

## Predictors of a Favorable Outcome of Physiotherapy in Fecal Incontinence: Secondary Analysis of a Randomized Trial

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**Aims:** It is unclear which patients with fecal incontinence (FI) are likely to benefit from physiotherapy treatment, which is relevant for medical decision making and patient counseling. This study aimed to identify patient characteristics predicting a favorable outcome of physiotherapy. **Methods:** Eighty patients with FI, with a mean age of 59.3 (SD ± 11.9), were recruited at the Maastricht University Medical Centre and enrolled in a randomized controlled trial, which assessed the effect of adding rectal balloon training to pelvic floor muscle training. Treatment groups were combined for prediction modeling. Candidate predictors were obtained from demographics, medical history, physical examination, baseline tests, questionnaires, and physiotherapy diagnostics. Favorable outcome was defined as a combination of: (i) Vaizey score reduction ≥ 5 points, and (ii) “slightly” to “very much improved” on the nine-point global perceived effect score. Predictors were identified by univariable and multivariable logistic regression analysis. **Results:** Thirty-seven patients (46.3%) had a favorable outcome. Multivariable analysis showed that longer time since FI onset appeared to be associated with an unfavorable outcome (odds ratio [OR], 0.68; 95% confidence interval [CI], 0.47–1.00;  $P = 0.05$ ), whereas the use of constipating medication (OR, 3.79; CI, 0.99–14.51;  $P = 0.05$ ), any obstetric factor (OR, 2.15; CI, 0.94–4.89;  $P = 0.07$ ), and experiencing minor embarrassment (OR, 2.12; CI, 1.10–4.09;  $P = 0.03$ ) predicted a favorable outcome. **Conclusions:** The small subset of identified predictors for a favorable outcome may be relevant in patient counseling and targeting physiotherapy treatment more efficiently, especially as they are available early in the diagnostic process. *NeuroUrol. Urodynam.* 31:1156–1160, 2012. © 2012 Wiley Periodicals, Inc.

**Key words:** biofeedback; fecal incontinence; physiotherapy; prediction; Vaizey score

### INTRODUCTION

Fecal incontinence (FI) is the complaint of involuntary loss of feces<sup>1</sup> and is associated with embarrassment, depression, and societal effects. Underreporting is a common feature of this patient group due to embarrassment about seeking help or lack of awareness of available and effective interventions.<sup>2</sup> The majority of patients who seek help respond favorably to physiotherapy treatment. Physiotherapy treatment may include pelvic floor muscle training, biofeedback (including rectal balloon training), electrical stimulation, and the provision of information and advice (on diet, incontinence material, defecation techniques, and toilet behavior) and has reported success rates of 49–72%.<sup>3</sup> However, a Cochrane review of controlled studies of biofeedback and exercises for FI showed insufficient evidence to determine which patients are most likely to have a favorable outcome.<sup>4</sup> Identifying patient characteristics that are amenable to change by physiotherapy treatment may prevent referral to surgical interventions, which are considered equally effective, but costly and burdensome because of their invasive nature and serious adverse events.<sup>5,6</sup> Identifying predictors based on pre-treatment assessments is essential to support early clinical decision-making and may lead to more realistic expectations of the outcome, as well as a more efficient use of resources and referral. Only a few studies have examined which patient characteristics are likely to predict the greatest benefit from

physiotherapy treatment. Conflicting data has been reported on predictive factors due to heterogeneity of study populations, outcome measures, treatment methods, and definition of favorable outcome.<sup>7,8</sup>

If individual patient characteristics can be related to treatment response, physiotherapy treatment can be made more effective by using targeted interventions. We recently completed a two-armed randomized controlled trial examining the effect of rectal balloon training as an add-on therapy to pelvic floor muscle training.<sup>9,10</sup> We performed secondary analyses aimed at identifying baseline characteristics that predict a favorable outcome of physiotherapy treatment for patients with FI.

Additional Supporting Information may be found in the online version of this article.

