

Supplement digital content 1: Surgical procedures involved in the Delphi process

Four specific surgical procedures were chosen for identifying core outcome domains of perioperative pain management. These surgical procedures cover a broad range of parameters that might influence the appropriate selection of outcome domains or measurement instruments, which might differ depending on the procedure, type of pain-related intervention and patient population (please also compare www.postoppain.org). This table highlights some of the aspects related to each surgical procedure explaining its inclusion in the project and the diversity of the chosen surgeries able to reflect several aspects related to postoperative pain.

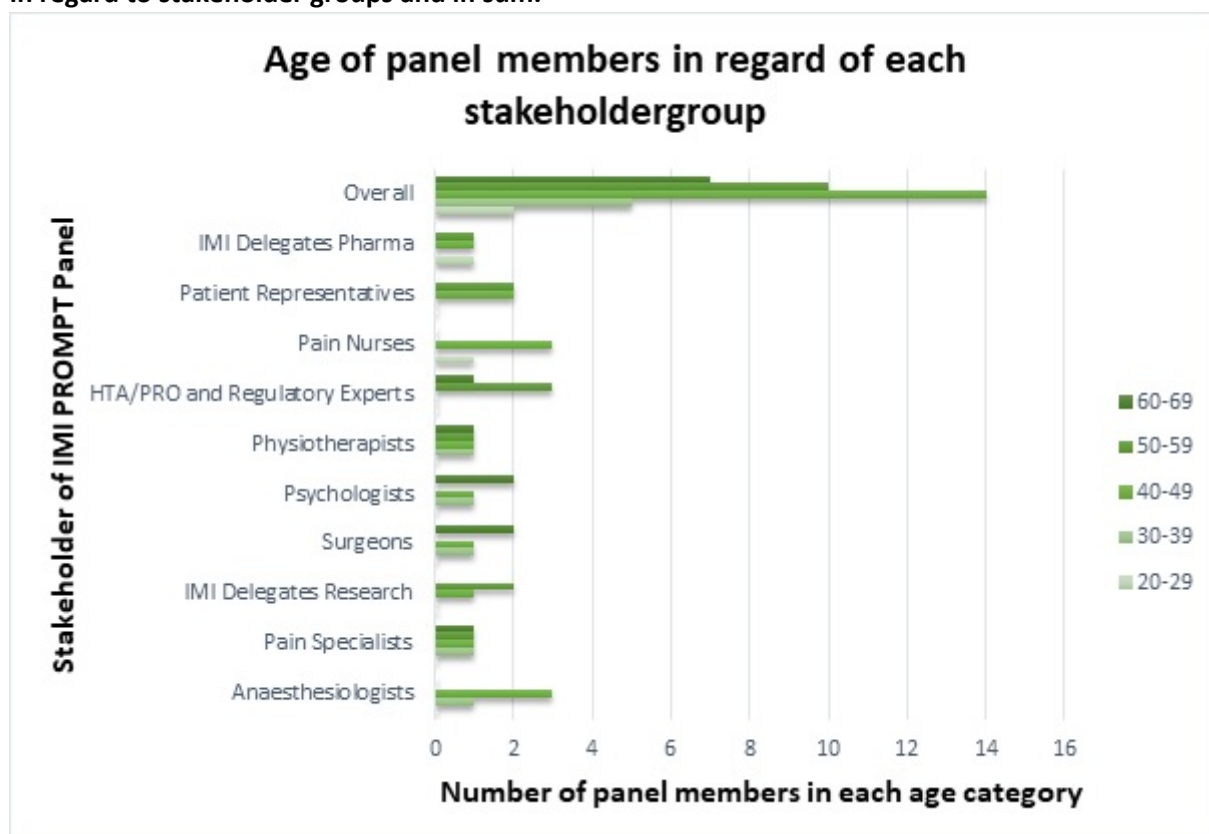
	Total Knee Arthroplasty (TKA)	Breast Surgery (BS)	Sternotomy (ST)	Endometriosis Surgery (ES)
Frequency	high	high	high	high
Main tissue affected	joint / bone	soft tissue and nerves (Axilla)	visceral (thorax) and bone	visceral (abdomen) and somatic (peritoneum)
Surgical service	in hospital	In hospital	In hospital	Mixed (in- and out-patient)
Patient population				
- Age	- old	- all ages	- older	- young
- Gender	- both	- females	- both	- females
Preoperative pain	frequent	as in general population	as in general population	Very frequent
Main anesthesiological treatment options	regional analgesia / systemic analgesia	systemic analgesia	systemic analgesia	regional analgesia/ systemic analgesia
Risk of chronic postoperative pain	high	high	high	not determined

