

This is the final draft, after peer-review, of a manuscript published in *J Health Serv Res Policy* 2013;18(4):233-41. The definitive version, detailed above, is available online at www.rsmjournals.com

Recruitment to clinical trials: A meta-ethnographic synthesis of studies of reasons for participation.

McCann, SK, Campbell MK, Entwistle, VA.

Health Services Research Unit, University of Aberdeen

ABSTRACT

Objectives Randomised controlled trials are important for evaluating healthcare interventions, but recruitment can be difficult. Studies of potential participants' perspectives on trial participation are accumulating but their collective contribution is not obvious. In 2007 we conducted a meta-ethnographic synthesis of people's reasons for accepting or declining participation. This paper reports a second synthesis, conducted separately on the same topic, using studies published subsequently. It discusses both the substantive findings and the methodological implications for updating meta-ethnographies.

Methods Systematic searches identified relevant papers published between 1996 and 2005 (first synthesis), then 2005 and 2010 (second synthesis). We used a meta-ethnographic interpretive process of translation to examine the relationships between study findings.

Findings The two syntheses were broadly compatible, but the line of argument developed in the second more clearly highlighted how potential participants' health states and healthcare situations at the time of recruitment could interact with other considerations. In particular they could influence the nature and significance for trial entry decisions of people's

judgements about: their communication and relationship with trial recruiters; the personal implications of trial interventions and processes; and the “common good” (helping others) and what their non/participation might say about their identity.

Conclusions Our work highlights the need for trialists to consider potential participants’ health and healthcare situations when designing recruitment approaches. It also provides the first empirical insights on the process of updating meta-ethnographies that we are currently aware of. Approaches to updating meta-ethnographies need further investigation.

Introduction

Randomised controlled trials (RCTs) can generate valuable knowledge about the effects of clinical interventions, but trialists often struggle to recruit sufficient participants.¹

Numerous qualitative research studies have generated insightful findings into potential participants’ perspectives on trial recruitment,²⁻⁵ but their collective contribution is hard to ascertain without a formal review. To complement broader systematic summaries of evidence and issues relating to trial recruitment^{6,7} we had undertaken, in 2007, a meta-ethnographic synthesis that specifically aimed to identify and build new conceptual knowledge about peoples’ reasons for accepting or declining participation in trials (we focused on phase III RCTs - trials of interventions in which basic safety and efficacy checks have already been completed).

This first meta-ethnography, covering papers published between 1996 and 2005,⁸ had established that people’s personal circumstances at the time of being invited to participate in a trial were salient to participation decisions, and that being able to perceive some

personal benefit from trial participation was clearly associated with willingness to take part. The synthesis also highlighted that potential participants could identify personal benefits and harms in both trial processes and interventions. Figure 1 illustrates the conceptual model developed from the first synthesis.

[Figure 1 here]

In December 2010 we re-ran the original literature searches and identified 12 papers published since September 2005 that fulfilled the original inclusion criteria. Although there have been a number of papers that consider methodological issues relating to meta-ethnographies,⁹⁻¹¹ we found no published guidance on how to update a meta-ethnography. After considering a range of possible options, we decided to conduct a new, “stand-alone” meta-ethnography. Our decision reflected a concern to avoid forcing the findings from the recent studies into the model generated by the earlier synthesis, and to facilitate clear identification of the additional insights generated by the more recent studies. We further reasoned that by comparing the two syntheses and reflecting on the strengths and limitations of this ‘standalone’ approach, we could inform a much-needed methodological discussion about updating meta-ethnographies.

Methods

Meta-ethnography facilitates an “essentially interpretive and inductive” approach to synthesising studies. It centres on “translating” the findings of individual qualitative studies so they can be considered in relation to one another. This allows re-interpretation and construction of interpretations accumulatively across studies.^{12,13}

While planning and conducting the second meta-ethnography, we avoided referring back to the findings of the first, but on its completion we compared the resultant syntheses and reflected on the 'standalone' update process. We focus now on the methods of the second synthesis.

Searching and identification of relevant studies

Medline, EMBASE, CINAHL, ASSIA, PsychInfo, SocAbs and the Cochrane Library were searched using the comprehensive search strategy developed for the first synthesis to identify English language publications (September 2005 –December 2010) reporting qualitative data on people's *own accounts* for accepting or declining participation in specific phase III RCTs. The reference lists of relevant papers were also searched.

