Host: Welcome to the *ANESTHESIOLOGY* journal podcast, an audio interview of study authors and editorialists.

Dr. BobbieJean Sweitzer: Hello. I'm BobbieJean Sweitzer, Professor of Anesthesiology at Northwestern University and an Associate Editor for *ANESTHESIOLOGY* and you are listening to an *ANESTHESIOLOGY* podcast designed for physicians and scientists interested in the research that appears in our journal.

Today we are speaking with two authors of publications that appear in the June 2020 issue of the journal. With us is Dr. Mark A. Shulman. Dr. Shulman is a lead author of an article titled "Defining the Minimal Clinically Important Difference in Patient-acceptable Symptom State Score for Disability Assessment in Surgical Patients."

Dr. Shulman is a full-time anesthesiologist in the Department of Anaesthesiology and Perioperative Medicine at Alfred Hospital and a Senior Lecturer at Monash University, Melbourne, Victoria, Australia. Welcome, Dr. Shulman.

Dr. Mark A. Shulman: Thanks, Dr. Sweitzer. It's a pleasure to be able to speak to you and Dr. Kalkman today. Thanks very much for the invitation to be on this podcast.

Dr. BobbieJean Sweitzer: Joining Dr. Shulman is Dr. Cor J. Kalkman who wrote an accompanying editorial "Minimal Clinically Important Difference, Maximum Impact." Dr. Kalkman is Professor, Department of Anesthesiology, University Medical Center Utrecht, Utrecht, the Netherlands. Welcome, Dr. Kalkman.

Dr. Cor J. Kalkman: Thank you, Dr. Sweitzer. Thank you, Dr. Shulman. It's a pleasure to be on the podcast with you both today.

Dr. BobbieJean Sweitzer: Let's start with you, Dr. Shulman. I'm a bit uncertain that those in our audience who are not already familiar with disability assessment may not fully grasp the essence of your manuscript or what we plan to discuss today simply from the title. Will you maybe give us just a 15-second elevator pitch about what this study is all about?

Dr. Mark A. Shulman: Certainly. Disability, as measured by the WHODAS, which stands for the World Health Organization's Disability Assessment Schedule, is a patient-centered outcome that's being used increasingly in clinical trials to measure the patient experience of the journey following surgery.

The aim of this particular study was to define the values on the WHODAS scale that correspond to a significant change in disability, being free of disability or having clinically significant disability.

Dr. BobbieJean Sweitzer: I understand that we have information already on measuring patient disability in medical populations or nonsurgical populations and even some information from postoperative studies. But apparently this is primarily from providers' determinations of that disability and apparently we have little to no information from actual patients' perspective on what is clinically meaningful to them. Can you tell us more about this?

Dr. Mark A. Shulman: Well, it's certainly true that providers' or clinicians' assessments of disability have traditionally focused on specific clinical parameters such as range of motion, strength or pain; however, it's important that we remember when we talk about disability, we're talking about an interaction between a person's health problem and their personal or environmental situation. This interaction may or may not lead to a person having problems performing certain tasks or participating in society in a way that they would want to.

In this way, a specific injury or health problem may lead to disability in one patient but not another. That's why it's so important to measure disability from a patient's perspective. We need to find out what matters to our patients. In the perioperative medicine world, we're now doing this with assessment tools like the WHODAS.

Dr. BobbieJean Sweitzer: Dr. Kalkman, why is it important to establish an objective, meaningful change in disability from the patient's perspective? And how important is disability—which is a bit of a broad term—compared to other patient outcomes?

Dr. Cor J. Kalkman: Well, I think that's (inaudible) the key issue here. We are perioperative physicians and we're always on the lookout to do things in better ways, find better drugs, anesthesia techniques, better ways of providing care and we do this to improve the outcomes for our patients.

And the most reliable way to find out what works and what doesn't is to do randomized controlled trials where we assign patients who consent to participate in either the new intervention or the control group which is often what we do now: care as usual.

Unfortunately, it's quite easy to select a study endpoint that does not always translate really well to the patient's experience. If I may give an example: so, the blood levels of an enzyme that indicates myocardial injury or an MRI scan where you find microscopic new brain lesions, now these are important outcomes, that's for sure. But disability as measured with the WHODAS questionnaire, that much better captures the effect of abnormalities on daily functioning and meaningful to the patient.

An alternative patient-centered outcome is quality of life. It's actually been with us much longer and there is, I have to say, considerable overlap with disability.

Dr. BobbieJean Sweitzer: Dr. Shulman, how did you actually conduct this research? Was this a prospective trial? And how was disability actually assessed? I know we've mentioned the WHODAS and we're going to get to the details of that a little bit more. But can you give us sort of the big picture of this study?