Supplement Digital Content 2: Composition of surgery groups by stakeholders

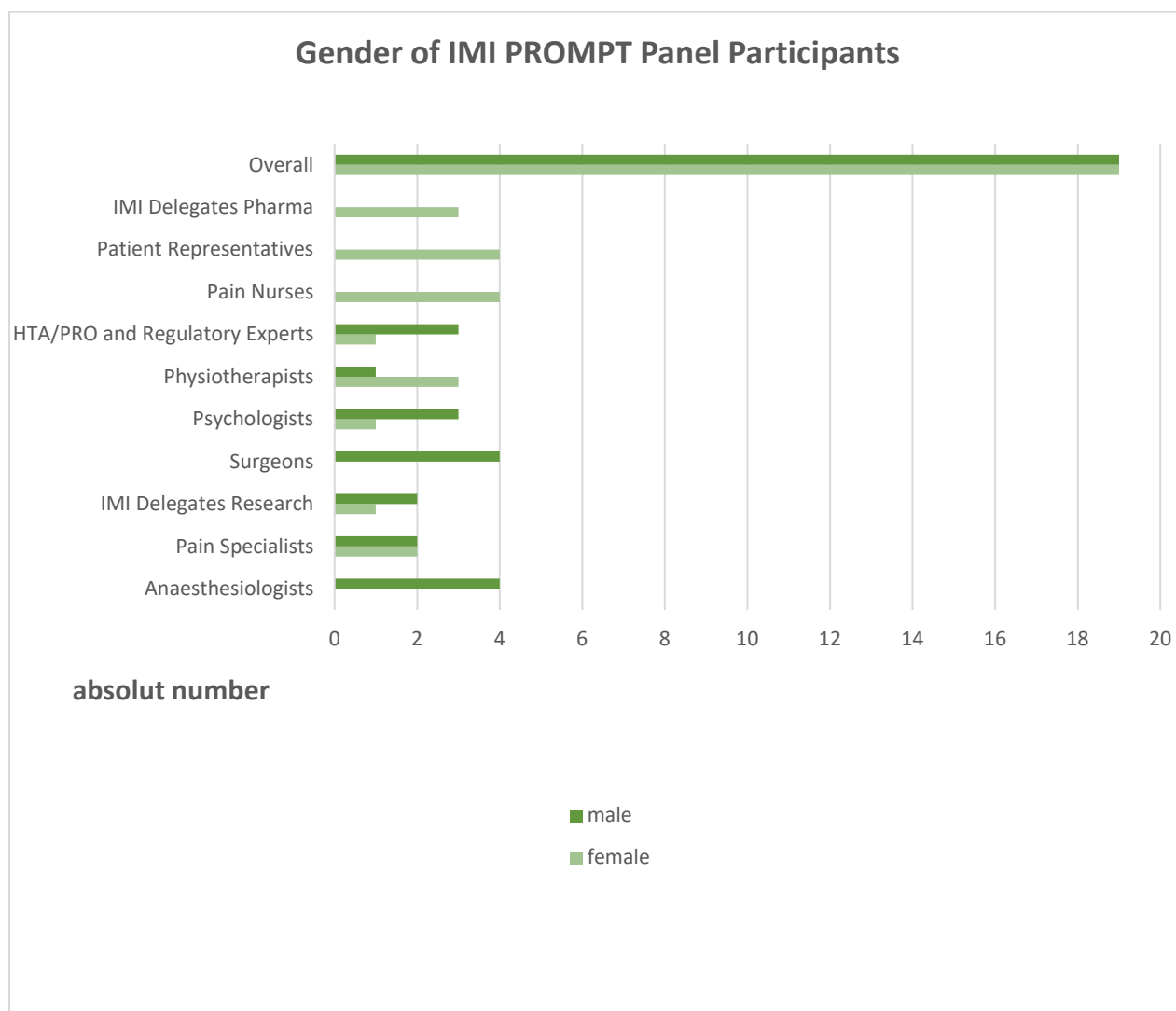
	<i>Surgery group</i>					Sum
		TKA	ST	BS	ES	
<i>Stakeholder Group</i>	Anesthesiologists	1	1	1	1	4
	Pain Specialists	1	1	1	1	4
	IMI Group (clinical)					3
	Surgeons	1	1	1	1	4
	Clinical psychologists	1	1	1	1	4
	Physiotherapists	1	1	1	1	4
	HTA/PRO experts and Regulatory experts	1	1	1	1	4
	Pain Nurses	1	1	1	1	4
	IMI-EFFPIA (pharmacists)					3
	Patient Representatives	1	1	1	1	4
Sum						38