One reviewer (SM) assessed the abstracts of the 2965 references from the bibliographic searches and identified 38 as potentially relevant. Two reviewers (SM, VE) screened the full text versions of these using a structured assessment form (paperwork available on request). The inclusion criteria specified that studies must have examined people's *own accounts* of what influenced their decision to participate or not in the trial. This restriction allowed us to focus on papers offering rich insights into peoples' reasons for accepting or declining participation. The 12 papers that met the inclusion criteria are summarised in Table 1. They report on 9 separate research studies associated with 12 RCTs.

Analysis & synthesis

Two reviewers (SM and VE) read and systematically extracted data from included papers, and discussed study findings and interpretations with a third reviewer (MC) throughout the process.

We initially organised papers in chronological order and followed Noblit and Hare¹² in focusing on the findings, concepts and themes used by the papers' authors. We generated a list of key categories that served as the basis for comparing the similarities and differences across studies. This enabled us to produce a "reciprocal translation" - a comparison of the concepts used in the different studies¹² (example in Box 1). The translated concepts were integrated in a new interpretation or 'line of argument.'¹²

[Insert Box 1]

It became clear that the health conditions and situations that people were dealing with at the time of trial invitation were important. We therefore decided to re-group the papers according to the broad types of health conditions and situations that were represented: situations perceived as urgent and/or life threatening; established long-term conditions; and recently diagnosed long-term conditions. We then examined the key concepts thematically within these groups, attending as far as possible to the contextual aspects of particular studies. (Alternative approaches to ordering and grouping studies are possible within meta-ethnography, although their relative merits are not fully understood⁹).

Findings

We developed a ‘line of argument’ synthesis¹² that identified how potential participants’ health and healthcare situations at the time of recruitment can interact with other considerations to influence trial participation decisions. These situations had implications particularly for people’s decision-influencing judgements about: (1) their communication and relationships with trial recruiters; (2) the trial interventions and processes; and (3) their concerns about helping others and what their decisions about trial participation might say about them as people (referred to below as ‘common good and identity implications’).

We summarise the study findings that underpin this synthesis below. To reduce repetition in the text we provide authors’ details only when we introduce the papers, then use the paper descriptor labels from Table 1.

[Insert Table 1]

Situations perceived as urgent and/or life-threatening

Seven papers studied people asked to participate in a trial in situations that most perceived as urgent and/or life-threatening (for themselves and/or their children): “pre-term labour” papers (a) and (b),^{3,14} “perinatal” paper,¹⁵ “breast and ovarian” papers (a) and (b),^{16,17} “stroke” paper,¹⁸ leukaemia” paper.⁵

The “pre-term labour” papers studied women who were asked to participate in a trial when they were experiencing pre-term labour or pre-labour membrane rupture. The “perinatal” paper studied parents of babies with life-threatening health problems. The authors of these three papers highlighted a dominant sense of “fear” amongst potential participants, who

were asked about trial participation when some faced the “dreaded possibility that their baby would die.”

The “breast and ovarian cancer” papers highlighted that nearly all the breast cancer patients “felt being in a life-threatening situation” although none reported feeling ill prior to treatment. Further, the authors drew attention to potential participants’ “fear” and “loneliness” at the time of being offered trial entry. The “stroke” paper described how some potential trial participants were experiencing “panic” and “anxiety” about further deterioration during the first few hours after stroke onset.

The “leukaemia” paper considered parents of children with newly diagnosed, life-threatening, acute lymphoblastic leukaemia who had been approached about entering their child into a trial which aimed to determine appropriate treatment. Parents expressed “very little negativity” about the trial, commenting only on the timing of the trial offer and having to make a relatively quick decision about randomisation so soon after diagnosis.

Communication and relationship with trial recruiters

Life-threatening circumstances apparently made potential trial participants’ perceptions of trial recruiters particularly salient. The “*pre-term labour*” paper (a), reported the centrality of “socio-emotional” aspects of interpersonal exchanges to responses to recruitment invitations. Women attributed their decisions to take part in the trial more to the health professionals who approached them rather than to any written trial information provided or to thoughts about the trial interventions or processes. The authors suggested that the

importance of the interpersonal relationship was heightened by the women's stress-compromised ability to absorb information.

Relationships with recruiting clinicians were also considered "highly influential" in the "perinatal" paper. The authors highlighted the significance of recruiters' presentations of the trial, particularly for "the inferences that parents drew" about the risks and time available for deciding about participation. Where a need for an immediate decision was perceived, a particular "type of trust" became apparent and some parents took "a leap of faith" not necessarily based on "a particularly clear understanding of what they were being offered."

