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DEATH BY VOLUNTARY CESSATION OF THERAPY BY NON-TERMINALLY ILL CYSTIC FIBROSIS PATIENTS – INTERNATIONAL SURVEY OF CLINICIANS*

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Abstract

Background: Little is known about non-terminally ill cystic fibrosis (CF) patients who die by voluntary cessation of therapy. The current study was undertaken to provide an international snapshot of this problem.

Methods: An online survey was distributed to the medical directors of the CF Centres affiliated with the US *Cystic Fibrosis Foundation* and *Cystic Fibrosis Australia* (with the inclusion of New Zealand); the same letter was sent to every clinician member of the *European Cystic Fibrosis Society*.

Results: More than 200 patients were reported as being in the situation described above. Data analysis was eligible in 102 patients (4 children, 25 adolescents and 73 adults). 92% were capable of judgement. Time-consuming and low immediate-impact therapies, such as respiratory physiotherapy, were most frequently discontinued first. Resignation was the main reported reason, followed by reactive depression and lack of familial support. 69% received palliative care and 72% died in the six months following refusal.

Conclusions: Death of non-terminally ill CF patients due to voluntary cessation of therapy exists. This challenging situation should be discussed in multi-disciplinary teams so that the most appropriate attitude, suited to the individual situation, is defined.

Key words: voluntary, cessation, stop, therapy, cystic fibrosis

Background:

Although recent advances have dramatically lengthened the average life span of people with cystic fibrosis (CF), the disease retains its distinctive clinical trajectory: periods of intermittent pulmonary exacerbation requiring intensive therapy followed by periods of relative disease quiescence which still require active (1–5) and time-consuming daily therapy (1, 6–9). As the disease progresses, there is rarely a clear signal for the transition from this pattern of acute care to a palliative care approach (10–12). For a seriously ill patient, each pulmonary exacerbation might be the one during which death occurs, but there might also be a return to baseline. This fundamental uncertainty can lead to the habit of aggressive in-hospital care (2,10–15) at a time when similarly ill patients with other disease trajectories, such as end-stage cancer, might be offered palliative care in non-hospital settings (2,10–13). Even when experiencing periods of being in a relatively stable condition, patients with CF must maintain a strikingly complex and time-consuming daily regimen. Adherence to this regimen is difficult even in times of relative health. As the patients' clinical conditions deteriorate, maintenance of this regimen, with often little chance of an observable clinical effect, becomes more burdensome. In particular, maintenance of daily respiratory physiotherapy (RP) can be challenging (1, 3–7, 9,16–21).

The combination of an uncertain disease trajectory without a clear signal for initiation of palliative care and burdensome, and only partially symptom-relieving, daily therapy can lead to substantial drops in adherence. Several cases became known to one of the authors (GH), in which CF patients appeared to decide to stop their daily treatments partially or completely in recognition of their perceived hopelessness or futility. Medical literature is virtually silent on patients taking this step: a challenging situation for a multi-disciplinary CF team.

The current study was undertaken to provide an international snapshot of this problem, as well as to get some preliminary (and potentially hypothesis-generating) data on clinicians' views of this topic. Our aim was to gather quantitative and qualitative data from clinicians about CF patients who died after choosing to interrupt their treatments, in order to improve medical practice and initiate further discussion on this difficult subject.

Methods:

An informative letter describing the study and containing a web link to an online survey was distributed by e-mail to the medical directors of the CF Centres affiliated with the US *Cystic Fibrosis Foundation* (CFF, n=250) and *Cystic Fibrosis Australia* (CFA) (with the inclusion of New Zealand, n= 45); the same letter was sent to every clinician member of the *European Cystic Fibrosis Society* (ECFS, n=723).

The questionnaire was sent in August 2013 to the CFF and CFA, in September 2013 to the ECFS and in October 2013 to New Zealand. A reminder to complete the survey was sent 3–8 weeks after the first delivery to enhance response rates. The link for the online questionnaire was closed at the end of November 2013.

The study was approved by the local ethics committee of the University of Lausanne in Switzerland (Study protocol 107/13).

The questionnaire *(text in the online supplement)* began with preliminary questions concerning the location of the clinic and the ages of the patients cared for there (paediatric/adolescent, adult, all ages); clinicians were then asked to report on their understanding of the law regarding voluntary refusal of treatment in their jurisdiction. To include a patient(s), the following "inclusion question" (Question 6) had to be answered with "yes": *"Have you ever had a CF patient (whom you did not consider terminal) tell you that he/she has decided to stop all or most of his/her treatments because of a wish to stop fighting the disease? Or have you ever suspected that a patient (whom you did not consider terminal) was discontinuing all or most of his/her CF treatments as part of a desire to die?"* If "no" was ticked, the survey concluded. If a case(s) was/were known, then additional questions concerning the case(s) were asked: in particular concerning the patient's judgemental ability; the patient's age and disease severity at the time of the voluntary refusal; the identity of the decision-maker; the duration of survival after the refusal; the order in which treatments were stopped; the use of palliative care; and the reasons of stopping care. It was possible to enter data only for three patients per questionnaire and the participants had the choice to remain anonymous or give their location.

We only included the fully completed questionnaires of patients who gave a positive answer to the "inclusion question" in this analysis. We did not further analyse incomplete surveys with a positive response to the inclusion question because of high heterogeneity and variability. Patients who were still alive at the completion of the survey were also excluded.

Analysis:

Patient age was categorised for analysis as follows: children (0–13 years), adolescents (14–17 years) and adults (18 years or over).

The most interesting themes and questions were selected and presented below following the application of a univariate analysis.

Response errors resulting from respondent data-entry mistakes limited the interpretation of some items of the completed surveys: the results for such items (Table 2) were therefore presented with regard to the interpretable responses as follows: number of interpretable responses/all the responses (e.g. 25/27).

Results:

231 clinicians returned the survey (a response rate of 22.7%; 231 responses/1,018 participants solicited), with at least 204 patients for whom the inclusion question was reported positive. 100 participants (100/231 or 43.3%) indicated that they have had patients who have stopped treatment: 28 participants (28%) had one patient, 37 participants (37%) had two patients, nine participants (9%) had three patients, 25 participants (25%) had more than three patients and one participant (1%) had an unknown number of patient(s) in this situation. Among these 204 patients, only 102 were eligible for analysis. For the other half, the inclusion question was answered positively but the clinicians stopped filling in the questionnaire.

Of these 102 patients, four were children (3.9%), 25 were adolescents (24.5%) and 73 were adults (71.6%) at the time of death. 71 were from the United States, 16 from Europe and 15 from Australia (see Table 1).

Most patients were considered by clinicians to be capable of judgement in order to voluntarily refuse care (94/102; 92.2%). Of the eight patients who were not considered to be capable of judgement (8/102; 7.8%), one was a child, six were adolescents and one was an adult. The mean age at which the refusal of care was made was 12 years for children, 16 years for adolescents, 25 years for adults and 22 years when the overall results were considered irrespective of age category.

In most cases, the decision to stop treatment was made by the patients themselves (98/102; 96.1%). In the remaining four patients (3.9%), both parents made the decision for the two children in this group and respectively the mother or the spouse in the case of the two adult patients. Of those four patients, one adult and one child, who were capable of judgement, had made advanced directives.

The mean age at death was 13.5 years for children, 17 years for teenagers, 26 years for adults and 23 years when the overall results were considered irrespective of age category. The difference between the mean age at the time of the decision and death – the overall survival time – was available in a total of 88 patients: it was less than 1 month in 23 patients, 1 to 2 months in 15 patients, 3 to 4 months in 10 patients, 5 to 6 months in 15 patients, 7 to 8 months in 2 patients, 9 to 10 months in 3 patients, 11 to 12 months in 7 patients and longer than a year in 13 patients. In other words, 72% of patients died during the six months following refusal.