Of 40 invited panel members 38 participated in the IMI PROMPT consensus process on outcome domains for perioperative pain management in total knee arthroplasty, breast surgery, sternotomy and endometriosis. Information regarding age and gender was provided by all participants, all other parameters had been provided by 30 IMI PROMPT Panel Participants.

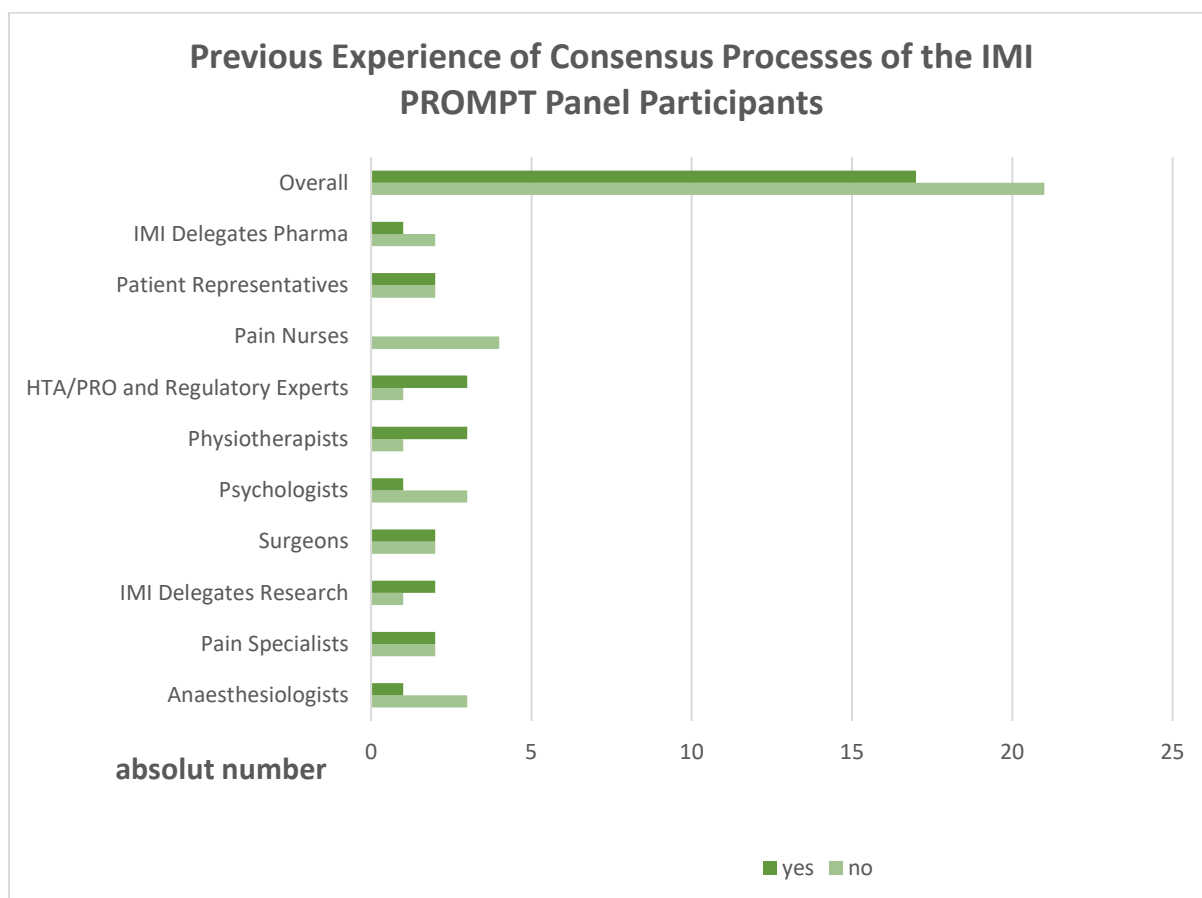
Supplement Digital Content 3. Diagram that displays the age of the IMI PROMPT Panel Participants in regard to stakeholder groups and in sum.