Dr. Mark A. Shulman: Certainly. This trial was conducted by retrospectively pooling data from over 4,000 patients enrolled in three different studies and in each of these studies, the data was collected prospectively. The studies included the RELIEF study which is a large randomized controlled trial; it also included our initial WHODAS validation cohort study; and, the third study was the MIDAS study which is an ongoing single-center cohort study which aims to identify the predictive and postoperative disability in the elderly.

In all three studies, disability was assessed before and after surgery using the 12-item WHODAS questionnaire. Just briefly regarding the WHODAS, each of the 12 WHODAS questions asks about the level of difficulty a patient has with a particular activity over the past 30 days and it's scored from 0 which equates no difficulty to performing that particular activity to 4 which equates to extreme difficulty with not being able to perform that activity at all.

This simple score out of 48 answers is then converted to a percentage score to arrive at a final WHODAS score between 0% for no disability and 100% which is complete disability.

Dr. BobbieJean Sweitzer: You mentioned that you assess disability preoperatively. I assume that was to establish baseline. But does that also mean that some of these patients actually were disabled or had some degree of disability before surgery?

Dr. Mark A. Shulman: That's right. We did want to establish a baseline. The majority of patients were free from disability, although about approximately 20% of patients we evaluated did have significant disability prior to surgery. This proportion remained approximately similar for male or female patients, younger and older patients.

Perhaps not surprisingly patients having neurosurgery, orthopedic and cardiothoracic surgery had higher rates of disability before surgery than those having other types of surgery; for example, plastic or abdominal surgery.

Perhaps a little more surprising, to me at least, was that patients having cancer surgery were much less likely to have significant disability prior to surgery than those patients not having cancer surgery.

Dr. BobbieJean Sweitzer: That is quite surprising, actually. I guess it's somewhat subjective, right, of a patient's assessment of being disabled? Were the cancer patients just very optimistic?

Dr. Mark A. Shulman: These measurements are supposed to be quite objective and reproducible. I think it may more reflect the fact that to have surgery for cancer you actually need to be more fit and healthy and free from disability. I suspect the older, sicker and more disabled patients perhaps may not end up having their cancer surgery. So, I think perhaps this group selects for, in general, less disabled patients and also doesn't include the kind of patients with orthopedic problems or mobility problems in general.

Dr. BobbieJean Sweitzer: Sure, that makes a lot of sense. So, Dr. Kalkman, at the center of this study is this 12-item disability questionnaire. The World Health Organizations' Disability Assessment Schedule, also referred to in our conversations here and in the paper as WHODAS, I think, 2.0. Can you tell us about this instrument? What does it actually measure and just give us some more details.

Dr. Cor J. Kalkman: So, as Dr. Shulman just told us, it is a questionnaire and most patients will fill it in on paper, but you can also do this over the phone. It's 12 simple questions and even if the patient is really disabled and cannot fill in the questionnaire, a spouse or informal preparer could do it. And it's designed to measure your level of disability and there are 12 questions and maybe I should just give you some examples of the kind of questions it would ask you as a patient.

It asks how much difficulty do you have standing for long periods such as a half an hour. How much difficulty do you have taking care of your household responsibilities? How difficult is it for you to learn a new task, for example, learning how to get to a new place? And how much of a problem did you have in the last 30 days joining your community activities, say, festivities or going to church?

So, it is a mix of physical but also emotional and psychological disabilities as viewed by the patients. So, in that sense it is, indeed, subjective. But at the same time it's also very meaningful. It asks you about difficulties maintaining friendship or dealing with people you do not know, difficulties with your day-to-day work or school activities. So, that is 12 questions that you can answer from no problems at all to very hard or impossible.

Dr. BobbieJean Sweitzer: What is the scale of the answers?

Dr. Cor J. Kalkman: So, each question is either a 0, 1, 2, 3 or 4. So, we have 12 questions that would give you a maximum scale of 48 which is hard to communicate or (sounds like: talk with) and that's why Dr. Shulman and his colleagues have transformed it to a 0 to 100 scale. So, 100% would be maximum disability, basically you can't do any of these activities; and, 0 would be no difficulties whatsoever, you can do all of these activities and you have no difficulties whatsoever.

Dr. BobbieJean Sweitzer: And each of these items are equally weighted?

Dr. Cor J. Kalkman: Yes, it's a simple summation. There is no magic. But help me here, Dr. Shulman. That's my understanding is no magical transformations.

Dr. Mark A. Shulman: That's correct.