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## MATERIALS AND METHODS

We report on secondary analyses of data from a randomized controlled trial conducted between August 2006 and May 2009. An extensive description of the design is provided elsewhere.<sup>9,10</sup>

### Patients

Eighty consecutive adults with FI, recruited at the Maastricht University Medical Centre in the Netherlands, were randomly assigned to receive rectal balloon training as an add-on therapy to pelvic floor muscle training ( $n = 40$ ) or pelvic floor muscle training alone ( $n = 40$ ). Inclusion criteria were: FI complaints lasting at least 6 months, Vaizey incontinence score of at least 12 (range 0–24), and failure of medication and dietary adaptations. Exclusion criteria were: having been diagnosed with an anorectal tumor within the past 2 years, absent squeeze pressure of the anal sphincter, chronic diarrhoea (always fluid stool three or more times a day), overflow incontinence, proctitis, ulcerative colitis, Crohn's disease, soiling (defined as leakage of a minimal amount of watery feces from the anal canal), previous ileo-anal or colo-anal anastomosis, and rectal prolapse in situ. Participants who had received physiotherapy during the previous 6 months or who were considered unable to comply with therapy were also excluded. Many patients appeared to have minor day- or nighttime soiling. Patients with minor soiling were included as long as it was not due to overflow incontinence. The total Vaizey score was exclusive of soiling.<sup>9,10</sup> The Medical Ethics Committee of the Maastricht University Medical Centre approved the study.

### Selecting Predictive Factors

Selecting distinct predictive factors based on literature reports in advance was not feasible due to conflicting conclusions of the articles. We therefore included a wide range of candidate predictors obtained from patient demographics, medical history, physical examination, baseline tests, questionnaires, and physiotherapy diagnostics at baseline (Supplementary Table I).

### Medical History and Physical Examination

The medical history and physical examination were obtained by one physician by means of a standardized case report form and included demographics, symptoms of incontinence (onset, type, and degree of FI, associated urinary incontinence, and underlying causes), bowel habits [stool consistency (thin, soft mushy, solid, firm, or varying) and constipation (use of digital support for defecation and/or straining to defecate)], previous history (systemic diseases or any reported anorectal, gynecological, urological, neurological, or metabolic factor), and any obstetric factor (including high birth weight ( $\geq 4,000$  grams), episiotomy, instrumental delivery (forceps delivery/vacuum extraction), prolonged second stage of labor ( $> 2$  hr), and breech delivery. Rupture after vaginal delivery was separately evaluated as independent predictor. Categorization of all variables is explained in Supplementary Table I. The primary outcome measure was the Vaizey grading system, ranging from 0 (complete continence) to 24 (complete incontinence).<sup>11</sup> This severity score assesses the frequency of loss of gas, liquid stool, and solid stool, the ability to defer defecation for 15 min, alterations in lifestyle, and the use of pads and constipating medication. To minimize bias, an independent research assistant performed double data entry for the medical history and physical examination data.

### Anorectal Functional Tests

Anorectal function was evaluated with the following series of tests: anorectal manometry using a solid state catheter (Konigsberg Instrument Inc., Pasadena, CA), rectal capacity measurement (as used in hospital setting and medical practice), anorectal sensation, anal endosonography (7.5 MHz, SDD 2000, Multiview, Aloka, Japan), and defecography (Supplementary Table I).

### Questionnaires

Condition-specific quality of life was measured with the Fecal Incontinence Quality of Life (FIQL) Scale, ranging from 4 to 16 and comprising four subscales: Lifestyle (10 items), Coping/Behavior (9 items), Depression/Self-perception (7 items), and Embarrassment (3 items).<sup>12</sup> A higher score indicates a better quality of life. We also asked patients to score their perceived change after the treatment, using a nine-point global perceived effect score (GPE), ranging from: 1 = very much improved to 9 = very much worse. These questionnaires were completed at home, minimizing bias as the physician and physiotherapist were unaware of the responses.

### Physiotherapy Diagnostics

All physiotherapists used standardized case report forms to record pelvic floor muscle assessment, including the Oxford grading Scheme,<sup>13</sup> endurance (submaximum contraction up to 30 sec), and fatigue (maximum contraction up to five repetitions) of the external anal sphincter and pelvic floor. In addition, they assessed rectal capacity measurements (as used by specialized physiotherapists), the presence of paradoxical lifting or straining and pain during palpation.

### Physiotherapy Treatment

After signing informed consent, patients were randomly assigned in a 1:1 ratio with a random permuted block size of four to either rectal balloon training and pelvic floor muscle training or pelvic floor muscle training alone. Patients received a standardized course of a total of 12 treatment sessions within 9 weeks. Pelvic floor muscle training included improving awareness of the pelvic floor and anal sphincter, strength, and endurance training, and home exercises. Exercises also comprised simulating daily life activities. Rectal balloon training was done according to the sensory and coordination training protocol.<sup>3,4</sup> Participating physiotherapists were instructed by means of a written protocol, and an educational meeting in which we showed them an instruction film on rectal balloon training. Ultimately, 25 out of the 90 trained physiotherapists treated all included patients.

