Supplementary File 1

This file describes the review protocol applied for the meta-analysis study entitled "Acupuncture relieves Opioid-induced Constipation in Clinical Applications- a meta-analysis and systematic review".

Review protocol

Title: Acupuncture relieves Opioid-induced Constipation in Clinical Applications- a meta-analysis and systematic review

Review questions:

1. Is acupuncture effective for clinical therapy of Opioid-induced Constipation (OIC)?
2. What are the effective rates for acupuncture treatment?
3. Will acupuncture be more efficient in relieving constipation symptoms when comparing with drugs for OIC patients?
4. What will be the influence of acupuncture on the quality of life for OIC patients after treatment?
5. What is the association between acupuncture and general drug prescriptions?

Searches:

The following electronic databases will be systematically searched:

PubMed, Embase, Cochrane library, and Web of science.

The search strategy will combine the following keywords:

Disease: "constipation", or "Gastrointestinal Transit", or "slow transit", or "bowel dysfunction"

Disease-associated condition: "opioid", or "opiate", or "opiate alkaloids", or "opioid analgesics", "Opioid-induced Constipation".

Therapy methods: "acupuncture", or "Electro-acupuncture", or "transcutaneous electric

stimulation".

Study design: randomized clinical trial (RCT)

There is no time or language restriction.

Example of search in the database PubMed:

(((((((("Constipation"[MeSH Terms] OR "Constipation"[Text Word]) OR "gastrointestinal transit"[MeSH Terms]) OR "gastrointestinal transit"[Text Word]) OR "slow transit"[Text Word]) OR "bowel dysfunction"[Text Word]) AND (((((((("analgesics, opioid"[MeSH Terms] OR "opioid"[Text Word]) OR "Opiate"[Text Word]) AND ("Constipation"[MeSH Terms] OR "Constipation"[Text Word])) OR "opiate alkaloids"[MeSH Terms]) OR "analgesics, opioid"[MeSH Terms]) OR "opiate alkaloids"[MeSH Terms]) OR "opiates"[Text Word]) OR "opiate alkaloids"[Text Word]) OR "analgesics opioid"[Text Word])) OR ("opioid-induced constipation"[MeSH Terms] OR "opioid induced constipation"[Text Word])) AND (((((((("acupuncture"[MeSH Terms] OR "acupuncture therapy"[MeSH Terms]) OR "Electroacupuncture"[MeSH Terms]) OR "acupuncture"[Text Word]) OR "Electroacupuncture"[Text Word]) OR "transcutaneous electric nerve stimulation"[MeSH Terms]) OR "transcutaneous electric nerve stimulation"[MeSH Terms]) OR "transcutaneous electrical nerve stimulation"[Text Word])

Example of search in Cochrane library

#1 (opioid):ti,ab,kw OR (opiate):ti,ab,kw OR (analgesics):ti,ab,kw (Word variations have been searched)

#2 (constipation):ti,ab,kw OR (gastrointestinal transit):ti,ab,kw OR (bowel dysfunction):ti,ab,kw (Word variations have been searched)

#3 ("opioid-induced bowel dysfunction"):ti,ab,kw OR (opioid-induced constipation):ti,ab,kw (Word variations have been searched)

#4 (acupuncture):ti,ab,kw OR (electroacupuncture):ti,ab,kw OR ("transcutaneous electric nerve stimulation"):ti,ab,kw (Word variations have been searched)

#5 ((#1 AND #2) OR #3) and #4

Type of studies to include:

All relevant peer-reviewed original RCT studies reporting on the clinical application of acupuncture on OIC patients will be reviewed.

The studied population:

OIC patients over 18 years old treated with acupuncture or accompany with other co-interventions, like drugs, are studied.

Exposure:

The review aims to evaluate the clinical therapeutic effects of acupuncture, including traditional handle acupuncture, and electric acupuncture, on opioid-induced constipation. There is no specific restriction on the conditions of patients or reasons for opioid administrations. The control groups are treated with prescribed drugs or placebo, while the acupuncture groups are subjected to acupuncture therapy with or without co-interventions, like the drugs or placebo applied to control groups.

Context:

This review summarizes the present available clinical trials in evaluating the effects of acupuncture application for treatment of Opioid-induced constipations. The information of study designs, sample sizes, group allocations, treatment methods and sessions, follow up periods, and the key questions of therapy effects including remission rate, symptom score, and quality of life, are described.