Based mainly on the FEV1 and/or BMI for 79% of all patients (81/102), the respondents considered the severity of the disease to be severe. The rest of the patients were classified as having an intermediate-severe disease (18/102; 18%) or a mild disease (3/102; 3%). In the sub-group of children, 75% were considered to have an intermediate-severe disease (3/4) and one child (25%) to be severely ill. In the sub-group of adolescents, 80% (20/25) were considered to be severely ill while the rest of the patients (5/25; 20%) were considered to have a mild disease.

Over half of the patients died in hospital (53/102; 52%); 44 patients died at home (44/102; 43.1%); one adolescent (1/102; 1%) died in a hospice and the location of death for four adult patients (4/102 or 3.9%) was unknown to the respondents. In the sub-group analysis: two children died in hospital and two at home, twelve adolescents died at home and twelve in hospital with one in a hospice and 39 adults died in hospital (53.4%) against 30 at home (41.1%).

The treatment regimen was stopped progressively by 73 patients (73/102; 71.6%), while 29 patients stopped it all at once (29/102; 28.4%), (see Table 2). For the patients that stopped treatments progressively, the most common sequence was to stop physiotherapy, antibiotics (oral or IV, not specified) or vitamins first, and pancreatic enzymes, diet or antibiotics last. These results are similar in the different age categories. Of the patients who stopped treatment progressively, some resumed taking various aspects of the regimen after the initial decision to refuse them (31/72; 43.1%). Antibiotics and pancreatic enzymes were the treatments most often resumed by adults, whereas in adolescents, the resumed treatments were more commonly pancreatic enzymes and dietary changes.

Of all the 102 patients, 70 (69%) received and/or accepted palliative care: 48/73 adults (66%), 19/25 adolescents (76%) and 3/4 children (75%) (see Table 3). Opioids and oxygen were given to almost all patients who received/accepted palliative care. Non-opioid analgesics and non-invasive ventilation were less frequently used alternatives. Anxiolytics followed by benzodiazepines and anti-nausea/anti-emetics are other palliative treatments that were frequently administered. Anti-spasmodics/spasmolytics were the least-used treatments.

The clinicians' reports about the patients' reasons for stopping or decreasing therapy is detailed in Tables 4 and 5. As Table 4 indicates, in the majority of cases, clinicians reported that the reasons for the patients' decisions were complex and overlapping; when asked to choose one primary main reason, clinicians most frequently reported that they assessed the patients as having concluded that "the disease will always have the upper hand" (resignation) (29/102; 28.4%) and "enough is enough/discontent regarding the treatments" (25/102; 24.5%). These reasons were followed by "reactive depression" in the adult sub-group (10/73; 13.7%) and "dysfunctional family and support" in the adolescent sub-group (6/25; 24%). 33 (33%) of the 39 patients assessed as having reactive depression were not reported as having received any specific therapy for this condition: the majority were adults (10/13; 77%), the rest were adolescents (3/13; 23%).

Discussion

Although the topic is largely absent in the literature, our results demonstrate that voluntary cessation of treatment in CF does exist: this research, while preliminary, uncovered at least 204 clinician reports of patients across three continents who voluntarily altered some or all aspects of CF treatment, presumably leading to shortened survival.

Our findings imply that there is, for many patients and clinicians, a time of resignation in which the burdens of the treatment regimen outweigh the perceived benefits. While the precise time of death is unpredictable (2,10–12,14), there may be a consensus between the patient and the clinician, even if only a tacit one, that the end of life is near enough to make changes to the regimen. This may be a sudden and striking change in the pattern of care for the CF patient for whom the importance of adherence to treatment has been an overriding theme since diagnosis, or it may be a more subtle shift towards a different perception of the "costs and benefits" of maintaining good adherence.

As found in the literature (5, 6, 21–23), our results suggest that changes in the regimen were based on the perceived burden and short-term lack of benefit of the therapy from the patient's perspective. RP was the most common treatment discontinued. This is no surprise as it is the most time-consuming and tiresome therapy in the patients' perception. It requires active patient collaboration and is known to have the lowest adherence rate (50% in the best cases) combined with difficulty in measuring the short-term benefits (1, 3–7, 9, 16–24). Low-burden but high immediate-impact therapies, such as oral pancreatic enzymes (6, 21–23), were more likely to be continued or resumed. This pattern indicates that patients with CF and maybe CF clinicians, most likely in recognition of the nearness of death and the lack of short-term efficacy of standard CF therapies, are shifting to a model of comfort care in which therapies are judged appropriate by their ability to simply relieve symptoms.

We could expect that this shift in the approach to care might be accompanied by the explicit use of palliative care. This was the case in the majority of patients described by the clinician respondents, but not all. Medications to relieve the symptoms of dyspnoea, primarily opioids, were most often used for palliative care, as would be expected given the clinical pattern of end-stage respiratory disease (4,10,13,14).

For most patients, the decision to reduce or restructure the CF regimen is made in a gradual way appropriate to the gradual decline in health. However, although our study lacks multivariate analysis and validated depression scales, its results also suggest that there are patients who discontinue the regimen out of despair or from a lack of familial and social support, at least according to the clinicians' reporting. This is especially true for adolescents. It is worrying to see clinicians reporting that medication, which might be able to relieve symptoms, was stopped due to depression, feelings of abandonment, dysfunctional families or insufficient familial support. Psychiatric and social evaluation and support should therefore be conducted. Palliative care services should be involved if appropriate, so that the regimen can be adjusted more explicitly to provide comfort.

Recognising that a patient is in the final stages of life is an imprecise process in CF, requiring knowledge of the patient's trajectory and response to previous interventions. Even experienced clinicians can be uncertain, and added to ethical considerations, that uncertainty may lead to difficulties in evaluating the burden of the treatment regimen. Our results suggest that a decrease in the clinical regimen, and acceptance of that modification by clinicians, may be a signal to begin a transition to a model of comfort care. This is likely to be especially true for patients that are free of major mood disorders, capable of judgement and receiving the appropriate familial and social support. Palliative care clinicians have long recognised that the expected trajectory of the illness strongly influences the timing of referral to palliative services (2,10,14), and that the standard model of palliative care, based on death from cancer, must be reconfigured to meet the needs of patients with CF (2,10,11,15).

Our results reveal that some patients may struggle with the balance of hope and realism that characterises the life of a patient with severe disease due to CF. If psychiatric conditions like a major depressive disorder must be ruled out, it is important to keep in mind that despair and resignation are human responses to a severe and chronic illness for which there is no cure. As clinicians we have a duty of compassion to these patients at all stages of life. Acceptance that patients have changed their feelings about the usefulness of the treatments, and a more explicit permission to make such changes, may even become part of the compassionate response to the suffering of seriously ill people with CF.

Finally, there seem to be patients that make the decision to cease treatment too soon, that is, when there is still an appreciable benefit expected from the point of view of comfort and survival length. Open discussion about the burden and benefits of the treatment may be helpful to these patients, and increasing psychosocial support accompanied by a temporarily flexible approach to adherence may help these patients to find their way back to an appropriate balance between the positive and negative aspects of treatment. Psychiatric conditions such as major depressive disorder should be referred to a psychiatrist for appropriate treatment. The decision to cease CF treatment in the context of insufficient familial support (nearly half of the adolescents in our sample) requires familial therapy or support.