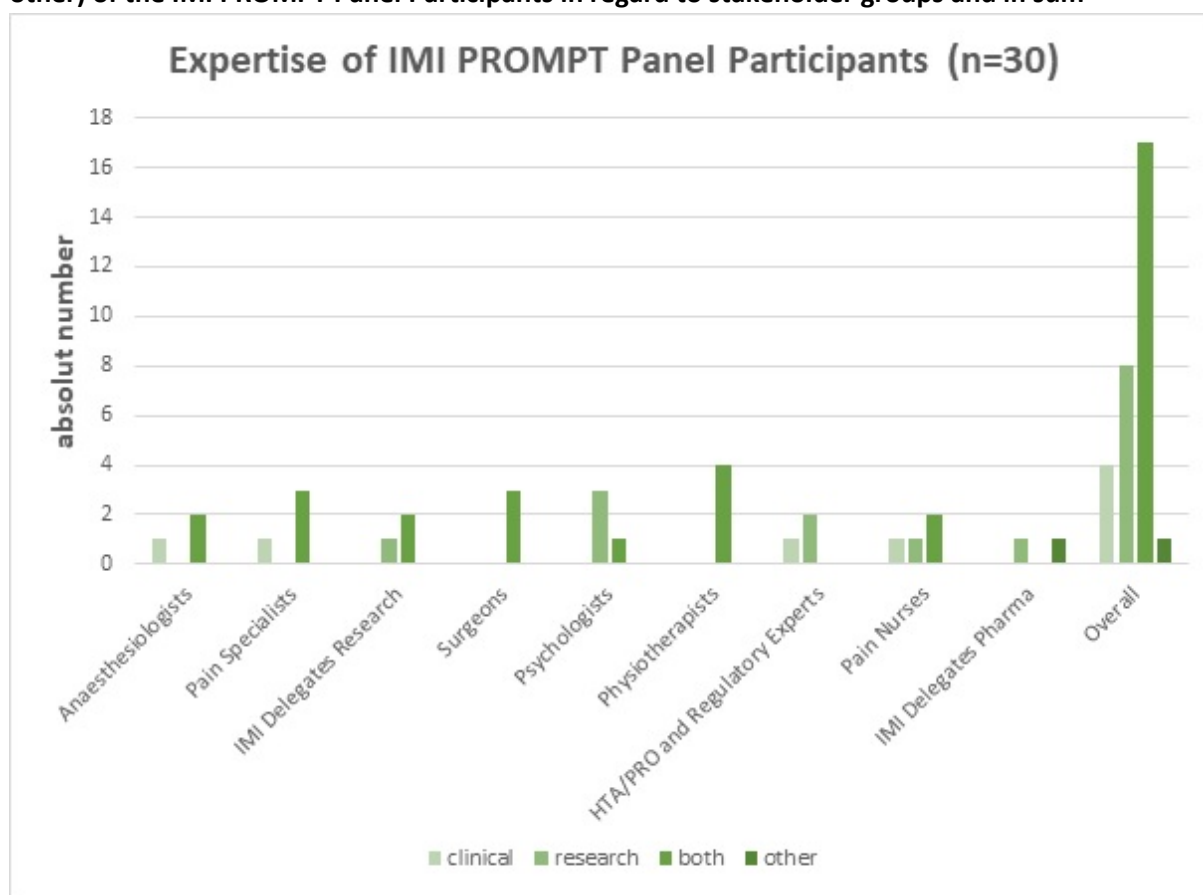
Supplement Digital Content 4: Gender distribution of the IMI PROMPT Panel Participants in regard to stakeholder groups and in sum



