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Placebo Effects of Nurses' Communication alongside Standard Medical Care on Pain and Other Outcomes: A Randomized Controlled Trial in Clinical Tonsillectomy Care

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Patient outcomes are not only influenced by medical technical interventions, but also by the context in which these interventions are provided. Such effects are called placebo effects [1]. They are elicited via several mechanisms, and can impact patient outcomes, most notably pain. The best-known mechanism is expectancy, whereby manipulating patients' expectations impacts pain [2, 3]. A lesser-known mechanism is empathy [4, 5].

A relatively unexplored, promising perspective is the role of clinician communication in eliciting placebo effects. A landmark study found that placebo-acupuncture delivered by a confident, empathic clinician produced significant changes in irritable bowel syndrome patients' outcomes [5]. In subsequent experimental studies, we disentangled the effects of clinician expectancy (affecting cognitive outcomes, e.g., expected pain treatment outcome) and empathy (affecting affective outcomes, e.g., anxiety) with most positive effects when expectancy and empathy were combined [6, 7]. To strengthen the clinical applicability of placebo effects, we need to know whether similar effects will be found in clinical care alongside standard evidence-based medical interventions. This study aimed to determine the separate and combined effects of: (i) expectancy-manipulation

(standard vs. enhanced) and (ii) empathy- manipulation (standard vs. enhanced) through nurses' communication alongside standard medical care on clinical tonsillectomy patients' outcomes.

Detailed information about the intervention and methods can be found in the published study protocol [8] and the supplemen-tary material (see www.karger.com/doi/10.1159/000503904 for all online suppl. material). A four-arm (2 × 2 design) single-blind randomized controlled trial was conducted at 2 daycare nursing wards. In total, 128 patients (> 18 years, scheduled for tonsillectomy in daycare, who could speak/understand Dutch and had no mental incapacity) were recruited and randomized to one of four groups (group 1: expectations+/empathy+; group 2: expectations–/ empathy+; group 3: expectations+/empathy–; group 4: expectation–/ empathy–).

The intervention consisted of a protocolled communication manipulation on top of the standard analgesic treatment protocol and daily routine care. For each group, daycare ward nurses manipulated their communication (either standard or enhanced expectations and empathy) during the patients' stay at the daycare ward (pre- and post-operation, day 1) and during the telephone consultation day post-discharge (day 2). Other clinicians standardized their communication. Nurses were trained in the delivery of the intervention using a half-day training course and several booster sessions. The research team was (onsite) available for feedback and information cards/posters were displayed. Norms and values of acceptable behavior were not crossed.

Within the expectancy manipulation the expectation that the pain medication would work very well was either not given (standard condition, example sentence: "This is your (pain) medication") or was given (enhanced condition, example sentence: "This pain medication is known for working very well"). Within the empathy manipulation a (non-)verbal empathic atmosphere was either not created (standard condition, example behaviors: reacting with standard empathy to patients' cues/concerns, not paying extra interest in the patient as a person) or was created (enhanced condition, example behaviors: reacting extra empathically to patients' cues/concerns, showing extra interest in the patient as a person).

The main analyses (detailed information is provided in the supplementary material) using STATA 14.0 consisted of ANCOVAs to determine the main and interaction effects of expectancy and empathy on patients' (pain) outcomes. Our results (detailed information is provided in the supplementary material) demonstrated that our sample was young (mean age 28 years), female (67%), and highly educated (63%; online suppl. Table 2). The manipulations were perceived as being in the right direction, but this remained non-significant (expectancy standard: mean = 6.63; high: mean = 7.18, t = –1.62, p = 0.11, range 0–10; and empathy standard: mean = 39.70, SD = 9.33; high: mean = 42.63, t = –1.56, p = 0.12, range 10–50). In contrast, the audio-recordings of nurse-patient interactions showed that 82% of the expectancy and 68% of the empathy manipulations were successfully displayed. Anxiety towards the operation had a significant effect on day 1 maximum pain (β = 0.14, p = 0.01), and was included as a centered covariate in the analyses. ANCOVA analyses showed no significant main and interaction effects of the manipulations on patients' perceivedpain (Table 1; online suppl. Table 4). Nurses' enhanced expression of the pain medications' effectiveness