Only 102 patients of the 204 reported were eligible for analysis. This is why great care should be taken in interpreting these results. The trajectory of care in the final months of life with CF is variable, and the course and meaning of the adjustments made in the regimen cannot be perfectly discerned given our methodology. Our study only canvassed the views of clinicians, and only in a retrospective manner. Further work interviewing patients and family members, as well as clinicians, would be able to uncover more precise differences among patients, as well as differences between care sites.

In conclusion, our study highlights the existence of situations where CF patients decide to stop daily treatment because of feelings of hopelessness or futility of the treatment. It is worth mentioning that such situations are very challenging for all persons involved: the patient, the family and spouse, and also for members of the multi-disciplinary team, as such cases can be easily interpreted as a failure of their own competence. Facing such a complex situation, a clinician should be able to discuss the case with a multi-disciplinary team (including an ethical specialist) so that the most appropriate attitude is defined, from the active psychiatric treatment of a severely depressed person to the compassionate support of a patient with the ability to judge that it is no longer useful to combat CF.

Table 1: Completed surveys according to age and CF-association categories

Number of completed patients	Global	Australia	Europe	USA
Total	102	15	16	71
Number of adults (18-more)	73	7	13	53
Number of adolescents (14-17)	25	8	2	15
Number of children (0-13)	4	0	1	3

Table 2: How, and which, treatments were stopped by the 102 CF patients

Treatments stopped	Global (n)	Children (n)	Adolescents (n)	Adults (n)
all at once	29	1	5	23
progressively	73	3	20	50
1st treatment stopped°				
Physiotherapy	21*	2	5**	14***
Antibiotics	16*	0	6**	10***
Vitamins	15*	1	5**	9***
Mucolytics	9*	0	1**	8***
Diet	6*	0	1**	5***
Pancreatic enzymes	1*	0	1**	0***
Others	1*	0	0**	1***
last treatment stopped°				
Pancreatic enzymes	23*	1	6**	16***
Diet	18*	2	7**	9***
Antibiotics	14*	0	4**	10***
Mucolytics	5*	1	1**	1***
Physiotherapy	4*	0	1**	3***
Vitamins	4*	0	0**	4***
Others	0*	0	0**	0***
Resumption of treatment(s)				
no	42	2	10	30
yes°	31	1	10	20
Antibiotics	19	1	5	13
Pancreatic enzymes	17	0	9	8
Physiotherapy	11	1	4	6
Diet	11	0	6	5
Mucolytics	6	0	2	4
Vitamins	2	0	1	1
Others	1	0	0	1

The treatment was stopped progressively by 73/102 patients, of which 72/73 stopped one treatment after the other and 1/73 (listed in “Others”) diminished them all progressively.

*°= Multiple choice questions, (hence the numbers do not add up to the total respondents). Results are presented with regard to interpretable responses as follows: number of interpretable responses/all the responses: *= (63/72) **= (19/20) ***= (41/49)*

Table 3: Use and type of palliative care treatments by the 102 CF patients

Palliative care	Global (n)	Children (n)	Adolescents (n)	Adults (n)
No	**32**	**1**	**6**	**25**
Yes°	**70**	**3**	**19**	**48**
opioids	61	2	15	44
oxygen	60	1	16	43
anxiolytics	45	1	13	31
benzodiazepines	32	1	6	25
anti-nausea/anti-emetics	28	0	12	16
non-opioid analgesics	20	2	4	14
non-invasive ventilation	16	0	4	12
others	5	0	4	1
anti-spasmosodics/spasmolytics	1	0	0	1

°= *Multiple choice question, (hence the numbers do not add up to the total respondents).*

Table 4: Reasons for stopping care by the CF 102 patients

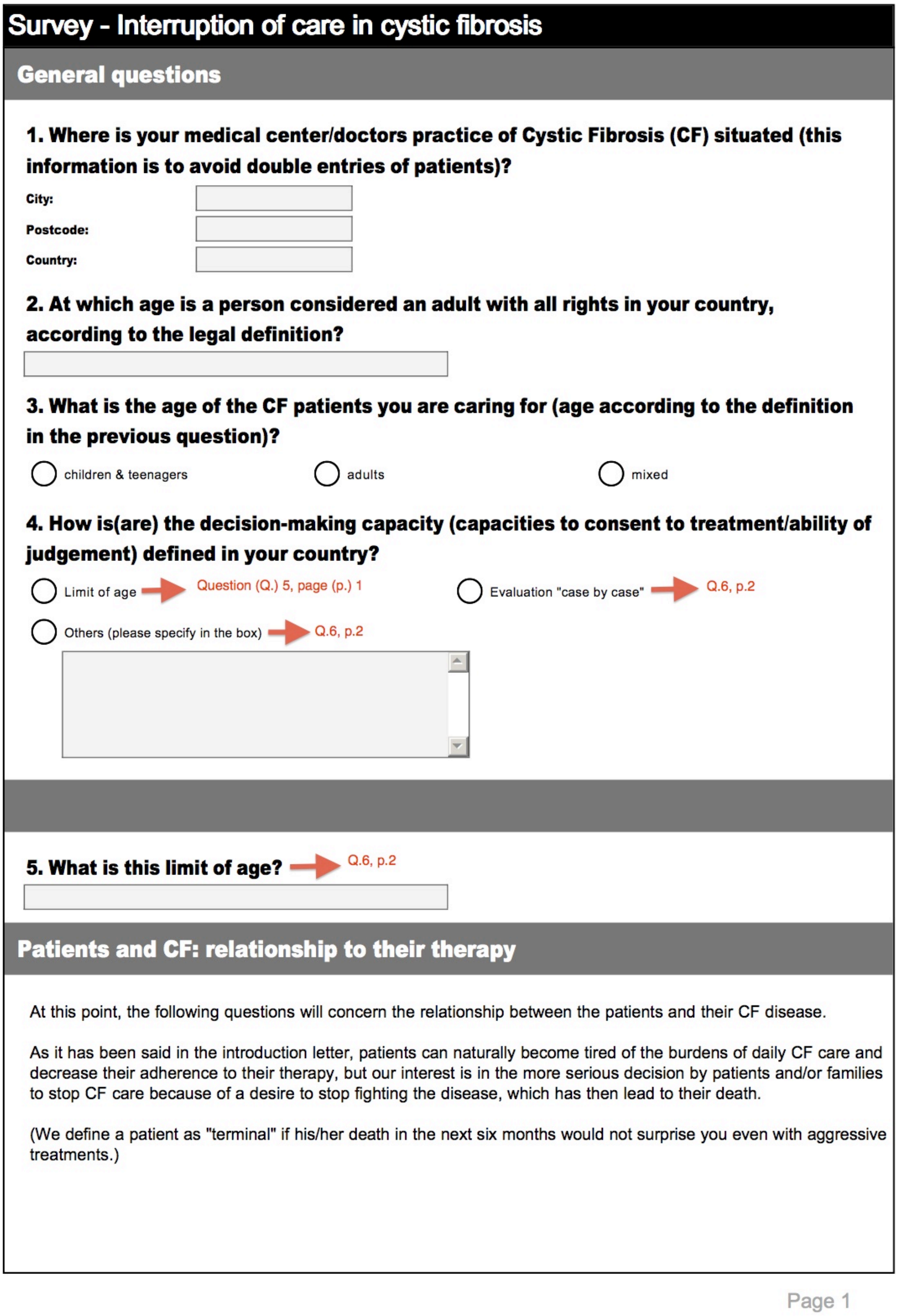
Reasons for stopping care°	Global (n)	Children (n)	Adolescents (n)	Adults (n)
Resignation	67	2	17	48
Enough is enough/discontent regarding the therapy	62	1	14	47
Reactive depression	39	1	10	28
Treatment				
no	13	0	3	10
yes°	26	1	7	18
Antidepressants	22	1	5	16
Psychotherapy	23	0	7	16
Others	4	1	0	3
Therapy gives more suffering than benefits	37	2	9	26
Dysfunctional family and support	27	1	11	15
Feeling of being different, not able to live normally	20	1	9	10
Absence of social/professional perspectives	13	0	5	8
Feeling of being abandoned and fighting alone	11	0	4	7
Others	11	1	2	8
Other psychiatric disease(s)	6	0	2	4

°= Multiple choice question, (hence the numbers do not add up to the total respondents).

