9. PCORI. Patient-centered outcomes research institute: about us (2014). www.pcori.org/about-us/our-story
10. PCORI. Patient-centered outcomes research institute: funding opportunities (2012). www.pcori.org/funding-opportunities/research-support-funding-opportunities
11. Forsythe LP, Ellis LE, Edmundson L *et al.* Patient and stakeholder engagement in the PCORI pilot projects: description and lessons learned. *J. Gen. Intern. Med.* 31(1), 13–21 (2016).
12. Selby JV, Forsythe L, Sox HC. Stakeholder-driven comparative effectiveness research: an update from PCORI. *JAMA* 314(21), 2235–2236 (2015).
   ● **Reports the definition, practices and implementations of stakeholder engagement.**

►13. Woolf SH, Zimmerman E, Haley A, Krist AH. Authentic engagement of patients and communities can transform research, practice, and policy. *Health Affairs* 35(4), 590–594 (2016).

►14. Concannon TW, Fuster M, Saunders T *et al.* A systematic review of stakeholder engagement in comparative effectiveness and patient-centered outcomes research. *J. Gen. Intern. Med.* 29(12), 1692–1701 (2014).

• **Reports the definition, practices and implementations of stakeholder engagement.**

►15. Lavery JV. Building an evidence base for stakeholder engagement. *Science* 361(6402), 554 (2018).

►16. Jackson T, Pinnock H, Liew SM *et al.* Patient and public involvement in research: from tokenistic box ticking to valued team members. *BMC Med.* 18(1), 79 (2020).

17. National Institute for Health Research. NIHR: about INVOLVE (2021). www.invo.org.uk/about-involve/

18. National Institute for Health and Care Excellence. Developing NICE guidelines: a guide for stakeholders and the public (2014). www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/developing-NICE-guidelines-information-for-stakeholders.pdf

►19. Brereton L, Ingleton C, Gardiner C *et al.* Lay and professional stakeholder involvement in scoping palliative care issues: methods used in seven European countries. *Palliat. Med.* 31(2), 181–192 (2017).

20. Liu C, Meyers K. Beyond clinical trials: social outcomes of structured stakeholder engagement in biomedical HIV prevention trials in China. *Cult. Health Sex* doi:10.1080/13691058.2019.1683230 1–17 (2019).

21. Wratil P, Helbing G, Wiens O. Research report I. Results of the legacy study - a first overview (2017). https://bibliothek.wzb.eu/pdf/2017/p17-006.pdf

22. Leiner DJ. SoSci Survey. Informationen über SoSci survey (2016). www.soscisurvey.de/de/about

23. Leiner DJ. SoSci survey (2016). www.soscisurvey.de

24. Rstudio Team. RStudio: integrated development environment for R (Version 1.1.419). MA, USA (2018). www.rstudio.com/

25. R Core Team. R: a language and environment for statistical computing (2017). R Foundation for Statistical Computing, Vienna, Austria. www.R-project.org/

►26. Deverka PA, Lavallee DC, Desai PJ *et al.* Stakeholder participation in comparative effectiveness research: defining a framework for effective engagement. *J. Comp. Eff. Res.* 1(2), 181–194 (2012).

27. Mallery C, Ganachair D, Fernandez J, Smeeding L, Robinson S, Moon M. Innovative methods in stakeholder engagement: an environmental scan. AHRQ Publication NO. 12-EHC097-EF (2012). https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/stakeholders-engagement-others_research-2012-1.pdf

►28. Guise JM, O'Haire C, McPheeters M *et al.* A practice-based tool for engaging stakeholders in future research: a synthesis of current practices. *J. Clin. Epidemiol.* 66(6), 666–674 (2013).

• **Reports the definition, practices and implementations of stakeholder engagement.**

►29. Thariani R, Wong W, Carlson JJ *et al.* Prioritization in comparative effectiveness research: the CANCERGEN experience. *Med. Care* 50(5), 388–393 (2012).

►30. Sebo P, Maisonneuve H, Cerutti B, Fournier JP, Senn N, Haller DM. Rates, delays, and completeness of general practitioners' responses to a postal versus web-based survey: a randomized trial. *J. Med. Internet Res.* 19(3), e83–e83 (2017).

►31. Af Wåhlberg AE, Poom L. An empirical test of nonresponse bias in internet surveys. *Basic Appl. Social Psychol.* 37(6), 336–347 (2015).

►32. Cook DA, Wittich CM, Daniels WL, West CP, Harris AM, Beebe TJ. Incentive and reminder strategies to improve response rate for internet-based physician surveys: a randomized experiment. *J. Med. Internet Res.* 18(9), e244 (2016).

►33. Eysenbach G, Wyatt J. Using the internet for surveys and health research. *J. Med. Internet Res.* 4(2), e13 (2002).

Lebenslauf

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

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