

time for person centered research in neuroscience: users driving the change

There is an exciting opportunity to change the landscape of clinical trials and new interventions. Research can now be tailored to the needs of the public through the use of public led online trials (PLOTs) and participatory research interventions in the form of user driven healthcare. We explore some of the advantages and pitfalls of collaborative participant centered research. Collaboration is made possible through online communication, social media, and the desire of researchers, the public and clinicians to work collaboratively for the common good.

The present clinical trials system shows a decline in enrolment and compliance and an increase in unreported serious adverse events, attrition, and clinical trials contamination. The situation is mirrored in clinical practice where 71% of individuals have searched online for health information and a growing percentage report the support they receive from other patients is superior to that they can get from their medical providers.¹

There are disturbing trends where patients do not understand the differences between the role of a patient and a participant, they know nothing about bias or how a trial works, and become disturbed when a trial is stopped for safety reasons in case they were getting some real or perceived benefit. When safety and bias are brought up as a way of rationalizing the cessation of an unsafe intervention, vulnerable participants become distraught because in their own eyes they would die anyway and the trialists and regulators, by halting the trial, have deprived them of life and hope.²

Participants, up until now, have been unable enter a trial and to learn interactively what takes place and why it might be necessary before they face life altering situations where the only hope for survival becomes a clinical trial.

A neglected area of methodologically sound research is in the area of the interventions that the informed public can do for themselves.³ This is partly due to the fact that much of biomedical research is funded through intervention sponsors, e.g. the pharmaceutical industry, as there

is little profit to be made from interventions people can do for themselves. Nonetheless, these questions are of intense interest to patients and have significant potential for lifestyle and behavioral health effects.⁵ Even when research is not funded by a sponsor, it tends to address the questions of most interest to the researcher rather than those of interest to the patients.³

The articles clinicians are exposed to in journals and in on-going education tend to be about drugs rather than about interventions or changes the patient can make in their own lives without medical assistance. It is reported that over half the articles selected by clinicians for abstracting for the Journal EBM are about drug trials, and yet, in focus groups, clinicians and specialists reported wanting fewer drug trials.⁶

The process below (figure 1) is taken from a stakeholders focus group on osteoarthritis of the knee and confirms that patients' priorities differ from those interventions most researched.⁷

This contrasts with the actual research in progress. DeBronkart and Sands urge medicine, science and industry to "Let Patients Help"⁴ pointing out that although they are not medically trained they can be a valuable source of information on their own conditions. They may, as a group,

be able to dedicate significant time to keep up with the new developments and research in their areas of concern. They point out that this also builds solidarity and community between all stakeholders as they can find out what is important to each group by observation and communication. It is claimed that 75 new trials and 11 systematic reviews are produced daily.⁸ A medical provider catering to clinical care that may be unable to keep up with the flood of new research on each patient's condition. A person, or a group of people with the condition can make knowing the research their priority and this is one area where other stakeholders could collaborate to provide tools for the public to become informed research partners. In addition, we think that crowdsourcing the research areas would better aid in addressing the needs of the various stakeholders involved rather than be dictated by personal preference of researchers or pharmaceutical interests.

The public is signalling that the present research mode fails to meet their needs and this is demonstrated by a reduction in clinical trials participation worldwide. Groups such as Quantified Self, 23 and Me and Patients Like Me are providing a platform where the public self experiment and analyse results, sometimes to their own detriment.⁹ It may be time to

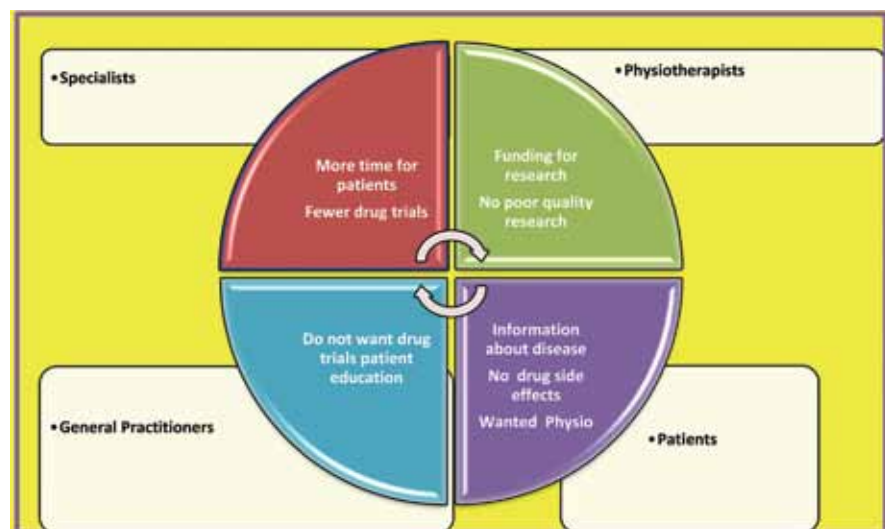


Fig. 1: Patient vs medical provider priorities for research in knee osteoarthritis [5]

place the focus on questions the public wants answered rather than those that do not meet their needs.¹⁰