Table 5: Main reason for stopping care by the 102 CF patients

Main reason for stopping care	Global (n)	Children (n)	Adolescents (n)	Adults (n)
Resignation	29	0	6	23
Enough is enough/discontent regarding the therapy	25	0	7	18
Reactive depression	12	0	2	10
Dysfunctional family and support	11	1	6	4
Therapy gives more suffering than benefits	10	2	2	6
Feeling of being different, not able to live normally	5	0	1	4
Others	4	1	1	2
Other psychiatric disease(s)	3	0	0	3
Absence of social/professional perspectives	2	0	0	2
Feeling of being abandoned and fighting alone	1	0	0	1

Questionnaire SurveyMonkey



Survey - Interruption of care in cystic fibrosis

General questions

1. Where is your medical center/doctors practice of Cystic Fibrosis (CF) situated (this information is to avoid double entries of patients)?

City:

Postcode:

Country:

2. At which age is a person considered an adult with all rights in your country, according to the legal definition?

3. What is the age of the CF patients you are caring for (age according to the definition in the previous question)?

○ children & teenagers ○ adults ○ mixed

4. How is(are) the decision-making capacity (capacities to consent to treatment/ability of judgement) defined in your country?

○ Limit of age → Question (Q.) 5, page (p.) 1
○ Evaluation "case by case" → Q.6, p.2
○ Others (please specify in the box) → Q.6, p.2

5. What is this limit of age? → Q.6, p.2

Patients and CF: relationship to their therapy

At this point, the following questions will concern the relationship between the patients and their CF disease.

As it has been said in the introduction letter, patients can naturally become tired of the burdens of daily CF care and decrease their adherence to their therapy, but our interest is in the more serious decision by patients and/or families to stop CF care because of a desire to stop fighting the disease, which has then lead to their death.

(We define a patient as "terminal" if his/her death in the next six months would not surprise you even with aggressive treatments.)

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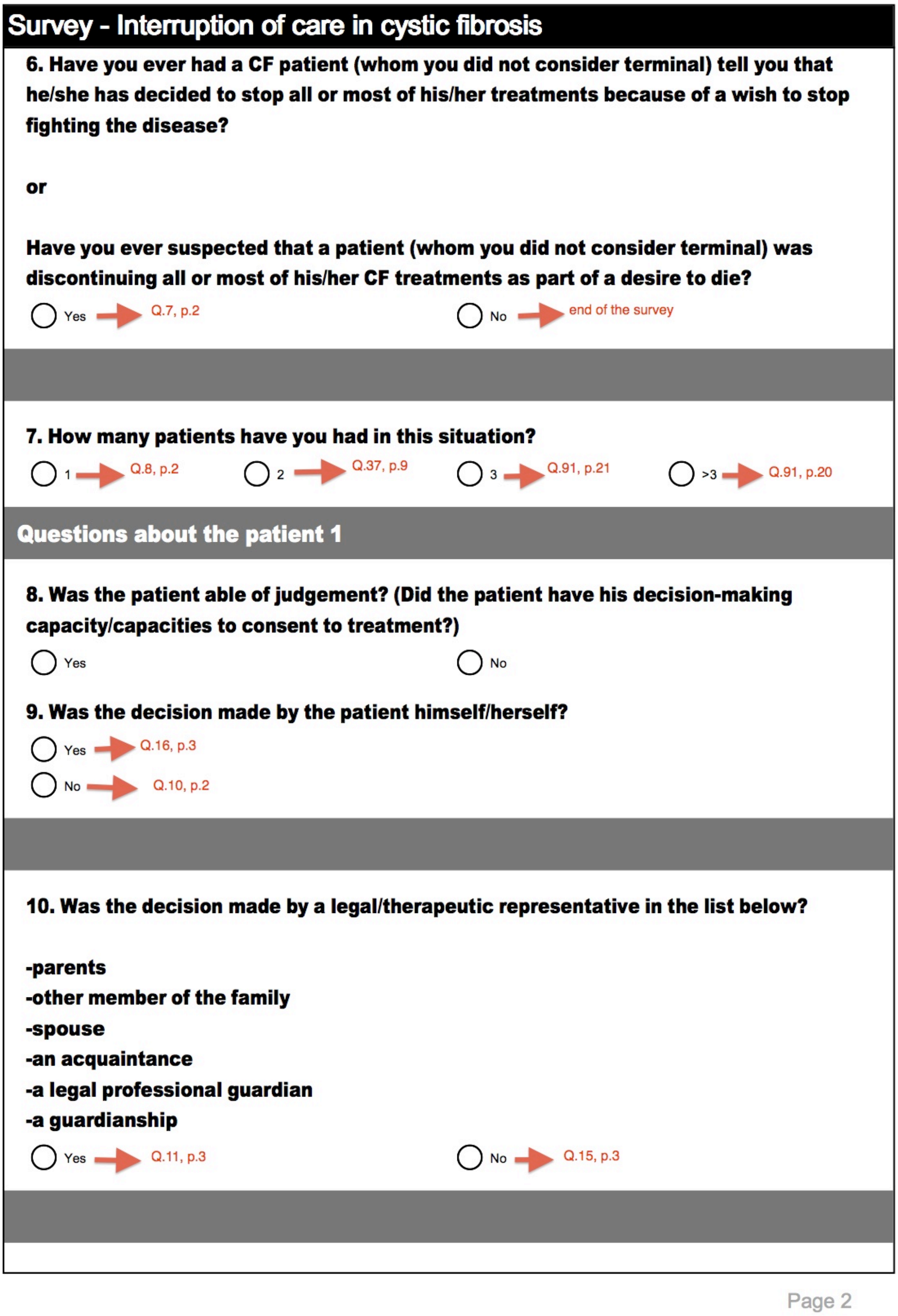

Survey - Interruption of care in cystic fibrosis

6. Have you ever had a CF patient (whom you did not consider terminal) tell you that he/she has decided to stop all or most of his/her treatments because of a wish to stop fighting the disease?

or

Have you ever suspected that a patient (whom you did not consider terminal) was discontinuing all or most of his/her CF treatments as part of a desire to die?

○ Yes → Q.7, p.2   ○ No → end of the survey

7. How many patients have you had in this situation?

○ 1 → Q.8, p.2   ○ 2 → Q.37, p.9   ○ 3 → Q.91, p.21   ○ >3 → Q.91, p.20

Questions about the patient 1

8. Was the patient able of judgement? (Did the patient have his decision-making capacity/capacities to consent to treatment?)