### Outcome

No single test or score exists that can benchmark favorable treatment of FI, due to the lack of a criterion standard.<sup>14</sup> Patient improvement after treatment was selected as favorable outcome, representing the dependent variable in the predictive model. In agreement with other studies,<sup>15</sup> favorable outcome was defined as the following combination: (i) a reduction of the Vaizey score by at least five points, and (ii) "slightly" to "very much improved" on the GPE score. The first criterion is derived from a study by the same authors who reported an estimate for the minimally important change in the Vaizey score.<sup>16</sup>

### Statistical Analyses

Missing predictive and outcome variables were completed using the multiple imputation procedure, in which each missing value was replaced by a set of multiple values, estimated from regression models and available data. We used the fully conditional specification imputation method (MCMC) with a maximum of 25 iterations and the predictive mean matching (PMM) as model type for the scale variables. We generated five multiple imputed datasets, separately for each intervention group.<sup>17</sup> The pooled results are presented.

We explored the assumption of linearity between the continuous predictors and the change in Vaizey score and GPE using visual inspection. In case of nonlinearity, the continuous variables were transformed to better approach linearity.

Multicollinearity was examined using the variance inflation factor (VIF) and the reciprocal tolerance statistic (1/VIF). VIF values indicate whether a predictor has strong linear associations with the other predictors. The average VIF value of all predictors should not be substantially larger than 1 and the reciprocal tolerance statistic should not be lower than 0.2.

The associations between the outcome immediately after treatment and each of the candidate predictors were analyzed using univariable logistic regression analyses. We used the Akaike Information Criterion, which corresponds to selection of predictors at a 0.157 significance level.<sup>18</sup> Univariable odds ratios (OR) and their corresponding 95% confidence interval were calculated. Selected predictors derived from univariable logistic regression were included in the multivariable logistic regression model.

For the multivariable analyses, a three-stage model was used. The initial prediction model included demographic and medical history variables available at the time the patients first visited the physician. The second model examined the added effect of anorectal functional tests in predicting the outcome of physiotherapy. Finally, the third model included variables available at the time the patient was referred to a physiotherapist. Hence, models 1 and 2 provide physicians with information before referral to physiotherapy, whereas model 3 examines the added effect of variables from physiotherapy diagnostics. To evaluate the influence of treatment allocation, we added this variable to the final set of predictors (model 4). Each model was based on 80 patients.

A forced entry approach with a significance level of 0.10 was used to build each multivariable model. A liberal *P*-value increases the chances of obtaining true predictors. Regression coefficients and related standard errors and *P*-values were then estimated across all multiply imputed datasets using Rubin's Rules.<sup>19</sup> Analyses were performed using SPSS software, version 17.0 (IBM Corporation, Somers, NY). Reported *P*-values are two-tailed.

## RESULTS

### Patients

Hundred and one patients had been assessed for eligibility. Eighty patients, predominantly female (90%), were included, with a mean age of 59.3 (SD ± 11.9).<sup>10</sup> Ten patients (12.5% missing data) dropped out before or during physiotherapy treatment. Patients were evaluated at a mean of 6.8 weeks (SD ± 5.3) after completing physiotherapy. Patients reported median of 4 years having elapsed since the onset of FI symptoms (interquartile range 2–6). The mean baseline Vaizey score changed from 17.8 (SD ± 2.8) to 12.8 (SD ± 5.9) after treatment, an average reduction of 5.0 points (95% CI, –6.3 to –3.7). A reduction in Vaizey score of at least five points was

achieved by 50.5% of treated patients, while 71% had a “slightly” to “very much improved” GPE score. Favorable outcome, defined as the combination of these two outcomes, was achieved by 37 patients (46.3%).

### Univariable Analyses of Response to Physiotherapy Treatment

Candidate predictors were first analyzed using univariable logistic regression (Supplementary Table I). The results for predictors with a *P*-value <0.157 are summarized in Supplementary Table I. We identified 10 factors predicting outcome of physiotherapy treatment. The following predictors, obtained from demographics and medical history, were associated with a favorable outcome (positive regression coefficient (B) and OR >1.0): a higher total score on the FIQL and its Embarrassment subscale, use of constipating medication, and any obstetric factor. Factors associated with an unfavorable outcome (negative B and OR <1.0) were longer time since onset of FI, liquid stool incontinence, and no distinction between flatus and feces. Predictors obtained from physical examination were not associated with a favorable or unfavorable outcome. Only one variable from the anorectal functional tests predicted the outcome of physiotherapy: a higher urge sensation threshold was associated with an unfavorable outcome. Finally, two predictive factors from physiotherapy diagnostics were identified: better results for endurance and fatigue of the pelvic floor were associated with an unfavorable outcome.