The importance of relationships between recruiting clinicians and patients also featured in the "breast and ovarian" papers. Some women's feelings of "loneliness" and "emotional turbulence" were reflected in a "need for confidence and trust" in the doctor. This need was reinforced because women felt "life threatened and lacked sufficient medical knowledge to make educated choices."

Similarly in the "stroke" paper, information about the trial appeared less important to patients' decisions than feelings of trust towards recruiting clinicians; a "tendency to perceive the information as a recommendation" was also reported. In the "leukaemia" paper there was little discussion regarding communication or trust issues *per se*, but the offer of trial participation was given in the same consultation as the diagnosis and the

authors highlighted the “dual” role of recruiting clinicians in terms of clinical management and research.

Trial interventions and processes

The interventions being evaluated in the “pre-term labour” papers were available outside the trial but not in the same context or combination. The authors reported that, although women acknowledged some uncertainty about whether the interventions would benefit their babies, they rationalised that outcomes would be “at worst no different from not taking part”, and some women believed that there was “no risk” to taking part. This apparently “intensified the feeling that there was no choice about whether to participate.” Women who expressed more concern about the risks of taking drugs in pregnancy seemed to weigh these against the possibly greater risks associated with premature birth.

The trials in the “perinatal” papers compared a range of drugs. Some, but not all, had been shown to be effective against placebo. The authors suggested that decisions *for* participation signified to parents that they were doing everything they could for their children (including gaining access to a potentially beneficial experimental treatment), while decisions *against* participation signified they were protecting children from the potential harm of a (risky) experimental treatment. The authors identified a “disproportionate focus on benefits rather than risks” among participants.

The three trials considered in the “breast and ovarian cancer” papers evaluated experimental treatments that were unavailable outside the trials. The authors reported that

almost all women perceived the 'new' treatments as superior, and that the prospect of randomisation appeared to cause some distress to women keen to access them. The availability of treatment interventions outside the trial studied in the "stroke" paper was not reported. Potential participants were strongly convinced of the importance of starting treatment, but did not seem fully aware that trial participation was voluntary. The authors judged that "time pressure and anxiety during the first few hours after stroke onset ... restricted the possibility of a free choice"

Common good and identity implications

"Pre-term labour" paper (a), highlighted that a desire to help other women and their unborn babies at risk of a pre-term birth was important, reflecting a "strong sense of solidarity with other women." However, the authors emphasised that acting on these feelings was "conditional on there being no risk" to themselves or their unborn children.

"Pre-term labour" paper (b) discussed how some trial participants perceived that "an invitation to serve the public good" enabled them to demonstrate their "moral character," but also recognised that in this life-threatening context "it would not be seen as morally deviant to decline the invitation."

The "perinatal" paper highlighted the "symbolism" of trial participation decisions: these decisions gave parents an opportunity for "involvement" and some control at a time of great uncertainty when there was little else they could do for their child."

The importance of helping with research featured strongly in the accounts reported in the “stroke” paper, but the authors noted that a general consensus towards helping with furthering medical research could become detached from a specific personal choice about taking part or not in the trial. Similarly the very positive attitudes that women in the “breast and ovarian cancer” papers expressed towards clinical trials in general seemed to become less important when they faced more “personal choices” about trial involvement.

The authors of the “leukaemia” paper reported many parents had a clear understanding that the scientific imperative of the trial was to help future children rather than explicitly helping their own child. However, few parents expressed “positive feelings” about helping future children (although agreeing to take part in the trial), reflecting possibly their immediate concerns for their own seriously ill child

Established long-term conditions

Four papers focused on people who were invited to participate in trials because they had established long-term conditions: “decision aid” paper,¹⁹ “lupus” paper,²⁰ “migraine” paper,²¹ and “reflux” paper.²²

The “decision aid” paper differed from the others because the trial it considered was of decision-support tools intended to support choices between treatments, rather than of treatments themselves. The authors interpreted the offer of taking part in this trial as a broader “research experience” for people living with a long-term condition.

The “lupus” paper highlighted the importance of people’s perceived state of health at the time of the trial invitation. This seemed primarily due to the “unpredictable course” of the condition and the potential for it to “flare precipitously” if treatment regimes changed.

The people invited to participate in the trial studied in the “migraine” paper all had migraines that had caused “major disruptions to their lives” for years. They had used a range of prescribed and over-the-counter medications as part of extensive self-management regimes. Many were taking a substantial amount of medication that was currently not controlling their symptoms satisfactorily.