did not lower pain levels on day 1 (p = 0.43), day 2 (p = 0.96), or day 3 (p = 0.33), and nurses' enhanced expression of empathy did not lower pain levels on day 1 (p = 0.34), day 2 (p = 0.57), or day 3 (p = 0.23). The pain protocol was well adhered to and received analgesia did not differ between conditions, apart from paracetamol day 3 (F = 0.08; online suppl. Table 5). Regarding our secondary outcomes (Table 1; online suppl. Table 4), neither expectancy nor empathy influenced patients' pain expectations for the upcoming days (p = 0.68; p = 0.33) or patients' pain improvement expectations after receiving medication (p = 0.12; p = 0.62). On day 3, patients receiving high expectations thought their post-operative pain had been better than expected (p = 0.02), which was unaffected by empathy (p = 0.71). Expectations and empathy did not significantly affect patients' psychological outcomes: anxiety (p = 0.60, p = 0.14), positive mood (p > 0.99, p = 0.88), negative mood (p = 0.30, p = 0.96), and satisfaction (p = 0.62, p = 0.70). Patients' overall benefit of analgesia was not influenced by expectations and empathy (day 2: p = 0.93, p = 0.83; day 3: p = 0.18, p = 0.21). When nurses' expressed high painrelieving expectations, patients tended to rate the quality of the received care higher (p < 0.10), which was unaffected by empathy (p = 0.71). The likelihood to recommend this hospital remained unaffected by expectancy and empathy (p = 0.24, p = 0.38).

[Table 1]

Although these results were not as anticipated based on previous evidence [2, 3, 6, 7, 9], we need to interpret them in light of the choppy waters of the clinical routine care reality we entered with this study. This included methodological complexities (e.g., effects to be found from communication alongside standard care might be smaller than anticipated; a pool of nurses delivering the intervention) and limitations (e.g., manipulations not being successfully perceived; missing data) that need to be overcome in future studies. Simultaneously, we should not dismiss the potential positive placebo effects of communication we did find, i.e., positive expectations led to better evaluations of perceived pain and received care. We hope our study will act as a starting point for further studies in this important yet fragile research field, disentangling the potential effects of expectancy and empathy on clinical patients' outcomes alongside standard care. In the meantime, raising positive yet realistic expectations in an empathic manner is recommended [10]. It is harmless, time-efficient, and has the potential to improve at least some patients' outcomes for the better.

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Statement of Ethics

All participants gave their written informed consent. The study received formal ethical approval from the ethics committee of theUMC Utrecht (No. 16/144, NL55225.041) and the institutional review board of the participating hospital (No. WO 16.506). It is registered at the Dutch Trial Register (Registration No. NTR5994), which is the Primary Registry in the Netherlands.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

J.M.B., L.M.v.V., M.B.G., G.W.v.D., T.J.K., S.v.D., and B.T. were involved in the planning of the study. All authors were involved in the conduct of the study and in reporting of the work. L.M.v.V. is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Figure1: Main effects of expectancy and empathy on outcomes

	Expectancy			Empathy		
	F	SS	*p*	*F*	SS	*p*
Pain primary						
Max. pain day 1	0.63	1.97	0.43	0.91	2.83	0.34
Max. pain day 2	0.00	0.01	0.96	0.33	1.05	0.57
Pain day 3	0.95	2.89	0.33	1.46	4.43	0.23
Pain secondary						
Pain expectation	0.17	0.50	0.68	0.97	2.81	0.33
Pain improvement expectation	2.50	831.80	0.12	0.25	82.30	0.62
Pain evaluation	5.58	23.98	**0.02**	0.14	0.59	0.71
Psychological						
Anxiety	0.27	11.43	0.60	2.28	94.99	0.14
Positive mood	0.00	0.00	>0.99	0.02	1.40	0.88
Negative mood	1.10	54.17	0.30	0.00	0.12	0.96
Satisfaction	0.25	0.70	0.62	0.15	0.40	0.70
Other outcomes						
OBAS day 2	0.01	0.13	0.93	0.05	0.75	0.83
OBAS day 3	1.85	29.80	0.18	1.58	25.40	0.21
General quality	2.80	3.07	**<0.10**	0.14	0.15	0.71
Recommendation	1.43	2.56	0.24	0.80	1.43	0.38

All analyses were controlled for (centered) effects of anxiety towards the operation. Interaction effects were insignificant and thus eliminated from the model. Bold *p* values are considered significant.