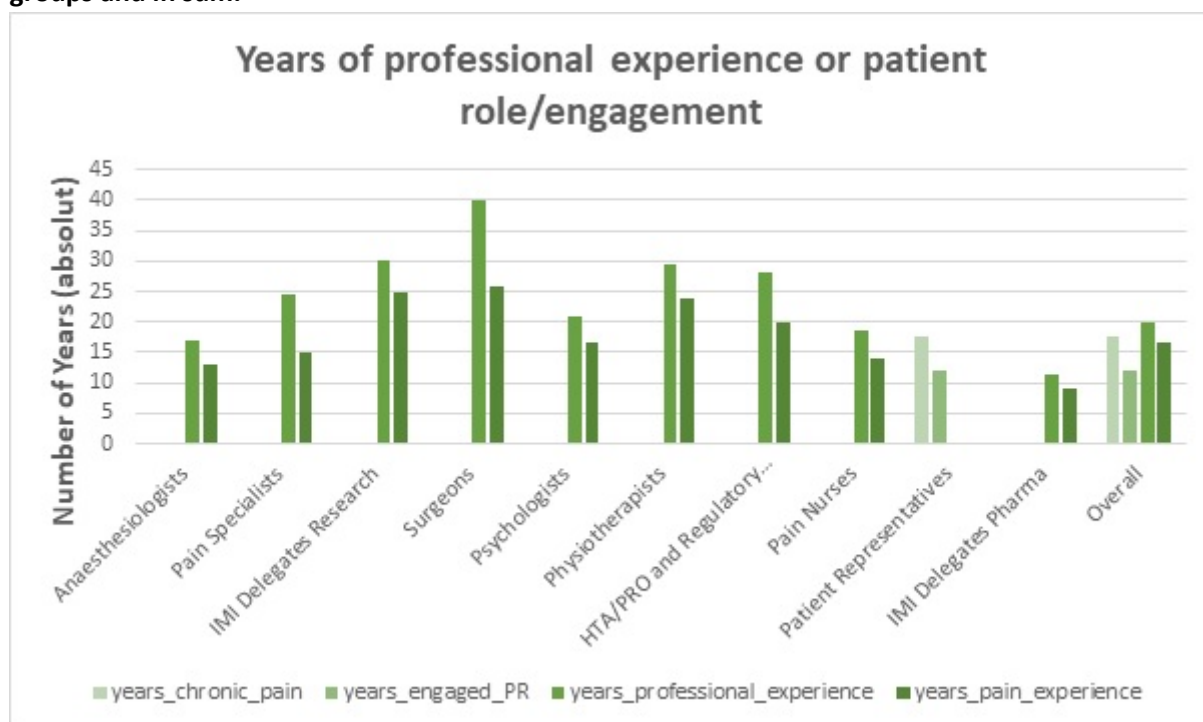
Supplement Digital Content 5: Previous Experiences in Consensus Processes of the IMI PROMPT Panel Participants in regard to stakeholder groups and in sum



Supplement Digital Content 6. Diagram that displays the expertise (clinical, research, both or other) of the IMI PROMPT Panel Participants in regard to stakeholder groups and in sum



Supplement Digital Content 7. Diagram that displays the years of Experiences (general and regarding pain management) of the IMI PROMPT Panel Participants in regard to stakeholder groups and in sum.



Supplement Digital Content 8. Definitions of the most important constructs for IMI PROMPT consensus meeting

Term (alphabetical order)	Working definition
Breast surgery	Surgery of the breast; here: Surgery related to breast cancer including mastectomy and lumpectomy
Clinical trial	An experiment to compare the effects of two or more healthcare interventions. Clinical trial is an umbrella term for a variety of designs of healthcare trials, including uncontrolled trials, controlled trials, and randomised controlled trials [8].
COMET	The COMET (Core Outcome Measures in Effectiveness Trials) Initiative brings together people interested in the development and application of agreed standardised sets of outcomes, known as ‘core outcome sets’ (↗Core outcome set) [2].
Consensus process	Coming to an agreement by generating a proposal, identifying unsatisfied concerns and modifying the proposal to generate as much agreement as possible; the transfer into decisions are made by predefined, definite rules (i.e. $\geq 70\%$ of agreement, $< 20\%$ of disagreement necessary).
Construct validity	An aspect of ↗ <i>validity</i> ; degree to which the scores of an HR-PRO instrument are consistent with hypotheses based on the assumption that the HR-PRO instrument validly measures the construct to be measured [5]
Content validity	An aspect of ↗ <i>validity</i> ; degree to which the content of an HR-PRO instrument is an adequate reflection of the construct to be measured [5]
Core area	An aspect of health or a health condition that needs to be measured to appropriately assess the effects of a health intervention; broad concepts consisting of a number of ↗ <i>domains</i> [1]
Core outcome set (COS)	Standardized set of outcomes which should be measured and reported (↗core domain set) or