Data extraction:

Study selection. Relevant studies to be reviewed by YL and CH according to the following inclusion/exclusion criteria. The review processes are conducted following three stages: title review, abstract review and full text review. The studies collected from literature searches are compiled into one database with duplications checked and removed before title review. The abstract review and full text review were processed following title review. Two reviewers conducted the review separately with a discussion after each step for contradistinction and

resolution of any discrepancy.

Inclusion criteria:

1. Study design: randomized clinical trials with two or multiple groups regardless of the blinding to patients or assessors.

2. Study subjects: Patients of 18 years old or over, who were diagnosed as constipation due to opioids application for management of cancer pain or non-cancer associated pain.

3. Treatment methods: The intervention group received treatment of acupuncture, electro-acupuncture, transcutaneous electric stimulation, or acupressure, with or without the combination of same medication as the control group. There is no limitation to the acupuncture types, acupoints, frequency, sessions, durations and follow up periods. There is no restriction to the treatment type of control groups, who received no treatment, placebo, sham acupuncture or conventional medication.

4. Outcome assessments: Clear criteria for therapy responses were defined. Number of patients who were cured or with effective relief of symptoms and patients responding with limited or no effects were reported. Assessments of constipation symptoms in any aspects, including stool property, defecation frequency or duration time, defecation comfortable level or difficulty, and colon motility or bowel movement, were reported.

Exclusion criteria:

1. Patients received opioids and acupuncture for pain relief with the main outcome assessment of pain and other sides effects. Any studies without clear diagnoses of constipation claimed before acupuncture treatments were excluded.

2. Studies on patients aged less than 18 years old with diagnoses of functional constipation were not included in the analysis.

3. Clinical trials with low quality, such as no randomization, which may lead to obvious bias in the evaluation were excluded.

4. Studies on specific populations, like pregnant women, colon cancer patients, and patients with other diseases (for example, irritable bowel syndrome) those influence bowel function directly or indirectly were excluded.

5. Study protocols of ongoing RCTs without completed data were excluded.

Data coding:

The extraction/coding form was developed to collect all data about study characteristics (Author, publication time, investigation time, locations, and study designs), patient characteristic (number of patients, patient genders and ages, patients diagnoses, diagnose guideline/criteria, group allocations, therapy methods, therapy durations, co-intervention strategies, and follow up periods), outcome evaluations (rate of curation or remission, symptom evaluation, quality of life scores, scales used for scoring, scores of sub-items like stool property, defecation time, or defecation difficulty). Data was extracted and recorded by YL and CH.

Risk of bias assessment:

All the included papers are evaluated on their reporting quality with Cochrane risk of bias tool [1], on random sequence generation, allocation concealment, participants and personnel blinding, outcome assessment blinding, incomplete outcome data and exclusions, selective reporting, and other sources of bias. According to the criteria, the studies are evaluated as "high risk", "low risk", or "unclear risk".

Data synthesis strategy:

Based on the general guideline of narrative synthesis [2], a preliminary synthesis firstly applied to explore the heterogeneity between studies. For I^2<50%, fixed effect model will be applied, while for I^2>=50%, the random effect model will be used. For dichotomous data, the risk ratio (RR) between treatment groups and control groups will be calculated. For continuous data, the standardized mean differences (SMDs) will be adapted to minimize the influence of variable scoring systems in different studies.

Subgroup analyses will be conducted to explain the potential factors influencing the heterogeneity between studies. The considered factors are acupuncture types, co-interventions, follow-up periods, and treatment sessions.

References:

1. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *Bmj.* 2011;343:d5928.

2. Rodgers M, Sowden A, Petticrew M, et al. Testing Methodological Guidance on the Conduct of Narrative Synthesis in Systematic Reviews: Effectiveness of Interventions to Promote Smoke Alarm Ownership and Function. *Evaluation.* 2009/01/01 2009;15(1):49-73.

Supplementary File 2

This file provides the supplementary data (Supplementary Table 1) and scales (Supplementary Table 2-5) supporting the descriptions and conclusions in the main text of "Acupuncture relieves Opioid-induced Constipation in Clinical Applications- a meta-analysis and systematic review".