Supplement

1. Materials and methods

1.1 Study design and randomization

A four-arm (2x2 design) single-blind randomized controlled trial was conducted at daycare nursing wards on two locations of a Dutch general hospital. Patients were randomized to one of four groups (see Figure 1) using a random number generator (1:1:1:1 allocation rate) via sequentially numbered sealed envelopes, independently generated and opened by a secretary. For each group, daycare ward nurses manipulated their communication, while keeping their standard medical practice constant.

1.2 Participants and recruitment

Eligible patients were adult (>18 years) patients, scheduled for tonsillectomy in daycare, who could speak/understand Dutch and had no mental incapacity (as observed by the clinical team during the consultation) were informed about the study while discussing their operation with their ENT doctor, and during preoperative screening with the anesthesiology clinician. Interested patients were then contacted by the research team who explained the study in more detail and asked the patient to return the Informed Consent (IC) form. Following a protocol amendment to increase recruitment numbers, patients were given the opportunity during the pre-operation examination to provide consent. Patients already scheduled in for an operation at study start were contacted by the anesthesiology team to be informed about the study, before being contacted by the research team.

During the study, participants were excluded if they experienced a post-operative bleeding or for other urgent medical reasons (e.g. if patients were not discharged on the day of operation). Participants were free to withdraw their participation in the study. Data collected until drop-out was used, unless the patient objected to this.

1.3 Analgesia protocol

A standard peri-operative analgesia protocol was developed by the involved clinicians (led by MBG) and consisted of day 1: pre-operative paracetamol (1000 mg); peroperative metamizol (2 gr) and morphine (5-10 mg); postanaesthesia care unit (PACU) cold application and morphine titration (2.5 mg, bolus) until satisfactory pain relief combined with tramadol (300 mg), paracetamol (2600 mg) and ibuprofen (1800 mg) at the daycare ward. The advice for day 2-3 was: tramadol (300 mg), paracetamol (2600 mg) and ibuprofen (1800 mg).

1.4 Intervention

The intervention consisted of a protocolled communication manipulation on top of the standard analgesic treatment protocol and daily routine care of the hospital. The intervention was delivered during the patients' stay at the daycare ward (pre- and post-operation, day 1) and during the telephone consultation between nurses and patients on the day post-discharge (day 2). One patient per room was included at any time point. All nurses were trained in the delivery of the intervention using a half-day training course and several booster-sessions. The research team was available

onsite and offsite to provide assistance and feedback, information-posters were displayed in the communal spaces, and pocket cards with examples of the manipulations were available to enhance standardized delivery of the intervention (documents, including training videos, available upon request from the authors).

Despite manipulating communication, norms and values of acceptable behavior were not crossed. Nurse-patient interactions are often interrupted (e.g. by telephone calls, other clinicians), impacting time and attention spent to patients' in pain(1). Variations in communication seem thus inherent to the clinical encounter, which was confirmed by field observations of the research team before study start. The training materials were tested in a pilot study to ensure they were realistic and not trespassing ethical boundaries, and finalized in collaboration with involved clinicians. More detailed information about the intervention and methods than displayed here can be found in the published study protocol(2).

1.4.1 Expectancy manipulation

In the standard condition no expectation that the pain medication would work very well was created, using sentences such as: "This is your pain medication", "This is your medication" (without mentioning pain), "The medications attempt to reduce your pain ever so slightly", or by given the pain medication in silence.

In the enhanced condition an expectation that the pain medication would work very well was created, using sentences such as: "The medications I am giving you now will lead to a strong decrease of your pain", "This pain medication is known for working very well", "With these medications your pain will decrease rapidly", or "The medication you are receiving is a strong pain killer"(3-5).

1.4.2 Empathy manipulation

In the standard condition a standard (non)verbal empathic atmosphere was created, using behaviors like reacting with standard empathy to patients' cues and concerns, keep standing when communicating, not exploring concerns in detail, not expressing extra interest in the patient as a person, not paying extra attention to not interrupting patients, and not making extra eye contact.

In the enhanced condition an extra warm and friendly atmosphere was created, using behaviors like proper introductions, sitting while communicating with patients, reacting extra empathically to patients' verbal/nonverbal cues and concerns and taking their concerns seriously, showing extra interest in the patient as a person, not interrupting the patient, and making adequate eye contact(6-14).