○ Yes   ○ No

9. Was the decision made by the patient himself/herself?

○ Yes → Q.16, p.3
○ No → Q.10, p.2

10. Was the decision made by a legal/therapeutic representative in the list below?

-parents
-other member of the family
-spouse
-an acquaintance
-a legal professional guardian
-a guardianship

○ Yes → Q.11, p.3   ○ No → Q.15, p.3

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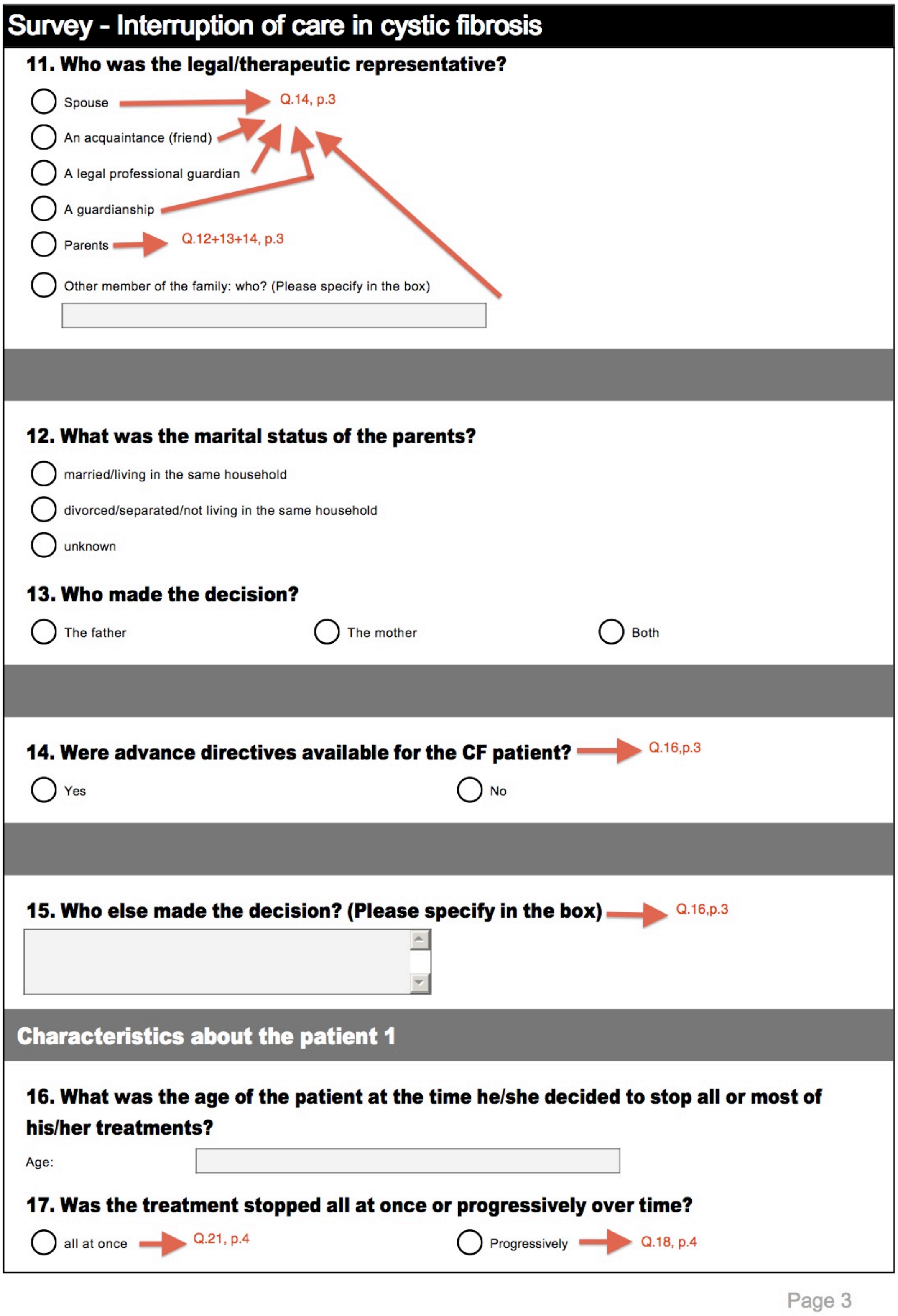

Survey - Interruption of care in cystic fibrosis

11. Who was the legal/therapeutic representative?

○ Spouse → Q.14, p.3

○ An acquaintance (friend)

○ A legal professional guardian

○ A guardianship

○ Parents → Q.12+13+14, p.3

○ Other member of the family: who? (Please specify in the box)

12. What was the marital status of the parents?

○ married/living in the same household

○ divorced/separated/not living in the same household

○ unknown

13. Who made the decision?

○ The father ○ The mother ○ Both

14. Were advance directives available for the CF patient? → Q.16,p.3

○ Yes ○ No

15. Who else made the decision? (Please specify in the box) → Q.16,p.3

Characteristics about the patient 1

16. What was the age of the patient at the time he/she decided to stop all or most of his/her treatments?

Age:

17. Was the treatment stopped all at once or progressively over time?

○ all at once → Q.21, p.4 ○ Progressively → Q.18, p.4

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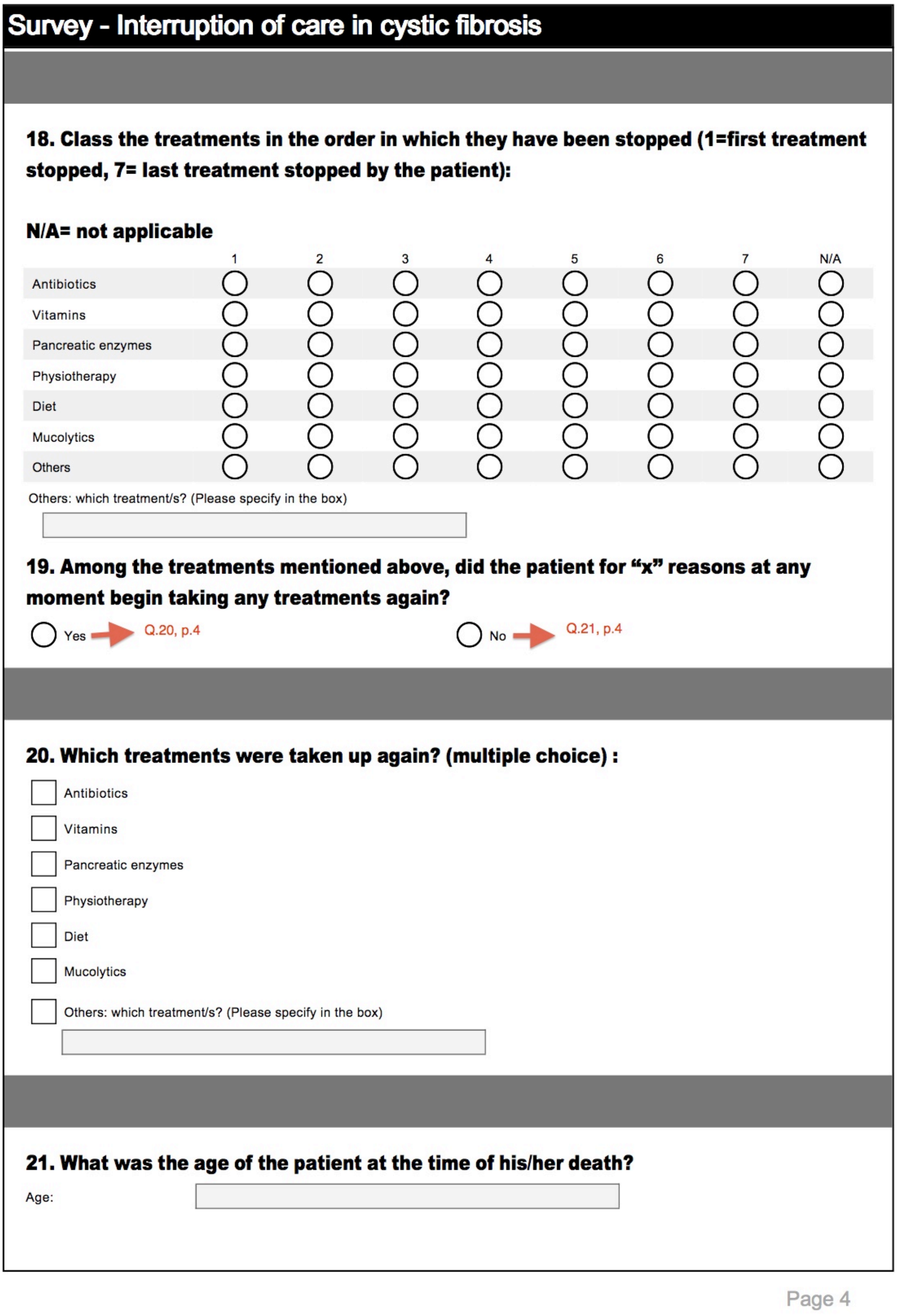