To be eligible for the trial reported in the “reflux” paper, people had to have been receiving medication for the previous twelve months and to have well controlled symptoms. Study participants expressed different attitudes towards their symptoms and medication, including long-term reliance on medication for symptom control.

Communication and relationship with trial recruiters

In this group, only the “lupus” paper reported interaction or relationship with trial recruiters as potentially significant for participation. Most of the people studied indicated that the recruiting physician’s opinion had “influenced their decision”, but participants to this trial were recruited by their usual clinicians, and many had developed strong relationships with these over a number of years. In the other three papers, potential trial participants were mostly reviewed by clinicians who were not usually involved in their care.

Trial treatment interventions and processes

The “decision aid” paper reported that some people valued the trial consultation as an “opportunity for an additional medical assessment or as a question and answer research meeting.” The “lupus” paper highlighted the significance of the ways trial interventions and processes related to people’s existing (already complicated) medical regimes for their decisions about participation.

The “reflux” paper reported that personal invitations to undergo specialist assessment of their condition and discuss possible trial participation, along with perceptions of additional monitoring as part of trial follow-up, tended to influence decisions towards participation. Both interventions compared in this trial were available outside the trial, and potential participants already took the medication. Potential participants considered the benefits and risks of the surgical intervention, including associated pre-surgical tests and hospital stays. Those who saw the surgical intervention as an opportunity to improve their symptoms and/or to stop taking long-term medications thought they might benefit from trial participation. Some also thought they might access surgery more quickly in the trial.

The “migraine” paper reported that some participants had used acupuncture previously with variable results, but as their current medication was not controlling their symptoms very well, they were inclined to consider acupuncture as an alternative. Participants also seemed to derive confidence from the university setting of the trial and liked “the flexibility in appointments” and “the fact treatment was free.”

Common good and identity implications

The “decision aid” paper discussed people’s sense of identity in relation to trial participation in some depth and described three main identity types. ‘Volunteers’ emphasised their desire to help others, albeit with expectation of some “indirect personal benefit.” ‘Patients’ perceived the trial primarily as an opportunity to benefit from individualised, tailored care, and those with a ‘hybrid identity’ had characteristics of both ‘patients’ and ‘volunteers’.

The “lupus” paper reported a strong sense of altruism as important for some people although “not the only factor” for those considering trial participation. Feelings of altruism seemed particularly linked to a sense of “responsibility” towards future patients.

The “migraine” paper identified a “desire to help with the research” as a feature of people’s decision-making. However, the authors suggested that decision-making was influenced primarily by people’s desires for improvement in their condition. The “reflux” paper reported an inclination to help others or contribute to a collective general good that predisposed people towards trial participation. However, the authors stressed that decisions ultimately depended on how people thought participation might impact on them personally, conceptualising this as “conditional altruism”.

Recently diagnosed long-term conditions

One paper, the “epilepsy” paper⁴, focused on people who had been very recently diagnosed with a long-term condition when they were asked to participate in a trial.

Similar to the situation in the “leukaemia” paper, trial recruitment consultations began with the clinician confirming a diagnosis. The diagnosis of epilepsy was reported as “generally unwelcome and for some, something of a shock.” People had to accept both diagnosis and the need for treatment before they were invited to participate in the trial. Some appeared “unprepared” for discussions about long-term drug treatment and possible participation in a trial comparing different regimens.

Communication and relationship with trial recruiters

Communication with recruiting clinicians was noted as particularly salient in this paper. The authors highlighted that participants’ accounts were “reflective of trust” in the doctor, even though this was often their first encounter, and that trust seemed important for decisions about participation.

Trial treatment interventions and processes

All drugs being compared in the epilepsy trial were available outside the trial, although two were not then licensed for monotherapy. The authors observed that trial acceptors thought the drugs being compared in the trial had been “tested and were safe” so perceived trial participation as a “low-risk enterprise.” Some also thought their care within the trial would be tailored to their individual needs.

Common good and identity implications

The authors suggested that attitudes towards trial participation could be characterised by a combination of a sense of “altruism or duty” and “personal desire and self-interest.” People

articulated a strong sense of “moral duty” to take part and of the importance of contributing to scientific knowledge, but were “happy to help others... only where they could also help themselves”. The authors conceptualised this as “weak altruism.”

LINE OF ARGUMENT

As indicated above, our line of argument synthesis highlights the significance of the way potential participants were situated in terms of their health states, treatment junctures, and perceptions about these at the time of trial recruitment. Potential participants’ sense of their situation can influence the nature and salience of judgements about: communications and relationships with trial recruiters; trial interventions and processes; and the implications of trial participation decisions for the common good and their own identity. All of these judgements can shape decisions about trial entry, although their particular significance varies between and within condition groups. Figure 2 illustrates the line of argument developed from the second synthesis.