Supplementary Table 1 Data records of included studies for meta-analyses

Study	Author	Year	Country	Centers	Start	End	Groups	Subjects	Defined age	Actual ages-control	Actual ages-treated	Dropout patients	Control group	Control male	Control female
1	Zhu, H. D.	2018	China, Zhejiang	Single center	2013	2016	2	198	18-80	59.54 ±10.77	57.12±9.93	6	100	45	55
2	Zhang, F. L.	2009	China, Beijing	Single center	2007	2008	2	66	18-80	63.55±11.02	59.61±12.49	0	33	14	19
3	Song, N.	2020	China, Chongqing	Single center	2017	2019	3	122	18-75	60.53±10.89	62.53±11.89	4	41		
4	Jiang, Y. L.	2010	China, Hunan	Single center	2008	2009	2	60	>18	59.2	61.4	0	30	12	18
5	Cai, H.	2019	China, Zhejiang	Single center	2013	2016	2	268	18-75	51.2±3.4	55.3±3.1	17	127	72	66

Supplementary Table 1 (Continued)

Control method	Cured (control)	Obvious remission (control)	Effective remission (control)	Limited remission (control)	Total remission (control)	Treat group	Treat male	Treat female	Treat method	Cured (treat)	Obvious remission (treat)	Effective remission (treat)	Limited remission (treat)	Total remission (treat)
Oral lactulose		21	49	30	70	98	52	46	IFC		30	45	23	75
Citrated mosapride tablet	1	2	26	4	29	33	17	16	EA	2	3	27	1	32
Polyethylene glycol electrolyte powder	0	15	17	9	32	40			Ultrasonic penetration	2	18	13	7	33
Kaysero	1	7	13	9	21	30	13	17	Handle acupuncture	4	14	10	2	28
lactulose solution	13	28	71	18	109	124	74	56	TENS combines traditional Chinese acupuncture with electrical stimulation	12	40	62	10	114

Supplementary Table 1 (Continued)

Trial Registered	Follow up period	Style of acupuncture	Acupoints	Acupoints number	Co-intervention	Co-intervention method	Treatment sessions (times)	Period of treatment (days)	Treat time each session
Yes	4 weeks	Transcutaneous acupoint interferential current (IFC) stimulation	Tianshu (ST25) and Zhongwan (RN12)	2	0		14	14	30 mins
No	2 weeks	Electro-acupuncture	Zusanli (ST36) and Tianshu(ST25)	2	0		5	5	30 mins
No	14 days	Electro-acupuncture with gel patch	Tiansu (ST25)	1	1	Chinese medicine gel pad	14	14	30 mins
No	4days	Handle acupuncture	bilateral 'Tiansu', 'Zhigou', 'Shangjuxu', 'Zusanli', 'Sanyinjiao', 'Qihai'	6	0		7	7	30 mins
No	14 days	TENS combines traditional Chinese acupuncture with electrical stimulation	'Guanyuan' point, 'Qihai' point, bilateral 'Tianshu' points, bilateral 'Zusanli' points and bilateral 'Shangjuxu' points	5	1	laxatives (15 mL of lactulose solution, twice per day)	14	14	30 mins

Supplementary Table 1 (Continued)

Scale of QOL	MQOL.c.baseline*	SDQOL.c.baseline#	MQOL.e.baseline	SDQOL.e.baseline	SMDQOL.baseline!	SpQOL.baseline&	MQOL.c.treat	SDQOL.c.treat	MQOL.e.treat	SDQOL.e.treat	SMDQOL.treat	SpQOL.treat
PAC-QOL	1.38	0.16	1.40	0.17	0.12	0.17	1.14	0.24	1.07	0.24	-0.29	0.24
PAC-QOL	3.51	0.13	3.53	0.16	0.14	0.15	2.61	0.63	1.58	0.33	-2.04	0.50
Karnofsky	2.79	0.31	2.77	0.28	0.05	0.29	2.76	0.37	3.03	0.36	-0.73	0.36
PAC-QOL	2.01	0.31	2.75	0.67	1.42	0.52	1.96	0.72	1.15	0.37	-1.41	0.57

Supplementary Table 1 (Continued)