Survey - Interruption of care in cystic fibrosis

18. Class the treatments in the order in which they have been stopped (1=first treatment stopped, 7= last treatment stopped by the patient):

N/A= not applicable

	1	2	3	4	5	6	7	N/A
Antibiotics	○	○	○	○	○	○	○	○
Vitamins	○	○	○	○	○	○	○	○
Pancreatic enzymes	○	○	○	○	○	○	○	○
Physiotherapy	○	○	○	○	○	○	○	○
Diet	○	○	○	○	○	○	○	○
Mucolytics	○	○	○	○	○	○	○	○
Others	○	○	○	○	○	○	○	○

Others: which treatment/s? (Please specify in the box)

19. Among the treatments mentioned above, did the patient for "x" reasons at any moment begin taking any treatments again?

○ Yes → Q.20, p.4 ○ No → Q.21, p.4

20. Which treatments were taken up again? (multiple choice) :

☐ Antibiotics
☐ Vitamins
☐ Pancreatic enzymes
☐ Physiotherapy
☐ Diet
☐ Mucolytics
☐ Others: which treatment/s? (Please specify in the box)

21. What was the age of the patient at the time of his/her death?

Age:

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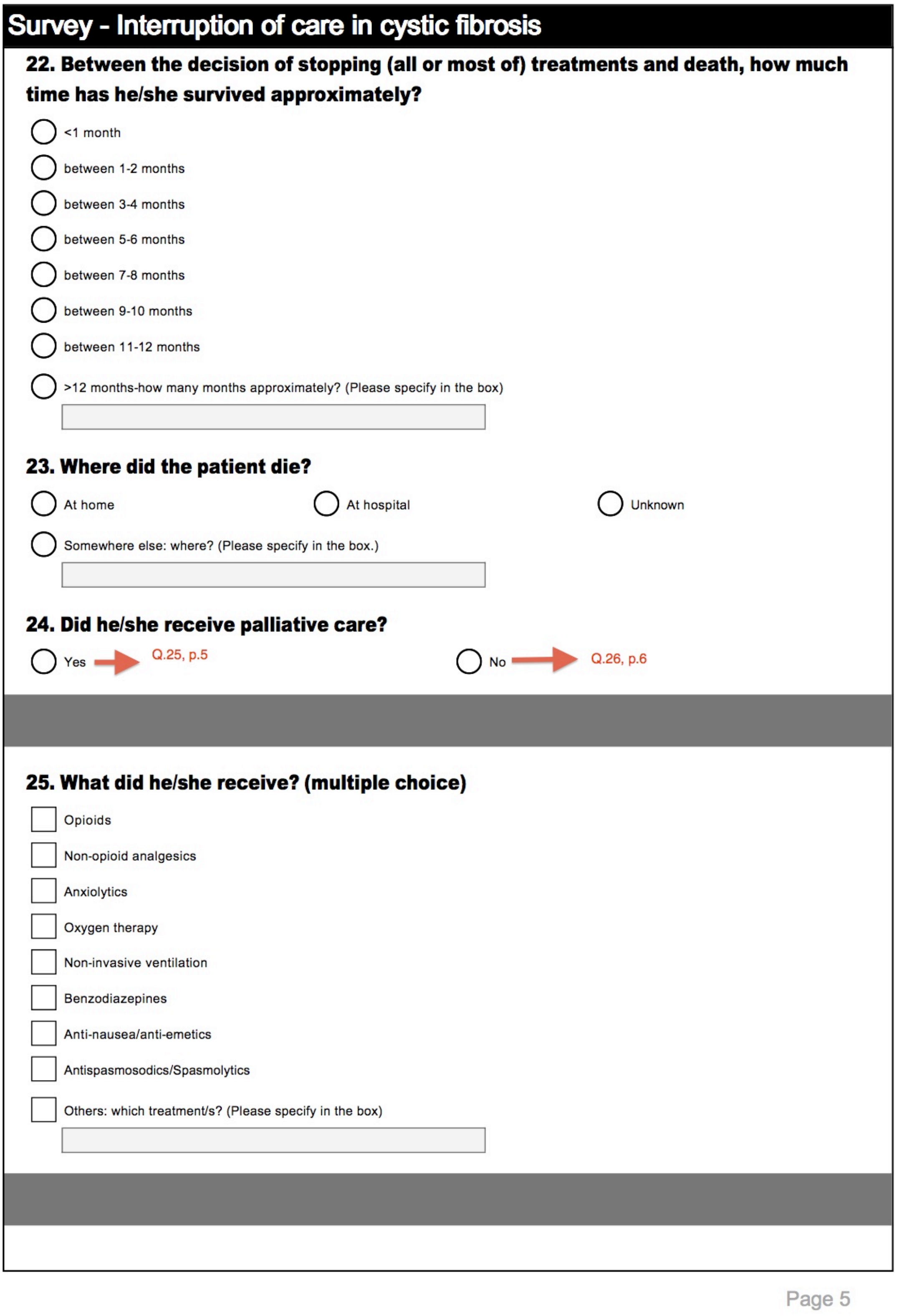

Survey - Interruption of care in cystic fibrosis

22. Between the decision of stopping (all or most of) treatments and death, how much time has he/she survived approximately?

○ <1 month
○ between 1-2 months
○ between 3-4 months
○ between 5-6 months
○ between 7-8 months
○ between 9-10 months
○ between 11-12 months
○ >12 months-how many months approximately? (Please specify in the box)

23. Where did the patient die?

○ At home ○ At hospital ○ Unknown
○ Somewhere else: where? (Please specify in the box.)