1.4.3 Standardization

All other clinicians (i.e. from the Ear, Nose and Throat (ENT) and anesthesiology department, operation theater, and the Post-anesthesia care unit (PACU) were instructed to standardize their communication (via personal communication and information leaflets). This included not providing extra empathy or raising extra expectations about pain.

1.4.4 Adherence

All nurse-patient interactions were audio-recorded and evaluated by a research assistant to determine adherence to the protocol, and 10% of audio-recordings were independently rated by two coders (as comparably done by Kaptchuk et al(15)). We originally planned to only code 10% of audio-recordings, but amended this to 100% in order to gather more thorough insight into the fidelity of the intervention.

1.5 Blinding

Patients were blind for specific study aims, but informed that the study focused on the effect of communication and that communication would be manipulated. At study end, they received a debriefing letter explaining the study aims and their treatment allocation. Involved health care professionals were not blinded, but either manipulated communication or standardized their communication. The research team analyzing the data was not blind to study allocation.

1.6 Sample Size

Sample size was based on of the primary outcome, i.e. patients' perceived pain, using data from a previous study(3) in which an open versus hidden administration of analgesic showed a difference of 1.2 and a total variance of 2.18. Based on a power of .80 and alpha of .05, and including an interaction-effect (with a within variance of 1.92), this results in a needed sample size of 32 patients per arm and 4x32=128 patients in total.

1.7 Outcomes

1.7.1 Background measures

Pre-operation (via patient questionnaire) we measured the following background characteristics: sociodemographics (in case of missing data, this was assessed via the medical record) and functional health status (COOP-WONCA)(16, 17)). Moreover, patients' i) general benefit/expectations/objections against medications (0-10 self-created Visual Analogue Scale (VAS), 'not at all'-'very much'); ii) general reporting of pain (0-10 self-created VAS, 'never'-'always'), and; iii) attitudes (dreading/anxiety) towards the operation (0-10 self-created VAS, 'not at all'-'very much') were assessed as we hypothesized they might influence pain perceptions(18-20). Background characteristics of the participating nurses were assessed.

1.7.2 Main outcome

Perceived pain was assessed (0-10 Numeric Rating Scale (NRS), 'no pain'-'worst imaginable pain'(21, 22) at several time-points. On day 1; pre-operatively at daycare ward, post-operatively at PACU, post-operatively at daycare ward (following routine care); Day 2: via telephone contact nurses, via patient questionnaire. Day 3: via patient questionnaire. Maximum levels of pain on day 1 and day 2 were used for all analyses (as comparably done by(23)).

1.7.3 Secondary outcomes

1.7.3.1 Pain related outcomes

Patients' post-operative pain expectations (0-10 self-created VAS, 'no pain'-'most intense pain imaginable', adapted from(24)), and pain improvement expectations following medication (0-10 self-created VAS, '0% improvement'-'100% improvement', adapted from the Credibility and Expectancy Questionnaire(25)) were assessed at day 1, post-operatively. Analgesic dosage was assessed during hospital stay (medical record) and at day 2 and day 3 (patient questionnaire). Whether post-operative pain has been better or worse than expected (self-created 0-10 VAS, 'much worse than expected'-'much better than expected', recoded into 'much better than expected'-'much worse than expected' for all analyses) was assessed at day 3 (patient questionnaire).

1.7.3.2 Psychological outcomes

Anxiety (STAI-state(26), range 10-40), positive/negative mood (PANAS(27), 10-50) were assessed at baseline and day 3 (patient questionnaires). Cronbach's alpha's for the STAI at baseline and day 3 was .93 and .88, respectively. Reliability for the PANAS positive mood was .89 and .86, and for the negative mood .89 and .85, respectively. Difference scores between baseline and day 3 were used in all analyses. Satisfaction with provided care by day care nurses (0-10 self-created VAS, 'not at all'-'very much') was assessed at day 3.

1.7.4 Other outcomes

An overall indication of the benefit of analgesia care (including pain, itch, nausea) (OBAS(28), range 0-28) was assessed at day 2 and 3 (patient questionnaire). Reliability was .59 and .68, respectively. Patients' rated quality of provided hospital care and the likelihood of recommending this hospital to other tonsillectomy patients was assessed (using two adapted items of the Consumer Quality Index (CQ-index)(29), 0-10 scale) at day 3. Success of the manipulations – perceived empathy of nurses (adapted version of CARE(30), range 10-50) and perceived induced expectation of effectiveness pain medication by nurses (0-10 self-created VAS, 'no effect at all'-'a lot of effect') – were assessed at day 3.