	also how they should be measured (\nearrow core outcome measurement set), as a minimum, in all effectiveness trials for a specific health area. For \nearrow daily record keeping, the concept of COS was adopted for \nearrow VAPAIN.
Core outcome set of domains	The minimum set of (sub)domains necessary to adequately cover all \nearrow core areas, i.e. fully measure all relevant concepts of a specific health condition within a specified setting; describes <u>what</u> to [1].
Core outcome set of measurement instruments	The minimum set of outcome measurement instruments that must be administered in each intervention study of a certain health condition within a specified setting to adequately cover a corresponding \nearrow core outcome set; describes <u>how</u> to measure [1].
COSMIN	“Consensus-based Standards for the selection of health Measurement Instruments”; an initiative to improve the selection of measurement instruments in medicine [3].
Daily record keeping	Daily record keeping is defined as assessment and documentation of outcomes in daily clinical practice/routine care (e.g. patients with comorbidities, limited time or resources).
Discrimination	An aspect of the \nearrow OMERACT Filter 2.0; captures issues of \nearrow reliability and \nearrow sensitivity to change [1].
(Sub)Domain	Component of \nearrow core area; a concept to be measured, a further specification of an aspect of health, categorized within a \nearrow core area [1].
Endometriosis	A condition in which tissue <i>similar</i> to the lining inside the uterus (called “the endometrium”), is found <i>outside</i> the uterus, where it induces a chronic inflammatory reaction that may result in scar tissue. It is primarily found on the pelvic peritoneum, on the ovaries, in the recto-vaginal septum, on the bladder, and bowel.
Endometriosis surgery	Primary surgery for suspected diagnosis of and with the aim to confirm the presence of endometriosis

	Abdominal surgery in patients with confirmed endometriosis
Feasibility	An aspect of the <i>OMERACT Filter 2.0</i> ; captures an essential element in the selection of measures, one that may be decisive in determining a measure's success [1]
IMMPACT	The mission of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) is to develop consensus reviews and recommendations for improving the design, execution, and interpretation of clinical trials of treatments for pain [4].
Interpretability	the degree to which one can assign qualitative meaning - that is, clinical or commonly understood connotations – to an instrument's quantitative scores or change in scores [5].
Measurement error	The systematic and random error of a patient's score that is not attributed to true changes in the construct to be measured [5].
OMERACT	OMERACT (Outcome Measures in Rheumatology) is an independent initiative of international health professionals interested in outcome measures in rheumatology. Over the last 20 years, OMERACT has served a critical role in the development and validation of clinical and radiographic outcome measures in rheumatoid arthritis, osteoarthritis, psoriatic arthritis, fibromyalgia, and other rheumatic diseases [6].
OMERACT Filter 2.0	A comprehensive framework and process for developing <i>core</i> outcome measurement sets, which has been fruitful within rheumatology [1].
Outcome	Any identified result in a <i>Domain</i> arising from exposure to a causal factor or a health intervention [1]
Patient-relevant	All “patient-reported outcomes” (PROs) (<i>patient-reported</i>) as well as treatment outcomes specifically relevant to patients but reported e.g. by physicians or spouses are defined as “patient-relevant outcomes.”

Patient-reported	A patient-reported (PRO) is a measurement that is directly assessed by the patient, i.e. without the interpretation of the patient's responses by a physician or anyone else (to be differentiated from \nearrow patient-relevant).
Perioperative	relating to, occurring in, or being the period around the time of a surgical operation
Perioperative pain management	Any intervention that is started pre- intra- or postoperatively aiming to improve pain outcome within 14 days after surgery
PROMIS	Patient Reported Outcomes Measurement Information System (PROMIS), funded by the National Institutes of Health (NIH), is a system of highly reliable (\nearrow reliability), valid (\nearrow validity), flexible, precise, and responsive (\nearrow responsiveness) assessment tools that measure patient-reported (\nearrow patient-reported) health status (PROMIS 2014).
Reliability	The proportion of the total variance in the measurements which is due to 'true' differences between patients [5].
Responsiveness	Responsiveness (\nearrow <i>sensitivity to change</i>) is the ability of an HR-PRO instrument to detect change over time in the construct to be measured [5].
Sensitivity to change	Please refer to \nearrow <i>responsiveness</i> .
Sternotomy	(Median) sternotomy, made in the thorax that gives a wide view of the thoracic cavity, usually used for CABG (heart surgery).
Structural validity	An aspect of \nearrow <i>validity</i> ; degree to which the scores of an HR-PRO instrument are an adequate reflection of the dimensionality of the construct to be measured [5].
Systematic literature review	Literature reviews that adhere closely to a set of scientific methods that explicitly aim to limit systematic error (bias), mainly by attempting to identify, appraise and synthesize all relevant studies (of whatever design) in order to