The above summary suggests several emergent patterns. Interpersonal interactions and relationships between potential trial participants and trial recruiters can be particularly important when people find themselves (or their children) in urgent, unfamiliar and apparently life-threatening situations. In part this may be because fear impairs information processing³ and loneliness enhances the need for relational support.¹⁷ The advice of trusted clinicians can also be particularly important for people with long-term conditions if trial

participation might involve a change of treatment that threatens the stability of their condition.

People sometimes perceive invitations to participate in trials as personal recommendations from recruiting doctors. The practical and ethical implications of this depend on the nature of their relationship (e.g. 'usual' or 'trial-specific') and the duration and quality of interactions between them.

The features of trial interventions and processes are obviously salient for people's decisions about trial entry, although their significance depends on how they are perceived and considered in relation to other issues. Perceptions of trial interventions as potentially beneficial and "low risk" incline people to participate, and some people strongly value trial participation as a means of possible access to treatments that are unavailable otherwise. Perceptions of trial interventions as more risky, on the other hand, can render declining participation as the better (because safer) option. In general, people may perceive the risks of trial participation as lower if all the interventions being compared are licensed for at least some kinds of clinical use, although judgements about the risks of these interventions still vary.

Attitudes towards participating in a trial can often be characterised by a sense of wishing to contribute towards the greater good, and thus demonstrating a positive moral identity, but also being concerned about self-interest. Self-interest considerations might be particularly strong among people in relatively 'good' situations that could be threatened by trial

participation. Some reports of the significance of trial participation as a moral imperative may have reflected more of a post-trial decision rationalisation than a prospective influence.

[Insert Figure 2]

Comparison with first synthesis

Our two meta-ethnographic syntheses were broadly compatible, but the second more clearly indicated *how* participants' health-related situations can mediate the significance for people's decisions about participation of key features of recruitment processes (including relationships with trial staff), of the interventions and processes involved in particular trials, and of participants' general inclinations to support research.

Discussion

Our second synthesis highlighted the significance of potential participants' health states and healthcare situations at the time of recruitment for mediating their interpretations and weighing up of: (a) communication and relationships with trial recruiters; (b) trial interventions and processes; and (c) common good and personal identity considerations. Trialists need to consider these issues when designing recruitment approaches.

Our literature searches were systematic, although searching for qualitative studies is a complex challenge and still requires further investigation.²³ We only included papers published in English and the 12 papers in this second meta-ethnography represented only 9 studies, so there may have been some over-representation of particular concepts and ideas.

The available studies did not cover the range of health-related trial situations comprehensively.

When we conducted the second “stand-alone” meta-ethnography, we were inevitably somewhat sensitised to the findings of the first, although we refrained from referring back to this until the second synthesis was completed. We were also particularly familiar (as authors) with one of the papers²² included in the second synthesis. However, the interpretive process of synthesising translations will always to some extent reflect the particular backgrounds of the research team involved.

On reflection, given the broad similarities of our two syntheses, our concerns about “forcing a fit” by trying to incorporate subsequently published studies into our first synthesis were perhaps too strong. However, if such a strategy had been adopted we would probably not have made the refinements to the initial line of argument that were facilitated by our decision in the second meta-ethnography to group studies according to the health and health care situations of potential participants at the time of recruitment.

Further investigation and debate about processes for updating meta-ethnographic syntheses will become increasingly important as more time elapses since early syntheses. This study provides the first empirical insights into the updating process that we are currently aware of. Our experience has suggested that a ‘standalone’ update can be appropriate, and consideration could be given to different kinds of study sampling²⁴ including time based approaches. These might be particularly useful when substantial numbers of relevant papers are available.