1.7.5 Adherence to communication protocol

For all audio-recordings a coding scheme was used to rate the occurrence of the (verbal) features of the manipulation to determine to which condition the audio-recording belonged to. For 10% of audio-recordings this was independently done by two raters. Interrater reliability of the conditions was 0.64 (Cohen's kappa), which is considered good(31, 32). Based on the audio-ratings of nurse-patient interactions, 82% of the expectancy- and 68% of the empathy-manipulations were successfully displayed. More specifically, standard expectancy (88%) and standard empathy (80%) were more successfully displayed than enhanced expectancy (77%) and enhanced empathy (56%). Overall, 56% of interactions were being rated as standard expectancies, and 62% as standard empathy.

1.8 Statistical Analysis

First, the four groups were checked on equality for background measures using $\chi 2$ tests or analyses of variance (ANOVA).

Second, for variables that differed between the groups their effects on patients' maximum pain day 1 were assessed using regression analyses and t-tests. This included the effect of patients' general benefit/expectations/objections, general reporting of pain, and attitudes towards the operation, as these variables might influence pain perceptions. Variables that influenced pain were entered as (centered) covariates in step four and further.

Third, the manipulation successes were determined.

Fourth, the effect of expectancy and empathy on patients' pain scores (maximum pain day 1 and day 2, pain day 3) was determined. Using ANCOVA, main and interaction effects were assessed (interaction effects were eliminated from the model when not significant). We also assessed whether the received analgesia per day varied between the conditions (using ANOVA) to help interpret our findings.

Fifth, the effect of expectancy and empathy on patients' secondary outcomes was determined. Using ANCOVA, main and interaction effects were assessed (interaction effects were eliminated from the model when not significant).

All data were analyzed using STATA 14.0 with two-sided significance testing at $p<0.05$ and using an intention to treat principle. If there was < 20% missing data on the questionnaires (STAI, PANAS, CARE, OBAS), these data were imputed with the mean of the remaining scores (as comparable done by(23)). Multiple imputation was not used as data might not have been missed at random. All other missing data was not imputed and participant data was not included for those specific analyses.

2. Results

2.1 Participant Flow

We enrolled patients between August 2016 and April 2018. Of the 639 assessed patients, 128 were included and randomized. Attrition on day 1 (n=15) was due to post-operative bleeding and complications for which patients were not discharged on day 1. Pain scores were available and analyzed for 125 patients on day 1, 99 on day 2 and 76 on day 3. See Figure 2 for details.

2.2 Background measures

Patients' background characteristics are displayed in Table 2. The four groups differed on marital status ($p<0.01$) and age ($p=0.03$). Nurses' background characteristics are displayed in Table 3.

2.3 Main outcome: pain

Patients' experienced levels of pain on day 1-3 are displayed in Table 4 for the different conditions. ANCOVA analyses (Table 1, Letter) showed no significant main and interaction effects of the manipulations on patients' perceived pain. As also mentioned in the letter, nurses' enhanced expression of pain medications' effectiveness did not lower pain levels on day 1 ($p=0.43$), day 2

(p=0.96) nor day 3 (p=0.33). Nurses' enhanced expression of empathy did not lower pain levels on day 1 (p=0.34), day 2 (p=0.57) nor day 3 (p=0.23). Interestingly, the covariate anxiety towards the operation kept an independent relation with pain throughout the days: day 1 (F=6.36, p=0.01), day 2 (F=8.81, p<0.01), and day 3 (F=11.89, p<0.01).

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Met opmaak: Lettertype: (Standaard) Segoe UI, Tekstkleur: Auto, Nederlands (standaard), Geen spelling- of grammaticacontrole uitvoeren