A review of published and unpublished reports in 2001 found research was dominated by studies of pharmaceutical (550, 59%) and surgical (238, 26%) interventions. Knee replacements were considered helpful by 5/6 respondents, while 40% of those surveyed did not find education and advice very helpful. Pain tablets were considered helpful by 66% of those surveyed but only 4.5% wanted more research on pain tablets. There is a mismatch between perceived need and effectiveness, and in many of the therapies like alternative interventions, patients wanted to know more about were the least studied.

Preferred choices among research priorities in a survey of 67 patients were as represented in figure 2.⁷

We can see in Figure 3 that although 23.9% of patients showed an interest in CAM trials, they represented only 3% of clinical research trials and that although only 4.5% of those surveyed found pain tablet research of interest, they dominated 82% of clinical trials.

Chronic conditions are often relapsing and remitting. This makes them particularly prone to direct to consumer marketing and bad science, as, without an RCT, it would be difficult to know when an individual gets better or if a temporary remission is the natural course of the disease.¹¹ Because of this, and the low success rate of complete remission, people with chronic and neurodegenerative disease also look for alternative therapies to drugs and orthodox treatments. Improved methodology and validity of these treatments are needed to assess efficacy.¹²

Open and extensive data collection presents possibilities to see data in new ways. Implications can be positive and negative. Pharamlot shares that unreported side effects are rapidly disseminated through social media but bypass standard FDA reporting mechanisms.¹³ Participants may be scooping official clinical trials by reporting through social media sharing prior to publication. They could potentially contribute to crossover contamination in research.¹⁴

Some data shared with patients is not portable and although the data appears to be de-identified, the owners of the databases seem unconcerned about sharing vulnerable persons' genomic information with insurance companies or pharmaceutical industries.⁹ There is merging of

organizations with direct consumer marketing, diagnostics, and interventional services.¹⁵ Without guidance, supervision and education, the public will conduct experiments on their own. This leads to

risk, bias and potential harm.⁹ In contrast, an educated and informed public may speak out against unregistered trials and incomplete reporting or hiding of trial reports that can mask ineffective or