24. Did he/she receive palliative care?

○ Yes → Q.25, p.5 ○ No → Q.26, p.6

25. What did he/she receive? (multiple choice)

☐ Opioids
☐ Non-opioid analgesics
☐ Anxiolytics
☐ Oxygen therapy
☐ Non-invasive ventilation
☐ Benzodiazepines
☐ Anti-nausea/anti-emetics
☐ Antispasmosodics/Spasmolytics
☐ Others: which treatment/s? (Please specify in the box)

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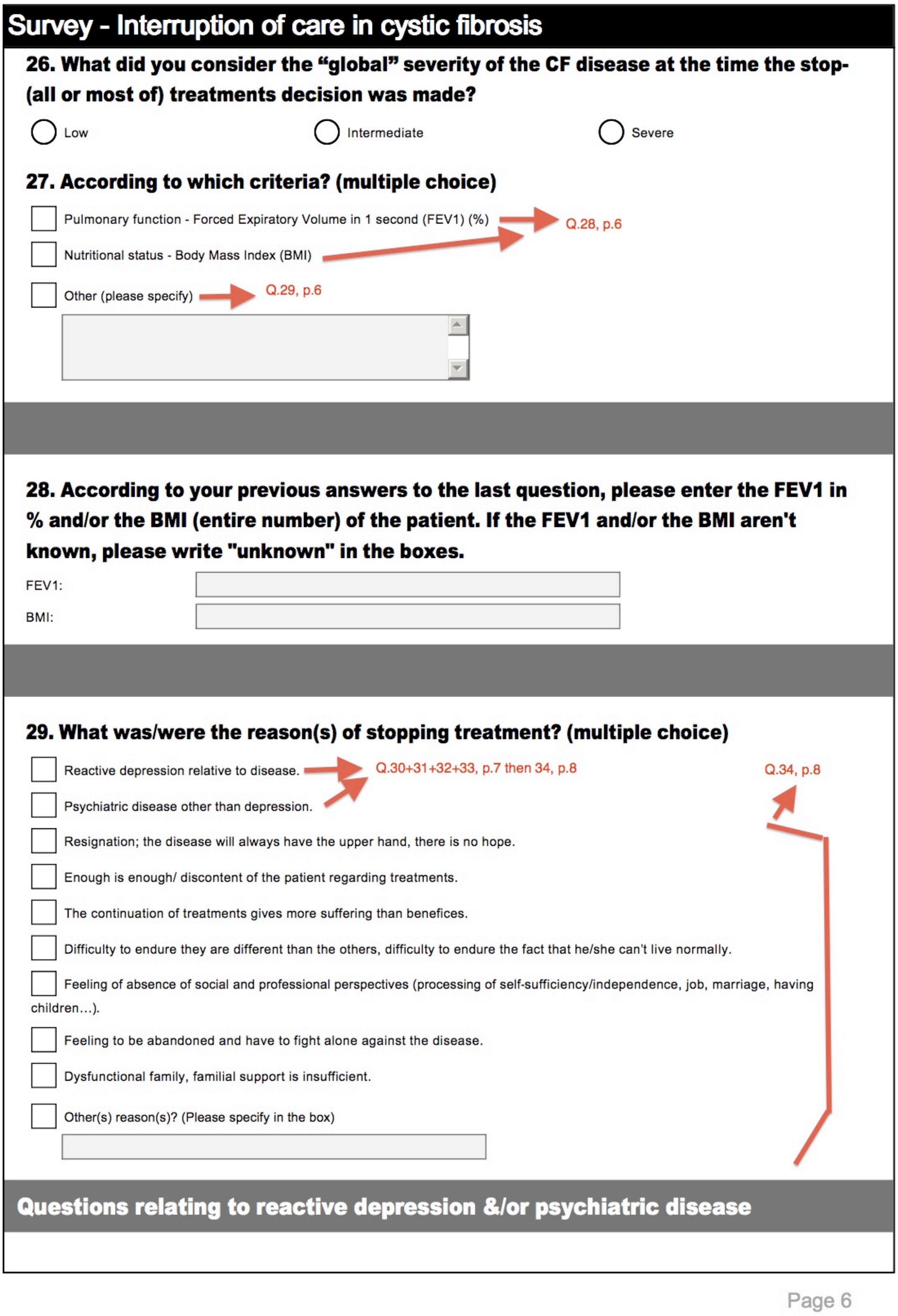


Survey - Interruption of care in cystic fibrosis

26. What did you consider the “global” severity of the CF disease at the time the stop-(all or most of) treatments decision was made?

○ Low ○ Intermediate ○ Severe

27. According to which criteria? (multiple choice)

☐ Pulmonary function - Forced Expiratory Volume in 1 second (FEV1) (%)

☐ Nutritional status - Body Mass Index (BMI)

Q.28, p.6

☐ Other (please specify)

Q.29, p.6

28. According to your previous answers to the last question, please enter the FEV1 in % and/or the BMI (entire number) of the patient. If the FEV1 and/or the BMI aren't known, please write "unknown" in the boxes.

FEV1:

BMI:

29. What was/were the reason(s) of stopping treatment? (multiple choice)

☐ Reactive depression relative to disease.

☐ Psychiatric disease other than depression.

Q.30+31+32+33, p.7 then 34, p.8

☐ Resignation; the disease will always have the upper hand, there is no hope.

☐ Enough is enough/ discontent of the patient regarding treatments.

☐ The continuation of treatments gives more suffering than benefices.

☐ Difficulty to endure they are different than the others, difficulty to endure the fact that he/she can't live normally.

☐ Feeling of absence of social and professional perspectives (processing of self-sufficiency/independence, job, marriage, having children…).

☐ Feeling to be abandoned and have to fight alone against the disease.

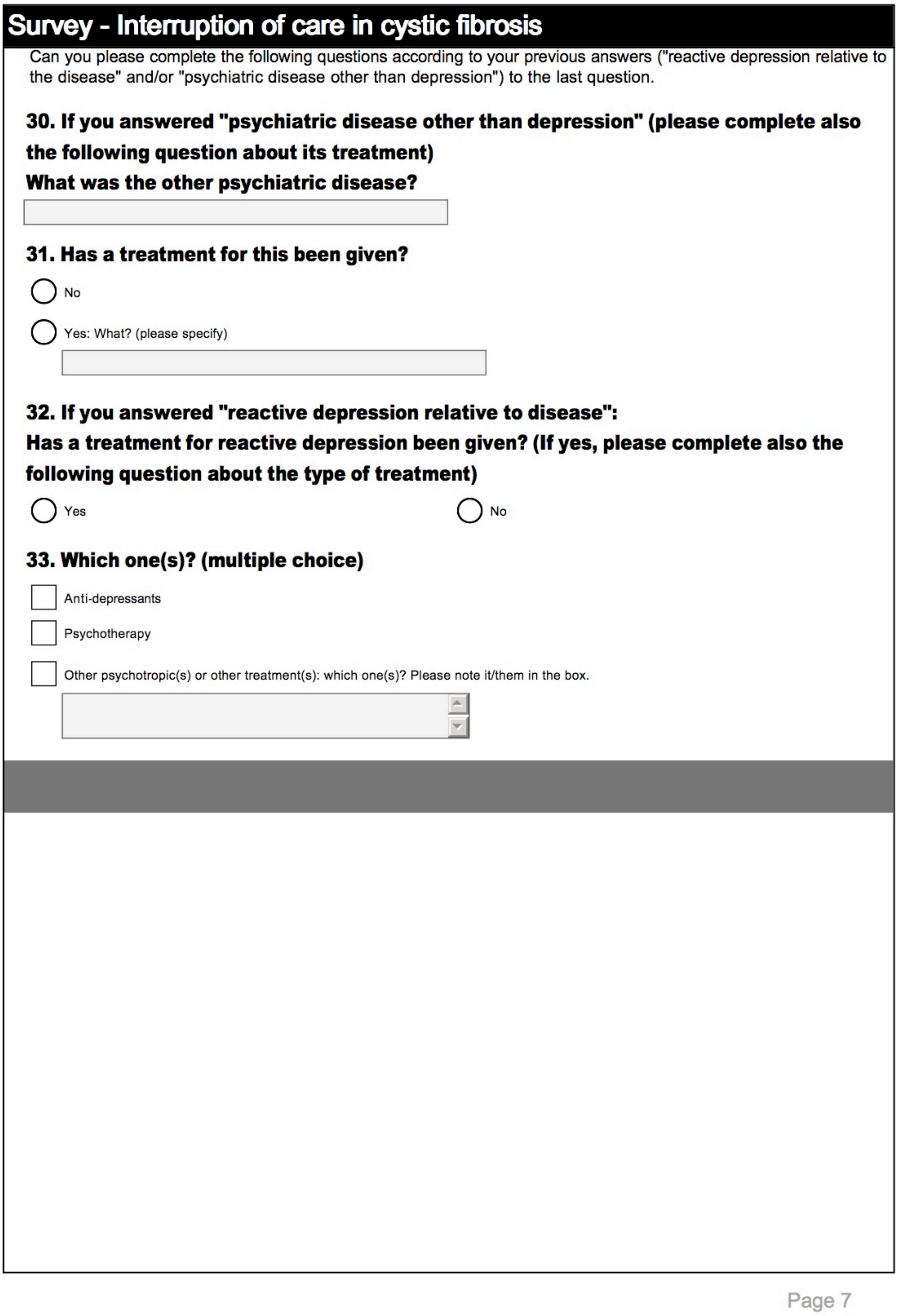
☐ Dysfunctional family, familial support is insufficient.