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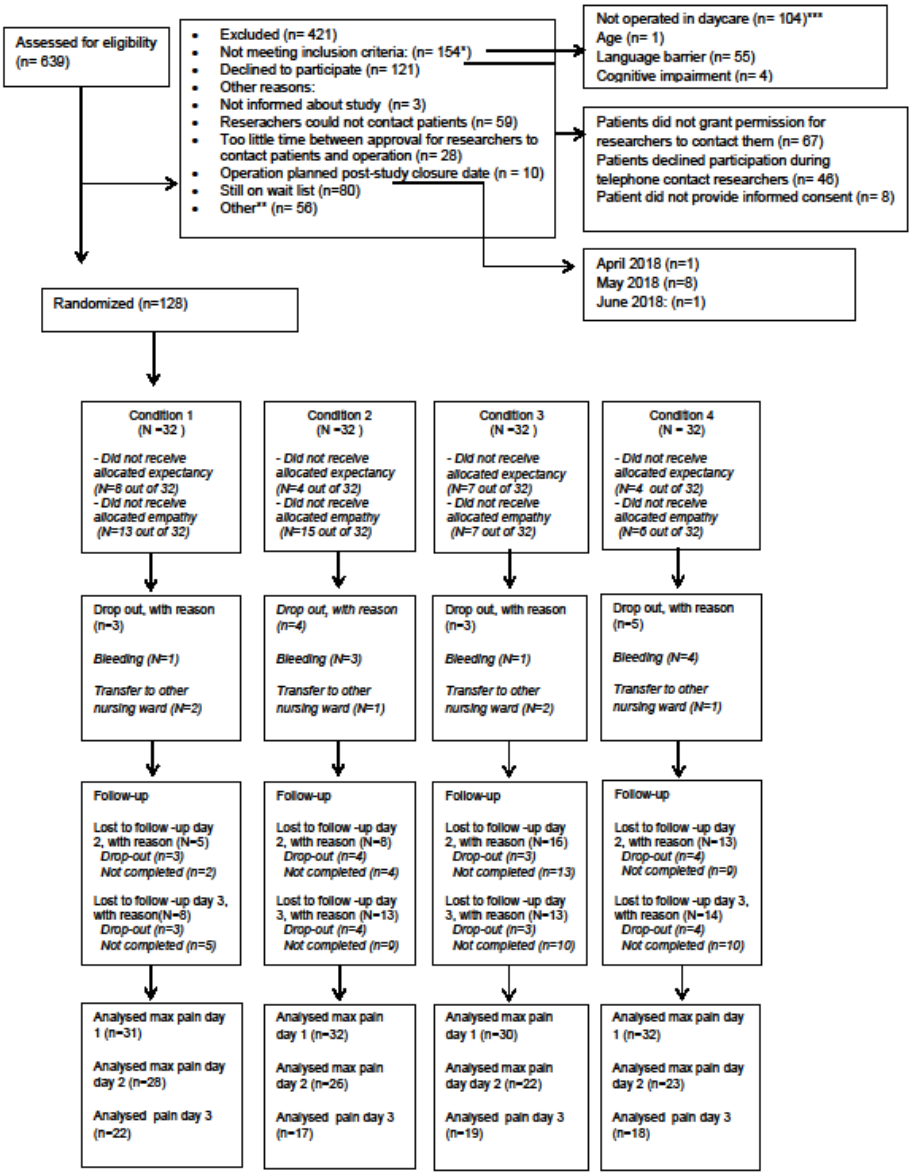
Figures

		Expectancy	
		enhanced	Standard
Empathy	enhanced	Group 1	Group 2
	standard	Group 3	Group 4

Figure 1 - Study design



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281 Fig. 2. Flowchart

Tables

Table 2 – Background characteristics participants

	Completed by nr of patients	Total (n=128)	Expectations + Empathy + (n=32)	Expectations – Empathy + (n=32)	Expectations + Empathy - (n=32)	Expectations - Empathy - (n=32)	
		M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	p
Age	128	28.01 (7.44)	28.69 (6.30)	30.91 (9.98)	26.34 (6.42)	26.09 (5.49)	**0.03 (F(3,124)=3.10)**
Health status [1]	112	13.69 (5.07)	14.00 (5.14)	13.13 (4.62)	13.07 (4.68)	14.56 (5.85)	0.64 (F(3,108)=0.57)
General benefit from medications[2]	106	6.39 (2.68)	6.47 (3.33)	6.66 (1.94)	6.63 (2.89)	5.84 (2.49)	0.64 (F(3,102)=0.56)
General positive expectations of effect medications [2]	106	7.04 (1.93)	7.04 (2.60)	6.80 (2.09)	7.15 (1.63)	7.13 (1.42)	0.91 (F(3,102)=0.19)
General objections against taking medications [2]	106	2.99 (2.63)	3.14 (2.38)	2.99 (2.55)	2.76 (2.69)	3.10 (2.93)	0.95 (F(3,102)=0.11)
General inclination to	106	6.31 (2.38)	6.66 (2.06)	5.97 (2.81)	6.66 (2.07)	5.97 (2.52)	0.53 (F(3,102)=0.73)