References

1. McDonald AM, Knight RC, Campbell MK, Entwistle VA, Grant AM, Cook JA, et al. What influences recruitment to randomised controlled trials? A review of trials funded by two UK funding agencies. *Trials* 2006; 7 (7 April)
2. Locock L, Smith L. Personal experiences of taking part in clinical trials – a qualitative study. *Patient Education and Counselling* 2011; 8:85-93
3. Kenyon S, Dixon-Woods M, Jackson CJ, Windridge K, Pitchforth E. “Participating in a trial in a critical situation: a qualitative study in pregnancy.” *Quality and Safety in Health Care* 2006; 15, 98-101
4. Canvin K, Jacoby A. “Duty, desire or indifference? A qualitative study of patient decisions about recruitment to an epilepsy treatment trial.” *Trials* 2006; 7, 32
5. Byrne-Davis LMT, Salmon P, Gravenhorst K, Eden TOB, Young B. Balancing high accrual and ethical recruitment in paediatric oncology: a qualitative study of the ‘look and feel’ of clinical trial discussions. *BMC Medical Research Methodology* 2010; 10:101
6. Edwards S, Lilford R, Thornton J, Hewison J. Ethical issues in the design and conduct of randomised controlled trials. *Health Technology Assessment* (1998); 2:1-132
7. Ross S, Grant A, Counsell C, Gillespie W, Russell I, Prescott R. Barriers to participation in randomised controlled trials: A systematic review. *Journal of clinical epidemiology* (1999); 52:12, 1143-56.
8. McCann, S.K. (2007). Patients’ perspectives on participation in randomised controlled trials. Ph.D. Thesis. University of Aberdeen
9. Atkins S, Lewin S, Smith H, Engel M, Fretheim A, Volmink J. Conducting a meta-ethnography of qualitative literature: Lessons learnt. *BMC Medical Research Methodology* 2008, 8:21

10. Malpass A, Shaw A, Sharp D et al. 'Medication career' or 'Moral career'? The two sides of managing antidepressants: a meta-ethnography of patients' experience of antidepressants. *Social Science & Medicine* 2009; 68 (1), 154-168
11. Bridges J, Nicholson C, Maben J, et al. Capacity for care: meta-ethnography of acute care nurses' experiences of the nurse-patient relationship. *Journal of Advanced Nursing* 2012 doi 10.1111/jan.12050
12. Noblit GW, Hare RD. *Meta-Ethnography: Synthesizing Qualitative Studies*. 1st edn, SAGE Publications, Newbury Park, California 1988
13. Britten N, Campbell R, Pope C, Donovan J, Morgan M, Pill R. Using meta-ethnography to synthesise qualitative research: a worked example. *Journal of Health Services Research & Policy* 2002, 7:209-215
14. Dixon-Woods M, Tarrant C. Why do people cooperate with medical research? Findings from three studies. *Social Science & Medicine* 2009; 68, 2215-2222
15. Snowdon C, Elbourne D, Garcia J. "It was a snap decision": Parental and professional perspectives on the speed of decisions about participation in perinatal randomised controlled trials. *Social Science & Medicine* 2006; 62, 2279-2290
16. Madsen SM, Holm S, Riis P. Attitudes towards clinical research among cancer trial participants and non-participants; an interview study using a grounded theory approach. *Journal of Medical Ethics* 2007(a); 33: 234-240
17. Madsen SM, Holm S, Riis P. Participating in a cancer clinical trial? The balancing of options in the loneliness of autonomy: A grounded theory interview study. *Acta Oncologica* 2007 (b); 46; 49-59.

18. Mangset M, Førde R, Nessa J, Berge E, Bruun Wyller T. "I don't like that, it's tricking people too much...": acute informed consent to participation in a trial of thrombolysis for stroke. *Journal of Medical Ethics*; 2008 34, 751-756
19. Heaven B, Murtagh M, Rapley T et al. Patients or research subjects? A qualitative study of participation in a randomised controlled trial of a complex intervention. *Patient Education and Counselling* 2006, 62, 260-270
20. Costenbader K H, Brome D, Blanch D, Gall V, Karlson E, Liang M H. Factors determining participation in prevention trials among systemic lupus erythematosus patients: a qualitative study. *Arthritis and Rheumatism (Arthritis Care and Research)*, 2007; 57(1), 49-55
21. Paterson C, Zheng Z, Xue C, Wang Y. "Playing their parts": the experiences of participants in a randomized sham-controlled acupuncture trial. *The Journal of Alternative and Complementary Medicine*, 2008; 14(2), 199-208
22. McCann, S.K., Campbell, M.K., & Entwistle, V. A (2010). Reasons for participating in clinical trials.
23. Jepson R, Ritchie, K. Methods of synthesizing qualitative research studies for health technology assessment. *International Journal of Technology Assessment in Health Care* 2011, 27:4, 384-390.
24. Dixon-Woods M, Agarwal S, Jones D, Young B, Sutton A. Synthesising qualitative and quantitative evidence: a review of possible methods. *Journal of Health Services Research & Policy* 2005; 10, 1, 2005: 45-53