Constipation symptom scale	MSYM.c.baseline	SDSYM.c.baseline	MSYM.e.baseline	SDSYM.e.baseline	SMDSYM.baseline	SpSYM.baseline	MSYM.c.treat	SDSYM.c.treat	MSYM.e.treat	SDSYM.e.treat	SMDSYM.treat	SpSYM.treat
Cleveland Constipation Scale	13.93	1.83	14.16	2.03	0.12	1.93	11.12	1.73	9.81	1.67	-0.77	1.70
Roman II-Bristol based	8.79	1.45	9.21	1.41	0.29	1.43	5.70	2.49	5.52	1.54	-0.09	2.07
Chinese new medicine guideline	11.99	0.48	12.07	0.40	0.18	0.44	7.93	0.34	5.47	0.73	-4.34	0.57
Constipation system score	18.00	3.20	16.37	3.82	-0.46	3.52	12.97	4.92	7.2	3.77	-1.32	4.38
Applied Research on Traditional Chinese Medicine	8.60	0.90	8.30	1.40	-0.26	1.17	6.70	1.10	5.10	0.60	-1.80	0.89

*, Mean values (M) ; #, Standard deviations (SD); !, The standardized mean differences (SMD); &, Standard errors (Sp) of SMDs. QOL: quality of life scores.

Supplementary Table 2 Remission definitions of opioid-induced constipation treatments used in each study *

Study ID	Criteria				
Study 1	Ministry of Health of People's Republic of China Guidelines for clinical study of new Chinese medicines	***Cured***	***Obvious efficacy***	***Effective***	***Invalid***
	General symptom		Constipation symptoms are improved totally or significantly		No improvement in constipation and other symptoms
	Defecation and stool		Defecation interval and stool quality are normal or close to normal, the stool is slightly dry and defecation interval is within 72 hours	Symptom of dry feces is improved, defecation interval is shortened by 1 day	
	Other symptoms		All or most other symptoms disappear	Other symptoms are ameliorated	
Study 2	Ministry of Health of People's Republic of China Guidelines for clinical study of new Chinese medicines	***Cured***	***Obvious efficacy***	***Effective***	***Invalid***
	General symptom		Symptom relieved remarkably		No improvement in constipation and other symptoms
	Defecation and stool	Regular defecation and stool, or recovered to condition before sickness	Defecation interval and stool quality are close to normal, or stool is slightly dry and defecation interval is within 72 hours	Symptom of dry feces is improved, defecation interval is shortened by 1 day	
	Other symptoms	Other symptoms disappear	All or most other symptoms disappear	Other symptoms are ameliorated	
Study 3	Criteria of clinical disease diagnoses and therapeutic effects judgement.	***Cured***	***Markedly effective***	***Effective***	***No effect***
			Symptom relieved remarkably		No improvement in constipation and other symptom
		Regular defecation, moist stool, Smooth bowel movement, Or recovered to condition before sickness	Defecation interval <48 hours and stool nature near to be normal or slightly dry stool	Defecation interval shortened 24 hours, or symptom of dry stoll relieved	
		Constipation symptom score 0 and other symptom disappears	Constipation symptom score reduced by or over 2/3, other symptoms disappear	Constipation symptom score reduced by and over 1/2, other symptoms improved	No change of constipation symptom score
		Retention time > 2 weeks	Retention time >2 weeks	Retention time > 2 weeks	
Study 4	Ministry of Health of People's Republic of China Guidelines for clinical study of new Chinese medicines	***Cured***	***Obvious efficacy***	***Effective***	***Invalid***
	General symptom		Constipation symptoms are improved totally or significantly		No improvement in constipation and other symptoms
	Defecation and stool	Regular defecation and stool, or recovered to condition before sickness	Defecation interval and stool quality are normal or close to normal, the stool is slightly dry and defecation interval is within 72 hours	Symptom of dry feces is improved, defecation interval is shortened by 1 day	
	Other symptoms	Other symptoms disappear	All or most other symptoms disappear	Other symptoms are ameliorated	
Study 5	Applied Research on Traditional Chinese Medicine Spleen and Stomach Theory	***Cured***	***Markedly effective***	***Effective***	***Ineffective***
	General symptom	Disappearance of symptoms	Significant mitigation of symptoms	Mitigation of symptoms	Slightly mitigation of symptoms or aggravation of symptoms
	Symptom scores	Scores of 0 for more than 2 weeks	Score decrease by over 2/3 for more than 2 weeks	Score decrease by over 1/2	Score decrease lower than 1/2

*, This table shows the exact definitions of cured or remission of opioid-induced constipation (OIC) after clinical therapy and their referenced criteria. Though slight difference in the descriptions between the referenced criteria, the overall observations for cured, obvious remission (obvious efficacy / markedly effective), effective remission (effective), and limited remission (invalid / no effect/ ineffective) are similar.