report pain[3]							
Attitude: dreading of operation[2]	105	5.03 (3.03)	5.54 (3.32)	5.40 (3.10)	4.73 (3.13)	4.58 (2.64)	0.59 (F(3,101)=0.64)
Attitude: Afraid of operation[2]	105	3.98 (3.03)	3.93 (3.53)	4.17 (2.96)	4.22 (2.79)	3.60 (3.03)	0.88 (F(3,101)=0.23)
		N (%)	N (%)	N (%)	N (%)	N (%)	
Marital status	112						**<0.01 (X=12.55)**
Married		16 (14)	8 (30)	6 (23)	1 (3)	1 (3)	
Single (incl divorced, widowed)		96 (86)	19 (70)	20 (77)	29 (97)	28 (97)	
Gender	128						0.49 (X=2.41)
Male		42 (33)	8 (25)	13 (41)	9 (28)	12 (38)	
Female		86 (67)	24 (75)	19 (59)	23 (72)	20 (63)	
Highest Education[4]	112						0.21 (X=8.37)
Low		-	-	-	-	-	
Intermediate-1		9 (8)	1 (4)	1 (4)	4 (13)	3 (10)	
Intermediate-2		33 (29)	7 (26)	5 (19)	13 (43)	8 (28)	

High		70 (63)	19 (70)	20 (77)	13 (43)	18 (62)	
Occupation	111						0.84 (X=0.84)
Paid job		77 (69)	19 (70)	19 (76)	20 (67)	19 (66)	
No paid job (incl unemployed, housewife, student)		34 (31)	8 (30)	6 (24)	10 (33)	10 (34)	
Ethnicity	112						0.49 (X=5.43)
Dutch		69 (62)	19 (70)	13 (50)	18 (60)	19 (66)	
Western Immigrants		10 (9)	3 (11)	4 (15)	1 (3)	2 (7)	
Non-Western Immigrant		33 (29)	5 (19)	9 (35)	11 (37)	8 (28)	

[1] *Scores range from 7-35 (higher is poorer)*

[2] *Score range from 0-10 (ranging from not at all to very much)*
[3] *Score range from 0-10 (ranging from never to always)*

[4.] *Low = primary education or less*

Intermediate-1 = lower secondary

Intermediate-2 = upper secondary

High = tertiary

Please note, due to rounding, nog all percentages add up to 100

Table 3 – background characteristics nurses

	N=23
	M (SD)
Age	47.83 (11.05)
	N (%)
Gender	
Male	2 (9)
Female	21 (91)
Type of nurse	
Regular nurse	16 (70)
Specialised nurse (e.g. children, dialysis, pain assistant)	7 (30)

Table 4 Description of outcomes within the four conditions

	Completed by number of patients	Expectancy + Empathy + (n=32)	Expectancy - Empathy + (n=32)	Expectancy + Empathy – (n=32)	Expectancy - Empathy – (n=32)
		M (SD)	M (SD)	M (SD)	M (SD)
Pain primary					
Max pain day 1[1]	125	4.77 (1.91)	5.06 (1.54)	4.50 (1.93)	4.47 (1.93)
Max pain day 2[1]	99	5.04 (1.86)	4.85 (1.91)	4.86 (1.78)	5.04 (2.08)
Pain day 3[1]	76	5.00 (2.00)	5.53 (1.84)	5.21 (1.78)	5.61 (2.17)
Pain secondary					
Pain expectation day 1[1]	104	5.97 (1.06)	5.76 (1.81))	6.41 (1.96	6.07 (1.76)
Pain improvement expectation day 1[2]	103	71.64 (14.95)	64.38 (18.09)	68.57 (15.67)	63.48 (21.63)
Pain evaluation day 3[3]	76	4.63 (2.13)	5.36 (2.46)	3.76 (1.57)	5.28 (2.35)
Psychological					
Anxiety[4]	64	-1.63 (7.97)	-2.6 (6.74)	-0.64 (6.66)	2.8 (6.27)
Positive mood[4]	62	-8.60 (7.05)	-8.4 (9.26)	-8.96 (6.34)	-9.07 (8.05)
Negative mood[4]	62	-0.2 (8.28)	-3.00 (7.90)	-0.94 (5.47)	-2.00(6.48)
Satisfaction[5]	71	8.44 (1.68)	8.52 (0.93)	8.63 (1.27)	7.90 (2.23)