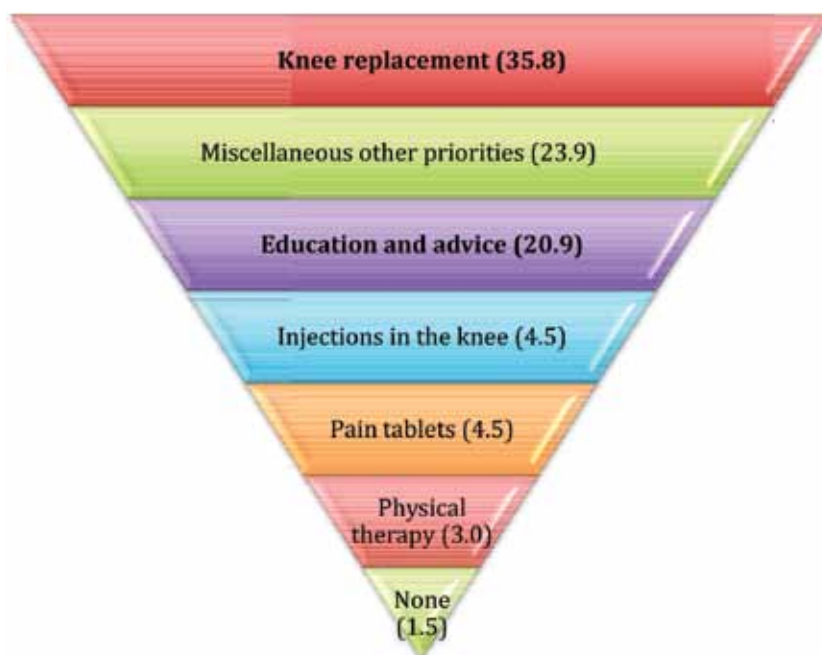


Fig. 2: Research priorities for 67 patients knee of osteoarthritis⁶

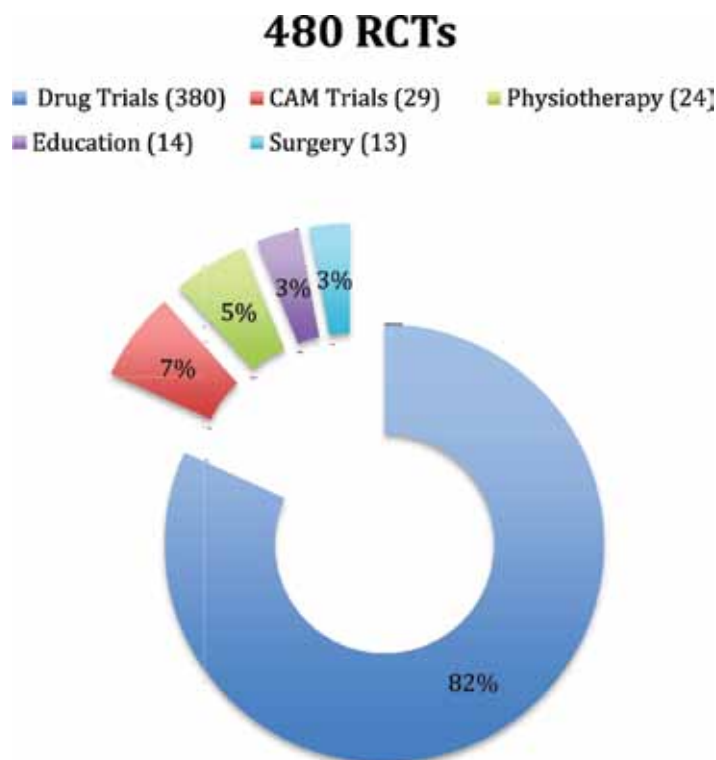


Fig. 3: Types RCTs for interventions in knee osteoarthritis

dangerous interventions. Multiple patient groups have joined the campaign where the AllTrials petition (<http://alltrials.net>) has been signed by 78240 people and 470 organisations who are urging their members to insist on a clinical trial being registered before they will take part.¹⁶

The present climate offers an excellent opportunity for science, medicine and industry to contribute in shared decision making for medical interventions and in clinical research. Participants can be empowered as they share in the prioritization, choice, trial design, and implementation of clinical trials. This can take place through user driven health care where the patient is at the center of the intervention.¹⁷ In this arena the possible research questions or interventions are discussed with the patient, participant, medical providers, researchers and other stakeholders and they brain storm best solutions together.¹⁸ A user-driven approach, additionally, has the benefit of not only crowd-sourcing the problems or community-needs, but also of obtaining solutions to complex clinical scenarios within a resource-constrained setting. Using online asynchronous interactions, it has been possible to deal with clinically complicated cases through a multidisciplinary approach.

For example, the current group of authors have worked on a case of porphyria presenting with hyponatremia and paralysis, with acute abdominal pain. The case was de-identified and presented on the user driven healthcare platform (<http://udhc.co.in>)¹⁹ and this was followed by an intense discussion on closed-to-public forums. Questions that were pondered over for future cases as the patient's life hung in the balance included the possibility of a 'person centered study design,' such as an adaptive trial that could be used to measure the efficacy of multiple interventions and eliminate those that were unsafe or ineffective to give the participant more options for a solution when time is at a premium.²⁰ Systematic reviews were diligently searched only to find the evidence around available treatments is not high.

"What else may work here in this woman fighting for her life now on a ventilator?"

Doctors discuss, "Would it be possible that the porphyrins may be getting deposited in her peripheral nerves as well as CNS (Hypothalamic deposition causing hyponatremia?) and possibly that too

is causing a leukemia like picture". They mourn together at their helplessness in the face of uncertainty and lament, "but then so very little is known due to the rarity of these cases. This is perhaps again because most of our current research focuses on 'populations' and rare diseases mostly happen to lesser number of persons".

These discussions not only contributed in the construction of a differential diagnosis for the presenting symptoms, but also raised several evidence gaps which could be adopted for future research question development.¹⁹

This multi-pronged approach also helped in finding cost-effective solutions for the patient, which is an important consideration in the setting of the developing world. This single case study helped to form a nidus around which research questions crystallised. These were not developed on the personal whims of a researcher or the less-than-altruistic needs of the pharmaceutical or diagnostics industry, but, rather, were stumbled upon while in quest for answers to questions raised by the patient. And finally, in this framework, the patient remains at the heart of all the endeavors, making it an ideal patient-centered model.

Person centered healthcare is a framework where the whole person (physical, neurological, cognitive, emotional, spiritual and social is seen as an ecosystem that can be fine tuned through competent care, quality research and sensitive informed interaction to optimise outcomes.²¹ In clinical trials we suggest a working environment where every aspect of the research is prioritised and discussed with the public as practised in the ThinkWell and then the public does the research with the backup of qualified professionals.²² While this "democratization of research" might increase the already overwhelming paperwork and online records associated with clinical trials, this would not just be a method of solving the "popular problems" but can also be a method to keep researching agencies accountable to the public. There have been multiple issues with publication bias which has resulted from suppressed publications and results. In a framework where the initiation of a registered trial is publicly acknowledged, "hiding" of results becomes more difficult. This has far-reaching implications, not just in the neurosciences but, in the larger context of medical research itself.

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