### Multivariable Analysis of Response to Physiotherapy Treatment

Variables with a *P*-value <0.157 based on univariable analyses were included in the multivariable logistic regression model. The initial multivariable model (model 1 from the three-stage modeling) included all predictors identified from demographics and medical history (Table I). Longer time since onset of FI, a higher score on the Embarrassment subscale of the FIQL, use of constipating medication, and any obstetric factor independently appeared to predict response and therefore remained in the model. In the second model, we added the significant predictor from the anorectal functional tests, i.e., urge sensation threshold, to the variables established in the first model, which did not add to the association with treatment response. Next, significant predictors from physiotherapy diagnostics (fatigue and endurance of the pelvic floor) were added to the variables determined in the first model, but yielded no additional predictors. After adding group allocation in the final multivariable model (model 4), the variables established in the first model remained significant. Ultimately, longer time since onset of FI proved to predict an unfavorable outcome (B, –0.38; OR, 0.68; *P* = 0.05), whereas the use of constipating medication (B, 1.33; OR, 3.79; *P* = 0.05), any obstetric factor (B, 0.77; OR, 2.15; *P* = 0.07), and a higher score on the Embarrassment subscale (B, 0.75; OR, 2.12; *P* = 0.03) proved to predict a favorable outcome. The Embarrassment subscale of the FIQL contains items with regard to feeling ashamed, worry about others smelling stool, and the concern about leaking stool without even knowing it.

## DISCUSSION

Longer time since onset of FI symptoms appeared to be associated with an unfavorable outcome of physiotherapy treatment in multivariable analysis. The multivariable analysis showed that three predictive factors were associated with a favorable outcome: a higher score on the Embarrassment subscale of the FIQL score (less embarrassment), use of constipating medication, and any obstetric factor.

TABLE I. Multivariable Logistic Regression Analyses

	Model 1		Model 2		Model 3		Model 4	
	B (SE)	P-value						
Longer time since onset of FI (m)	-0.49 (0.22)	0.03	-0.40 (0.19)	0.04	-0.56 (0.23)	0.02	-0.38 (0.19)	0.05
Embarrassment subscale	1.13 (0.50)	0.03	0.67 (0.34)	0.05	0.97 (0.40)	0.02	0.75 (0.34)	0.03
Current constipating medication	1.35 (0.70)	0.05	1.36 (0.69)	0.05	1.33 (0.77)	0.08	1.33 (0.69)	0.05
Any obstetric factor	0.95 (0.45)	0.04	0.93 (0.44)	0.04	0.95 (0.47)	0.04	0.77 (0.42)	0.07
Liquid stool incontinence	-0.46 (0.36)	0.19						
No distinction flatus/faeces	-0.22 (0.16)	0.16						
FIQL total score	-0.21 (0.17)	0.22						
Urge sensation (ml)			-0.01 (0.01)	0.12				
Endurance pelvic floor					-0.05 (0.04)	0.17		
Fatigue pelvic floor					-0.27 (0.23)	0.23		
Group allocation							-0.24 (0.53)	0.65

B (SE), estimate with corresponding standard error; FI, fecal incontinence; m, months; FIQL, Fecal Incontinence Quality of Life Scale.

Our findings indicate that only a small subset of predictive factors is important in predicting favorable or unfavorable physiotherapy outcome. Only predictive factors obtained from the medical history were associated with response to treatment. Results of physical examination, diagnostic tests, and physiotherapy assessment did not provide additional predictive factors, indicating that patients who are suitable candidates for physiotherapy treatment can be identified in an early stage of the diagnostic process, which is useful for medical decision making and patient counseling.

Potential study limitations should be taken into account when interpreting the results. Predictors of favorable outcome of physiotherapy treatment are inconsistently reported in the literature, which complicated pre-specification of the most important predictors to be included in the prediction model. To overcome this problem, we initially tested the association between each potential predictor and the outcome. Selection of predictors was based on the Akaike Information Criterion, which uses a liberal P-value. This limits the possibility that a true predictor would be missed.

Symptom severity and subjective perception of improvement do not seem to correlate.<sup>20</sup> Therefore, we defined favorable outcome as a combination of subjectively reported improvement and a reduction in the Vaizey score, which means we were stricter than most other studies, which used only one criterion.<sup>21,22</sup> This reduced the reported number of patients with a favorable outcome. Furthermore, we performed a sensitivity analysis in which we analyzed the demographic variables using univariable logistic regression, with a more stringent criteria for the GPE score in the outcome (“moderately” to “very much improved”). However, our results and conclusions did not alter.