Dr. BobbieJean Sweitzer: Dr. Shulman, so I understand that the patients actually use this WHODAS to assess their own disability. Did the clinicians also assess these patients? Did you compare the two?

Dr. Mark A. Shulman: That's right. The patients themselves used the WHODAS questionnaire to self-rate their level of disability and clinicians did not influence these assessments in any way. And no, we did not compare a clinician-based assessment to the patient's self-rated assessment.

Dr. BobbieJean Sweitzer: Dr. Kalkman, maybe one more question about WHODAS. Is this the best method, do you think, to get the information that you think we need to assess patients' perspectives of their outcomes and disability and how they're doing postoperatively?

Dr. Cor J. Kalkman: Well, I would assume that nowadays we are all much more convinced that we need the patient perspective and that's a large departure from how we used to do clinical trials maybe 10, 20 years ago where we would go for surrogate outcomes or pathophysiology.

So, WHODAS captures, as you could hear from all those questions, what are the needs for the patients and how the disease or the postoperative state influenced their daily activities. So, I would consider it certainly one of the better patient-centered outcome measures.

Of course you have quality of life; it's been with us for a long time and there is overlap, as I said. But a problem with measuring quality of life, I find, is that many patients have an amazing ability to adjust to a new situation or a new disability. And I have spoken to patients with even spinal cord injuries in a wheelchair who would rate their quality of life very high despite the considerable disability.

So, this is obviously a wonderful thing that we have this capacity to adapt, but I would say that directly measuring disability is probably a better reflection of the outcomes of the perioperative process.

And, of course, there are additional more targeted questionnaires that I would also call patient-reported outcome measures and they could be more focused to the type of surgery; say after orthopedic surgery you would ask specific questions about mobility and pain.

Dr. BobbieJean Sweitzer: Thank you. That was a nice explanation. Dr. Shulman, at what timepoint after surgery were patients contacted and asked to do this evaluation?

Dr. Mark A. Shulman: Patients who were approached before surgery took time (inaudible) level of disability and then patients from all three studies were then also contacted by telephone at 3 and 6 months following surgery to assess their recovery and their level of postoperative disability.

Dr. BobbieJean Sweitzer: And did you measure anything else to determine whether patients had done better or worse than expected after surgery?

Dr. Mark A. Shulman: Yes, we did, as well as other clinical variables that differed between the studies. All three studies measured readmission to hospital within three months of surgery. We included this data in our analysis because we felt it represented a key patient objective which is being well enough to go home and not return to hospital after surgery. And we thought that people who had complications after surgery would be more likely to be readmitted as several previous studies have shown.

The initial WHODAS validation study also asked patients about whether they felt better after surgery and whether surgery had improved their daily lives. We used these two patient-centered outcomes as the anchors or clinical endpoints that could help us determine the minimal change in WHODAS consistent with the clinically important difference in disability for the patient.

Dr. BobbieJean Sweitzer: Dr. Kalkman, can you explain to us what is the best and the minimal clinically important difference and the patient acceptable symptom state that Dr. Shulman reported on and mentioned here?

Dr. Cor J. Kalkman: Well, first of all, I have to admit myself, this is tough. This is not simple material and I had to read the paper several times before I grasped the concept. So, Dr. Shulman just mentioned they asked the patients whether they felt better after surgery and whether the surgery actually improved their daily lives and they were able to indicate whether it was just a little better or much better or a little worse or much worse.

And then they linked the little better or the little worse, so I tend to agree that as a little bit better to the change in the actual WHODAS score from the patients' answers to the questionnaire and so they arrived at the minimum clinically meaningful difference.

In other words, if you perform the clinical study and you found statistically significant difference in disability, if these differences are less than

what the patient could consider a little better or a little worse, they cannot be considered clinically meaningful even if statistically significant.

Well, and for the patient-acceptable symptom state, the researchers looked at those patients who would consider themselves improved after surgery and then they looked at the distribution of the disability scores in that subset of patients and then said, "Well, if you really think you have considerably improved after surgery, you now must have an acceptable symptom state" and then they arrived at scores up to 50 out of the 100 scale that are compatible with an acceptable level of disability for most patients.

Dr. BobbieJean Sweitzer: First off, thank you for acknowledging that you had to read the paper maybe perhaps more than once. I have to tell you, I did as well. I think it was a fascinating paper and I really encourage our listeners to read it, but I also want to encourage them to stick with it and I hope this conversation will also really augment their understanding when they do read the paper.

Back to you, Dr. Shulman, did Dr. Kalkman get it right there or is there anything that you want to clarify or disagree with?