Supplementary Table 3 Symptom scoring scales for opioid-induced constipations used in each study

Study ID	Scale or referenced scale	Sub-Items										
Study 1	Cleveland Constipation Scale	Defecation frequency	Defecation straining	Complete emptying	Abdominal pain	Defecation time	Defecation help	Failed defecation frequency per 24 hours	Constipation course			
Scores	0	1-2 times per 1-2 days	Never	Never	Never	< 5 mins	Without	Never	0			
	1	2 times per week	Rarely	Rarely	Rarely	5-10 mins	Stimulative laxatives	1-3 times	1-5			
	2	Once a week	Sometimes	Sometimes	Sometimes	10-20 mins	Digital assistance or enema	3-6 times	5-10			
	3	Less than once per week	Usually	Usually	Usually	20-30 mins		6-9 times	10-20			
	4	Less than once per month	Always	Always	Always	>30 mins		>9 times	>20			
Study 2	Roman II and Bristol	Defecation frequency	Defecation strain, discomfort, and incomplete			Defecation duration				Stool property		
Scores	0	1-2 days	No difficulty			<10 mins				Smooth or soft sausage		
	1	3 days	Sometimes			10-15 mins				Sausage with cracks		
	2	4-5 days	Occasionally			15-25 mins				Lumpy sausage		
	3	>5 days	Frequently			>25 mins				Separated hard lumps		
Study 3	Constipation symptom score		Defecation difficulty		Distension in chest or abdomen					Dry stool	Depression or irritability	Poor appetite
Scores	0		No		No					No	No	No
	1		Straining		Very mild, <0.5 hour					Hard stool	Occasionally	No appetite, usual amount
	2		2-3 exertion than defecation		Alleviated 0.5-1 hour, need medicine					Dry and lumpy	Easy to be angry	No appetite, reduce by 1/3 amount
	3		Failed after straining, need laxatives or other aids		No improve after 1 hour					Like sheep's droppings	Very easily	No appetite, reduce by >1/3 amount
Study 4	Constipation scoring system (CSS)	Bowel movement frequency	Defecation difficulty	Completeness: feel incomplete evacuation	Abdominal pain	Duration	Assistance	Failure defecation per 24h	Duration of constipation (year)			
Scores	0	1-2 times per 1-2 days	Never	Never	Never	< 5 mins	Without	Never	0			
	1	2 times per week	Rarely	Rarely	Rarely	5-10 mins	Stimulative laxatives	1-3 times	1-5			
	2	Once a week	Sometimes	Sometimes	Sometimes	10-20 mins	Digital assistance or enema	3-6 times	5-10			
	3	Less than once per week	Usually	Usually	Usually	20-30 mins		6-9 times	10-20			
	4	Less than once per month	Always	Always	Always	>30 mins		>9 times	>20			
Study 5	Applied Research on Traditional Chinese Medicine Spleen and Stomach Theory	Defecation frequency	Defecation strain, discomfort, and incomplete			Defecation duration				Stool property		
Scores	0	1 day	Easy			<10 mins				Soft		
	1	2-3 days	Sometimes feeling tired			10-20 mins				Hard, then soft		
	2	4 days	Occasionally			21-30 mins				Dry and hard		
	3	5 days	Usually			>30 mins				Dry and hard with blood		

Supplementary Table 4 The sample copy of Karnofsky Performance Status Scale (KPS)

Condition	Percentage	Comments
A: Able to carry on normal activity and to work. No special care is needed.	100	Normal, no complaints, no evidence of disease.
	90	Able to carry on normal activity, minor signs or symptoms of disease.
	80	Normal activity with effort, some signs or symptoms of disease.
B: Unable to work. Able to live at home, care for most personal needs. A varying degree of assistance is needed.	70	Cares for self, unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his needs.
	50	Requires considerable assistance and frequent medical care.
C: Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly.	40	Disabled, requires special care and assistance. [In bed more than 50% of the time].
	30	Severely disabled, hospitalization is indicated although death not imminent. [Almost completely bedfast].
	20	Hospitalization necessary, very sick, active supportive treatment necessary. [Totally bedfast and requiring extensive nursing care by professionals and/or family].
	10	Moribund, fatal processes progressing rapidly. [Comatose or barely arousable].
	0	Dead.

KPS describe three states (conditions): A (100–80%), B (70–50%) and C (40–0%).