☐ Other(s) reason(s)? (Please specify in the box)

Q.34, p.8

Questions relating to reactive depression &/or psychiatric disease

Page 6



Survey - Interruption of care in cystic fibrosis

Can you please complete the following questions according to your previous answers ("reactive depression relative to the disease" and/or "psychiatric disease other than depression") to the last question.

30. If you answered "psychiatric disease other than depression" (please complete also the following question about its treatment)
What was the other psychiatric disease?

31. Has a treatment for this been given?

○ No

○ Yes: What? (please specify)

32. If you answered "reactive depression relative to disease":
Has a treatment for reactive depression been given? (If yes, please complete also the following question about the type of treatment)

○ Yes ○ No

33. Which one(s)? (multiple choice)

☐ Anti-depressants

☐ Psychotherapy

☐ Other psychotropic(s) or other treatment(s): which one(s)? Please note it/them in the box.

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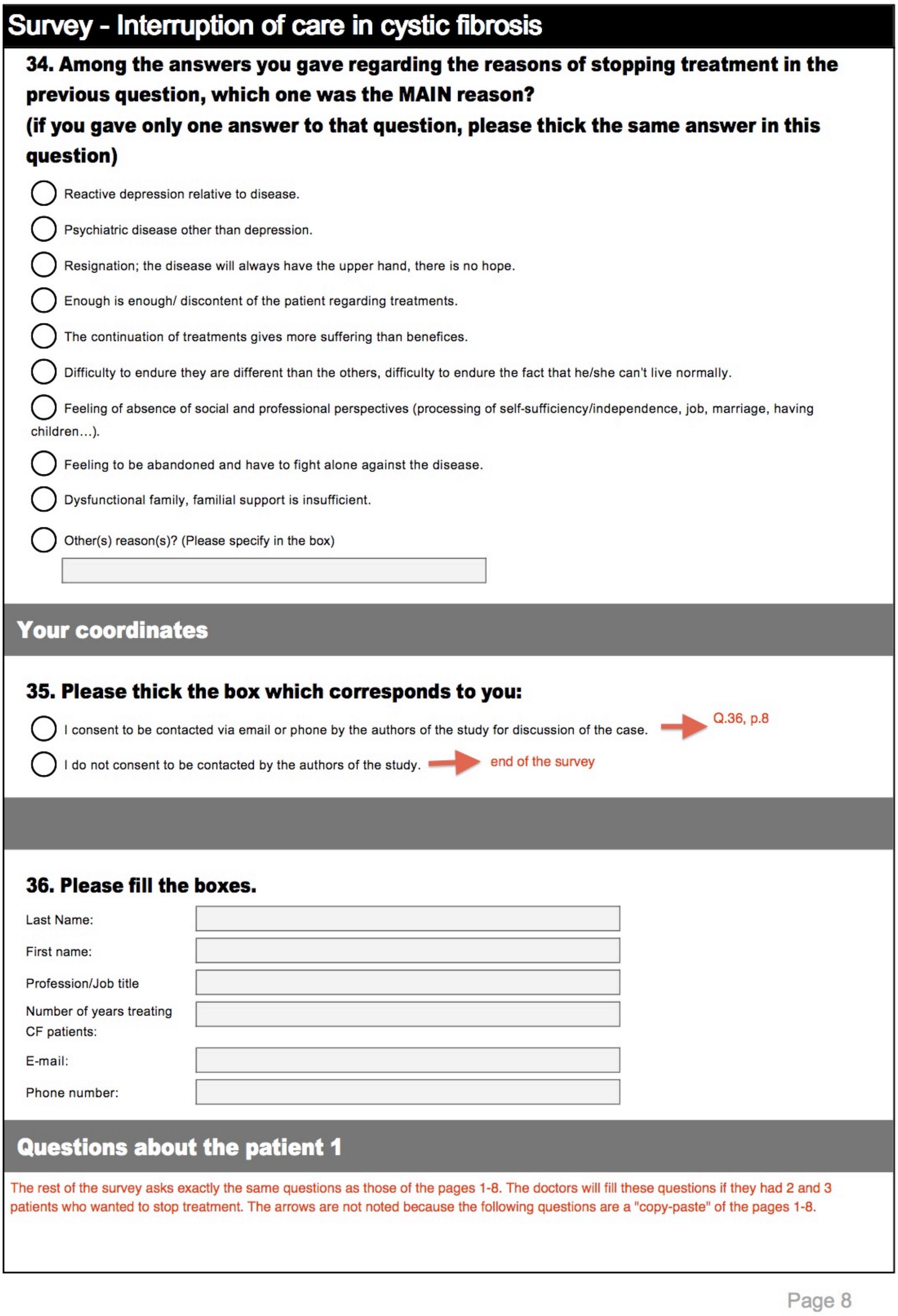

Survey - Interruption of care in cystic fibrosis

34. Among the answers you gave regarding the reasons of stopping treatment in the previous question, which one was the MAIN reason?
(if you gave only one answer to that question, please thick the same answer in this question)

○ Reactive depression relative to disease.

○ Psychiatric disease other than depression.

○ Resignation; the disease will always have the upper hand, there is no hope.

○ Enough is enough/ discontent of the patient regarding treatments.

○ The continuation of treatments gives more suffering than benefices.

○ Difficulty to endure they are different than the others, difficulty to endure the fact that he/she can't live normally.

○ Feeling of absence of social and professional perspectives (processing of self-sufficiency/independence, job, marriage, having children…).

○ Feeling to be abandoned and have to fight alone against the disease.

○ Dysfunctional family, familial support is insufficient.

○ Other(s) reason(s)? (Please specify in the box)

Your coordinates

35. Please thick the box which corresponds to you:

○ I consent to be contacted via email or phone by the authors of the study for discussion of the case. → Q.36, p.8

○ I do not consent to be contacted by the authors of the study. → end of the survey

36. Please fill the boxes.

Last Name:

First name:

Profession/Job title

Number of years treating CF patients:

E-mail:

Phone number:

Questions about the patient 1

The rest of the survey asks exactly the same questions as those of the pages 1-8. The doctors will fill these questions if they had 2 and 3 patients who wanted to stop treatment. The arrows are not noted because the following questions are a "copy-paste" of the pages 1-8.

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