Other outcomes					
OBAS day 2[6]	84	8.85 (4.83)	8.50 (4.29)	7.67 (3.48)	8.83 (4.31)
OBAS day 3[6]	76	8.36 (3.92)	8.59 (4.17)	5.68 (4.36)	8.61 (4.02)
General quality[1]	68	8.74 (0.99)	8.33 (0.98)	8.79 (1.03)	8.20 (1.26)
Recommendation[1]	68	8.58 (1.39)	8.27 (1.28)	9.00 (1.15)	8.13 (1.55)

All analyses were controlled for (centered) effects of anxiety towards the operation

[1] *Scores range from 0-10 (ranging from low to high).*

[2] *Scores range from 0-100 (ranging from low to high).*

[3]*Score range from 0-10 (ranging from better to worse)*

[4]*Difference score (pre and post hospitalization)*

[5]*Score range from 0-10 (ranging from not at all to very much)*

[6]*Score ranged from 0-28 (ranging from high to low benefit)*

Table 5– Pain medication within the four conditions

	Number of patients reported receiving med	Expectations + Empathy + (n=32)	Expectations – Empathy + (n=32)	Expectations + Empathy - (n=32)	Expectations - Empathy - (n=32)	
		M (SD)	M (SD)	M (SD)	M (SD)	p
Day 1 - Perioperative						
Morphine	118	7.80 (4.26)	7.77 (4.48)	8.88 (3.32)	8.44 (4.48)	0.66 (F=0.53)
Paracetamol	127	1000.00 (254.00)	1031.25 (176.78)	1031.25 (176.78)	1062.50 (245.93)	0.72 (F=0.44)
Ibuprofen	4	-	18.75 (106.01)	18.75 (106.01)	37.5 (147.56)	0.57 (F=0.68)
Metamizol	116	1750.00 (567.96)	1781.25 (608.24)	1625.00 (793.12)	1906.25 (390.15)	0.33 (F=1.16)
Pain protocol deviations peri-operative						
Naproxen	2	-	15.63 (88.39)	-	15.63 (88.39)	
Diclofenac	1	2.34 (13.26)	-	-	-	
Day 1 – post-operative daycare						
Tramadol	91	57.81 (36.72)	63.28 (37.02)	46.88 (35.64)	46.09 (36.54)	0.17 (F=1.71)
Paracetamol	91	487.50 (330.20)	570.31 (352.15)	437.50 (377.33)	510.94 (427.81)	0.56 (F=0.70)
Ibuprofen	60	318.75 (304.20)	262.50 (338.64)	318.75 (340.24)	262.50 (302.41)	0.33 (F=0.81)
Pain protocol deviations post-operative						
Naproxen	3	-	-	15.63 (88.39)	31.25 (122.97)	
Oxycodon	3	-	0.47 (2.65)	0.16 (0.88)	0.16 (0.88)	

Day 2						
Tramadol	69	284.21 (81.31)	251.79 (64.02)	219.23 (92.93)	222.66 (103.80)	>0.10 (F=2.15)
Paracetamol	72	2561.90 (631.84)	2358.33 (695.22)	2192.86 (984.22)	2292.19 (930.00)	0.56 (F=0.69)
Ibuprofen	61	1750.00 (464.76)	1482.35 (565.95)	1714.29 (616.26)	1928.57 (1083.04)	0.38 (F=1.05)
Pain protocol deviations day 2						
Diclofenac	1	-	-	-	50.00	
Oxycodon	1	5.00	-	-	-	
Day 3						
Tramadol	55	275.00 (67.48)	266.07 (71.80)	252.27 (100.75)	217.50 (82.89)	0.23 (F=1.48)
Paracetamol	59	2430.56 (576.79)	2396.43 (694.61)	2545.83 (932.06)	1885.00 (718.37)	**0.08 (F=2.39)**
Ibuprofen	53	1569.23 (303.82)	1909.09 (1059.67)	1671.43 (347.36)	1480.00 (549.29)	0.34 (F=1.13)
Pain protocol deviations day 3						
Diclofenac	1	-	150.00	-	-	

All measurements are in mg units