Dr. Mark A. Shulman: No, that was a fantastic description of the process which is a complicated process for someone who hasn't come across the concepts of distribution- and anchor-based assessment of the minimum clinically important difference. So, I think that was a very good explanation.

Dr. BobbieJean Sweitzer: Thank you both. Dr. Shulman, what do we already know about WHODAS, I guess, from other studies and meaningful disabilities from either WHODAS determination or other ways that set the background for your study?

Dr. Mark A. Shulman: The main data we have is from the World Health Organization group that initially developed and validated the WHODAS. They suggest that a WHODAS score of greater than 25% is consistent with moderate disability and that a score of greater than 50% is consistently severe disability.

We also obtained data from an Australian cohort which looked at disability in the community and from that data we extrapolated that a change in score of 8% was consistent with new disability.

It's important to note, though, that these recommendations were based on disability assessments in people in the community who had a range of physical and emotional health problems leading to disability. However, it's important that these kind of definitions or scaling properties be assessed in a population of interest.

So, in our case that's patients having surgery and that's why we felt it was important to do this study.

Dr. BobbieJean Sweitzer: Dr. Kalkman, Dr. Shulman notes in his paper that experts recommend that multiple approaches—I guess, using a combination of anchor- and distribution-based methods—would average in the results are the optimal methods of determining this minimal clinically important difference.

What are the advantages or disadvantages of either of these methods and what do you think of the approach that Dr. Shulman used?

Dr. Cor J. Kalkman: I would consider the anchor-based method, again, that's where you compare changes in the score with patients – how patients actually tell you they have experienced the surgery. I would consider those the most valuable also in this study, the most relevant.

So, with these distribution-based methods, that's actually purely statistical. Like, you compare 1.3 times the standard deviation or 5% of the score range and these experts who recommend to use both methods basically tell you do the anchoring. That's where you get the link with the patient experience and then you use the distribution method actually to check whether you are way off or in line.

And having said that, it's, of course, very reassuring that in this particular study both methods arrived at the same 5% clinically meaningful difference.

Dr. BobbieJean Sweitzer: Dr. Shulman, before you tell us what you found out, is there anymore background that you think would help our listeners to understand about how you did this study or what you were trying to determine?

Dr. Mark A. Shulman: I think we've probably summarized the most important background already. I mean, we did this study because we wanted to find out the change in WHODAS score that was meaningful to patients and we wanted to set some clear parameters in surgical patients that would define patients who were free of disability or patients who had serious clinically important disability.

I think the way we did this was to retrospectively analyze the prospectively collected data from the three studies I mentioned earlier. I think that's the main gist of the study and why we did it.

Dr. BobbieJean Sweitzer: Yes, that was a nice summary. So, what did you find out?

Dr. Mark A. Shulman: Well, we estimated that a 5% increase or decrease in the WHODAS score is consistent with the minimal clinically important difference. This estimate was remarkably consistent across both distribution- and anchor-based methods that Dr. Kalkman describes.

And then it was also very consistent across different patient groups and this increases our confidence that it's an accurate estimate. We also estimated that in surgical patients, the patient acceptable symptom state or PASS score, which the patients would consider themselves to be free of significant disability, is defined by a WHODAS score of less than 16% and that a WHODAS score of greater than 35% is consistent with at least moderate clinically significant disability.

Dr. BobbieJean Sweitzer: How did you classify the patients who did not fit, I guess, in either of those two categories, meaning that they were not considered to be in an acceptable symptom state and considered disability-free, but they were also not considered as having at least a moderate clinically significant disability?

Dr. Mark A. Shulman: So those patients fit into the WHODAS scores of between 16% and 35% and we classify these patients as having mild disability. It's possibly not the ideal term, but I think it's consistent with previous WHODAS descriptions.

And I think while they don't have moderate clinically significant disability, I think this group can probably be thought of as being an at-risk or vulnerable population that may in the future develop more significant disability. But this is certainly a concept that hadn't been proven yet and requires future research.

Dr. BobbieJean Sweitzer: And I think you'd mentioned earlier that previously a WHODAS score greater than 50 was severe disability. Did you determine patients with severe disability or you just had them moderate to least moderate?

Dr. Mark A. Shulman: No, we just determined at least moderate.

Dr. BobbieJean Sweitzer: There was a reason you did not try to determine severe disability?

Dr. Mark A. Shulman: We wanted to define a point at which disability became clinically significant. We didn't look to define severe disability because we didn't want to overcomplicate the story and try and split the scale up into many parts, especially for use in randomized controlled trials or that sort of thing. We felt it would be more straightforward to have a simple cut point.