	answer a particular question (or set of questions) [7].
Test-retest-reliability	An aspect of reliability (<i>↗reliability</i>); extent to which scores for patients who have not changed are the same for repeated measurement over time [5].
Total knee replacement	<i>Surgery</i> that replaces a <i>knee joint</i> with an artificial <i>joint</i> (prosthesis)
Truth	An aspect of the <i>↗OMERACT Filter 2.0</i> ; captures issues of face, <i>↗content</i> , and <i>↗construct validity</i> [1].
Validity	Degree to which an HR-PRO instrument measures the construct(s) it purports to measure [5].

- 1 Boers M, Kirwan JR, Wells G, Beaton D, Gossec L, d'Agostino M-A, Conaghan PG, Bingham CO, Brooks P, Landewé R, March L, Simon LS, Singh JA, Strand V, Tugwell P. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. *J Clin Epidemiol* 2014;67(7):745–53.
- 2 COMET. COMET (Core Outcome Measures in Effectiveness Trials) Initiative. <http://www.comet-initiative.org>.
- 3 COSMIN. CoOnsensus-based Standards for the selection of health Measurement INstruments. <http://www.cosmin.nl/>.
- 4 IMMPACT. Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials. <http://www.immpact.org/>.
- 5 Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, Bouter LM, Vet HCW de. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. *Qual Life Res* 2010;19(4):539–49.
- 6 OMERACT. The OMERACT handbook: OMERACT, 2018.
- 7 Petticrew M, Roberts H (eds.). *Systematic Reviews in the Social Sciences*. Oxford, UK: Blackwell Publishing Ltd, 2006.
- 8 The Cochrane Collaboration. Cochrane Glossary. <http://www.cochrane.org/glossary/5#letterc>.

Supplement Digital Content 9: Therapy aims for perioperative pain management after four surgical procedures Part I (WC)

Total knee arthroplasty	Sternotomy	Breast surgery {Comment: Breast (cancer & reconstructive)}	Endometriosis
{Early [crossed out: quick] movement} [connected with acceptable [added: manageable] pain with knee movement, reduce fear, anxiety with movement]	{Improve sleep}	{ <u>Survival</u> } {Comment: not related to pain in 2/52}	{Improve quality of life}
[1 dot=1. relevance; 7 dot=2. relevance]			[2 dot=relevance]
{Patient realistic and timely information}	{Low pain intensity} [connected with reduced functional impairment]	{ <u>Pain relief</u> (individualized)} {Quick reduction of pain} {Pain free breathing}	{Pain} {No/mild pain or less pain intensity}
[1 dot=1. relevance; no dot=2. relevance]	[2 dot=relevance]	[dot=relevance]	[2 dot=relevance]
{[crossed out: no pain]} {Not for short term}	{Low death rate, side effects, complications due to surgery, pain manifestation}	{ <u>Well informed patient/relatives</u> } {Realistic expectations} {[connected with pain relief, good quality of life, shared decision making]}	{↓analgesics compared to before surgery} {[crossed out: Reduced/Minimize adverse effects]}
	[2 dot=relevance]	[dot=relevance]	
{Acceptable/manageable pain with knee movement and at rest! In all situations}	{Effective surgery (long term)}	{Good sleep/eating}	{Function- restore}

	[connected with red[uced] functional impairment]	[connected with pain relief and normal adequate function]	{With or without pain} {[Addition by] -intestinal [crossed out: -illegible] [crossed out: -sexual] -Psychological -Urological -Social -Physical -Sexuality}
[no dot=1. relevance; 4 dot=2. relevance]			[2 dot=relevance]
{Follow up [...] of pain after discharge}	Low costs	{ <u>Good quality of life</u> } {-Depressive} {-Anxiety}	{Promoting self care/self management} {↑ self pain care strategies}
		[dot=relevance]	[3 dot=relevance]
Being alive ? Aim of acute pain therapy ?	Patient at the centre [connected with tailored provision of information to set] [dot=relevance]	(removal of tumor) not pain related	Reduce hospital stay The shortest time in hospital as possible without compromising care [dot=relevance]
{Acceptable side effects}	{Red[uced] Functional impairment- low discomfort, physical function}	{[circle: Self management]/ empowerment}	{Tailored provision of information to set realistic expectations} {Information for multidisciplinary pain treatment}
[no dot=1. relevance; 1 dot=2. Relevance; 1 dot=2. relevance together with restore function]	[2 dot=relevance]		[dot=relevance]