Supplementary Table 5 The sample copy of PAC-QOL scale

Sample copy, do not use without permission

PAC-QOL contact information and permission to use: Mapi Research Trust, Lyon, France, https://eprovide.mapi-trust.org

PAC-QOL ©

PATIENT ASSESSMENT OF CONSTIPATION ©

The following questions are designed to measure the impact constipation has had on your daily life **during the past 2 weeks**. For each question, please tick one box.

The following questions ask you about the intensity of your symptoms. To what extent, during the past 2 weeks...	**Not at all 0**	**A little bit 1**	**Moderately 2**	**Quite a bit 3**	**Extremely 4**
1. have you felt bloated to the point of bursting?	☐	☐	☐	☐	☐
2. have you felt heavy because of your constipation?	☐	☐	☐	☐	☐

The next few questions ask you about the effects of constipation on your daily life. How much of the time, during the past 2 weeks...	**None of the time 0**	**A little of the time 1**	**Some of the time 2**	**Most of the time 3**	**All of the time 4**
3. have you felt any physical discomfort?	☐	☐	☐	☐	☐
4. have you felt the need to open your bowel but not been able to?	☐	☐	☐	☐	☐
5. have you been embarrassed to be with other people?	☐	☐	☐	☐	☐
6. have you been eating less and less because of not being able to have bowel movements?	☐	☐	☐	☐	☐

Supplementary Table 5 The sample copy of PAC-QOL scale

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PAC-QOL contact information and permission to use: Mapi Research Trust, Lyon, France, https://eprovide.mapi-trust.org

The next few questions ask you about the effects of constipation on your daily life. To what extent, during the past 2 weeks...	**Not at all 0**	**A little bit 1**	**Moderately 2**	**Quite a bit 3**	**Extremely 4**
7. have you had to be careful about what you eat?	☐	☐	☐	☐	☐
8. have you had a decreased appetite?	☐	☐	☐	☐	☐
9. have you been worried about not being able to choose what you eat (for example, at friend's)?	☐	☐	☐	☐	☐
10. have you been embarrassed about staying in the toilet for so long when you were away from home?	☐	☐	☐	☐	☐
11. have you been embarrassed about having to go to the toilet so often when you were away from home?	☐	☐	☐	☐	☐
12. have you been worried about having to change your daily routine (for example, travelling, being away from home)?	☐	☐	☐	☐	☐

The next few questions ask you about your feelings. How much of the time, during the past 2 weeks...	**None of the time 0**	**A little of the time 1**	**Some of the time 2**	**Most of the time 3**	**All of the time 4**
13. have you felt irritable because of your condition?	☐	☐	☐	☐	☐
14. have you been upset by your condition?	☐	☐	☐	☐	☐
15. have you felt obsessed by your condition?	☐	☐	☐	☐	☐
16. have you felt stressed by your condition?	☐	☐	☐	☐	☐
17. have you been less self-confident because of your condition?	☐	☐	☐	☐	☐
18. have you felt in control of your situation?	☐	☐	☐	☐	☐

Supplementary Table 5 The sample copy of PAC-QOL scale

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The next questions ask you about your feelings. To what extent, during the past 2 weeks...	**Not at all 0**	**A little bit 1**	**Moderately 2**	**Quite a bit 3**	**Extremely 4**
19. have you been worried about not knowing when you are going to be able to open your bowels?	☐	☐	☐	☐	☐
20. have you been worried about not being able to open your bowels when you needed to?	☐	☐	☐	☐	☐
21. have you been more and more bothered by not being able to open your bowels?	☐	☐	☐	☐	☐

The next questions ask about your life with constipation. How much of the time, during the past 2 weeks...	**None of the time 0**	**A little of the time 1**	**Some of the time 2**	**Most of the time 3**	**All of the time 4**
22. have you been afraid that your condition will get worse?	☐	☐	☐	☐	☐
23. have you felt that your body was not working properly?	☐	☐	☐	☐	☐
24. have you had fewer bowel movements than you would like?	☐	☐	☐	☐	☐

The next questions ask you about how satisfied you are. To what extent, during the past 2 weeks...	**Not at all 0**	**A little bit 1**	**Moderately 2**	**Quite a bit 3**	**Extremely 4**
25. have you been satisfied with how often you open your bowels?	☐	☐	☐	☐	☐
26. have you been satisfied with the regularity with which you open your bowels?	☐	☐	☐	☐	☐
27. have you been satisfied with your bowel function?	☐	☐	☐	☐	☐
28. have you been satisfied with your treatment?	☐	☐	☐	☐	☐