Dr. BobbieJean Sweitzer: Thank you. I think you mentioned earlier about certain surgeries, like orthopedic and spine or neuro that were more likely to have disability and those with cancer less. But what were other predictors at which patients are more likely to have significant disability from surgery or change from pre- to post-[surgery].

Dr. Mark A. Shulman: Sure. Just to clarify, the patients, our orthopedic and neurosurgical patients, had a higher rate of disability preoperatively. So, this wasn't a prediction of future outcome; that was their preoperative state.

Dr. BobbieJean Sweitzer: Got it.

Dr. Mark A. Shulman: While looking at predictors of postoperative disability was really beyond the scope of this study, it wasn't a prediction study, but having said that, we did concern our findings from the WHODAS validation study which showed that patients with a higher ASA score tended to have higher WHODAS scores equating with more disability after surgery, And just higher ASA scores continued for their entire recovery trajectory over the 3, 6 or even 12 months after surgery.

In terms of prediction, we're hoping that the future data from the MIDAS study, which I mentioned earlier, will be able to answer the question of what the patient and surgical factors are that predict postoperative disability.

Dr. BobbieJean Sweitzer: Good. Dr. Kalkman, can WHODAS be used in all surgical settings for all procedures and with all patients? And what do you think the limitations of Dr. Shulman's study are?

Dr. Cor J. Kalkman: Of course the true answer, as Dr. Shulman says, we don't really know yet. But I would say WHODAS can be used after every surgical procedure to estimate what happens with the patient's disability, whether it improved, stayed the same or it got worse.

And it is true and Dr. Shulman and his coauthors, they acknowledge that in their paper that more than half of the patients participated in this fluid management study, the RELIEF trial and they all had upper abdominal surgery. So, that may have colored the study sample a little bit and I would say orthopedic and spine surgery was less well-represented.

So, I do believe that the disability approach can be used in many types of surgery, but maybe we need to adjust for specific types of surgery as we do trials with this endpoint in large numbers of, say, spine or cardiac surgical patients.

And obviously have to keep in mind to the goal of surgeries: is it to prevent future disability, say, carotid endarterectomy or a colectomy when a tumor was found during screening? Or is it to solve current disability, like if you have spine surgery for lower back pain or cardiac surgery for angina?

So, maybe that for such different goals that this (sounds like: bulky) approach may need more refinement. It's my expectation that as we will use this endpoint in our perioperative clinical trials, we'll learn much more and we can be able to refine this endpoint along these lines.

Dr. BobbieJean Sweitzer: Dr. Shulman, is there any advantage, do you believe, in asking caregivers how they assess patients' disabilities?

Dr. Mark A. Shulman: I think the main advantage lies when patients are so severely disabled or perhaps not severely but have a specific problem which prevents them from being able to answer those questions themselves. Otherwise, I think it's always preferable and best if we have the patient's own self-assessment rather than a proxy assessment.

Dr. BobbieJean Sweitzer: So, I think you recommended in your paper that specific scoring definitions should be used as standard clinical trial endpoints. Can you tell us about that?

Dr. Mark A. Shulman: Certainly. So, a bit of background is that the COMPAC StEP group is a group that's published consensus definitions for patient-centered outcomes. They recommend including a standard clinical trial endpoint. WHODAS is one of three patient-centered outcomes included. At the time of this publication, though, they used the old 25% cutoff to define clinically significant disability which is the cutoff we suggested in our previous work.

Based on our current research, I think I would recommend the following definitions of clinical trial endpoints: the first is minimal clinically important difference which is an increase or decrease of WHODAS score of at least 5%; the next is disability-free survival which is a patient who is alive with a WHODAS score of less than 16%; the next is clinically significant disability which is a patient who has a WHODAS score of at least 35%; and, finally, new onset clinically significant disability which is a patient who has had an increase in WHODAS score of at least 5% to a final WHODAS score of at least 35%.

And just to add to those definitions, I think I wanted to add to what Dr. Kalkman said earlier which is that I agree the way we use the WHODAS score probably does need to be modified depending on the patient group. For example, when patients get very low levels of preoperative disability who become disabled versus patients who may have – a more heterogenous group who may have deferring trajectories of disability after surgery.

But I think rather than modifying the WHODAS or thinking of changing the WHODAS, I think one of the best ways to approach that is by using these different measurements that I've just described and choosing the one that best suits the trial you're planning.

Dr. BobbieJean Sweitzer: I hope today's discussion will interest many of our listeners and lead you to read this important article to learn more. Thank you, Drs. Shulman and Kalkman, for discussing your work with us today. I wish you well as you continue your efforts to enhance the practice of anesthesiology and strive to improve the care of our patients.

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