{Restore function}	{Prevention of chronic pain/neuropathic pain}	{Shared decision making}	{Reduce anxiety and stress}
[no dot=1. relevance; 4 dot=2. Relevance; 1 dot=2. relevance together with acceptable side effects]	[dot=relevance]	[dot=relevance]	
{Reduction of complications}	{Tailored provision of information to set realistic expectations} {→timely education =right information at the right time} {preop[eratively] – in hosp[ital]-before discharge}	{{acceptance of the disease}} {Acknowledgement}	{Fear of movement}
{{(social inclusion) long term}}	{Reduce anxiety}	{Adequate referral to rehabilitation}	{Well informed patient} {- Realistic and accurate information}
			[dot=relevance]
{Shared decision making}	{Improve Self Care: general and pain relat[ed]}	{Avoidance adverse events}	{Avoid chronification} {- Further +/-or diagnosing when symptoms present}
	[dot=relevance]		
{Choice of right implant}	{Information on non-pharm[acological] pain managem[ent]}	{Minimize fear of movement}	{Acknowledgement} {{crossed out: survival; dot=relevance}} {{crossed out: realistic information; dot=relevance}} {{crossed out: reduction of postoperative complications (pneumonia, [illegible])}}
	[dot=relevance]		
{Cost effective treatment}	{Adequate pain follow up before and after discharge}	{Acceptance of new body image/self esteem}	

{Minimize distress}	{Think and consider fast tracking}	{Adequate pain assessment in follow up period (pre/post discharge)}
	[dot=relevance]	
{Minimize unnecessary medication}		<u>{Normal adequate function}</u>
{A level below preop[erative] analgesics}		{Disability}
		[dot=relevance]
{Restore function}		{{crossed out: no} side effects}
{{Crossed out: Standardized drainage/wound management}}		{Early mobilization}
{No therapy aim}		
{{crossed out: cheapest possible therapy}}		{Patient satisfaction/patient centeredness}
{2 nd opinion ?}		{Short hospitalization}
{Aim?}		{{(low cost)}
{Tailored approach for high/low pain responders}		<u>{Prevention of chronic pain incl. neuropathic pain}</u>
		[dot=relevance]
{Reduce fear anxiety with movement}		{{(satisfaction w/ social role)}
[1 dot=1. relevance; no dot=2. relevance]		
{Adequate movement !!}		{Social engagement}
[Connected with painless rehabilitation]		
{Painless rehabilitation ?}		{{crossed out: low} appropriate analgesic use}
{Acceptable pain!}		{{crossed out: consumption}}
{Facilitate rehab[ilitation]}		
{Be able to walk independently}		Optimal wound healing/↓odema

[3 dot=1. relevance; no dot=2. relevance]			
{Quality of sleep}			
{Manage daily routine/ active[ity]}			
{Active[ity] of daily living}			
[no dot=1. relevance; 3 dot=2. relevance]			
{Enhance inclusion in social interaction (e.g. hobbies)}			
{Motivation of p[a]t[ient]s (incl.[usive] coping)}			
[3 dot=1. relevance; no dot=2. relevance]			
{P[a]t[ient]- individualized therapy/aims (consid[erring] pts preferences)}			
[6 dot=1. relevance; no dot=2. relevance]			
{Access to rehabilitation}			
Comments: {Patient centered} {Well informed p[atien]ts} {Educated/expect ations realistic} {Participation in daily activities}	Comments: {Mortality is a surrogate of function}	Comments: {Pain relief →individual!} {Self management (empowerment) Patient at centre} {Patient well informed etc.} {→implementation in trial design?}	Comments: none

{...} term indicated by panel members

[...] additions by authors (e.g. when abbreviations had been provided, or when terms had been changed during the discussion indicated by crossing out, additions or similar