As a rule of thumb, multivariable logistic regression models should be used with a minimum of 10 outcome events (i.e., favorable outcome) per predictor variable.<sup>23</sup> In our study, events per variable ranged between 5.3 (model 1) and 7.4 (model 2 and 4). However, others consider this rule too conservative and conclude that this rule can be relaxed, based on the finding that model performance problems were uncommon with 5–9 events per variable.<sup>24</sup>

The generalizability of the predictive factors is limited by our study’s stringent inclusion and exclusion criteria. The population under study included patients with moderate to severe FI complaints, who were unresponsive to medical or dietary measures. The predictive factors need further exploration for use in other FI patients not represented in this study.

Candidate predictors from the medical history and physical examination were obtained by one physician by means of a standardized case report form, however some of the measures lack a validated assessment such as stool consistency (Bristol Stool Scale) or constipation (Rome III Diagnostic Criteria).

To our knowledge, embarrassment as a predictive factor has never been studied before. Less embarrassment (subscale of the FIQL) was associated with a favorable outcome of physiotherapy treatment. It is possible that compliance, motivation, cooperation, and expectations from patients who are less embarrassed are different, and this may have influenced treatment outcome. Since the degree of embarrassment was not related to the time since the onset of symptoms (Pearson  $r = -0.05$ ,  $P = 0.69$ ), the association was not explained by patients seeking help at an earlier stage and the prevention of symptom worsening. Degree of embarrassment was also not related to the severity of FI symptoms (Vaizey score) prior to physiotherapy treatment (Pearson  $r = 0.09$ ,  $P = 0.42$ ), so a favorable outcome of physiotherapy treatment for less embarrassed patients is unlikely to be explained by mild symptoms.

The use of constipating medication was associated with favorable outcome of physiotherapy treatment. We recently determined that the use of constipating medication showed poor responsiveness following physiotherapy treatment.<sup>16</sup> This may indicate that the use of constipating medication is associated with a patient’s self-confidence and a more favorable coping strategy, rather than with symptom severity.

The variable “any obstetric factor” appeared to predict a favorable outcome, although this factor may be prone to recall bias (patient’s report). Obstetric factors included high birth weight, episiotomy, instrumental delivery, prolonged second stage of labor, and breech delivery. These factors may result in perineal, anal sphincter, or nerve damage. Patients with one or more obstetric factors (55.6%) seem to have the potential to benefit from physiotherapy treatment, which is a promising finding in view of the large group of patients having obstetric factors. Rupture after vaginal delivery was not included in the “any obstetric factor” predictive factor, as there was a high prevalence in our patient group (66.7%). This factor was found to have a favorable but non-significant association with treatment outcome in univariable analysis. This is in agreement with previous studies,<sup>7,21,22,25,26</sup> although others found that biofeedback was most beneficial in patients with structurally intact sphincter muscles.<sup>27</sup> Unfortunately, we were unable to differentiate between degrees of rupture, which hampered our interpretation for patients with severe ruptures. As third- and fourth-degree ruptures are an important etiological factor

for postpartum FI,<sup>28</sup> knowing whether these patients will benefit from physiotherapy treatment is of great interest.

In contrast to other studies,<sup>7,21,26</sup> longer time since onset of symptoms was associated with an unfavorable outcome of physiotherapy treatment. This may be explained by the prior ineffective attempts to treat the disorder, like failure of medication and/or dietary adaptations as defined by our inclusion criteria, resulting in decreased motivation and possibly poor outcome. Symptoms may also worsen if patients seek help only after years.

We did not find an association between demographics (age or gender) and outcome, whereas one study found that treatment success was more likely in women,<sup>15</sup> and a few studies have reported a positive association between favorable treatment outcome and older age.<sup>15,21,22</sup> In line with most studies, we found that the physiological variables obtained from anorectal functional tests had no predictive value.<sup>21,26,29</sup> Nevertheless, a few studies reported better outcomes for patients with a higher squeeze pressure<sup>7,26</sup> and lower rectal sensory thresholds.<sup>29</sup> Hence, our results add evidence to the belief that test results may be proxy measures of symptoms, but at the same time attempt to explain the underlying pathophysiology of FI.<sup>7</sup> Interpretation of the association between physiological variables and favorable treatment outcome is further impeded by the substantial variation in test protocols.

We did not find an association between the severity of symptoms and outcome of physiotherapy treatment, as was reported by other authors,<sup>21,22,25,29</sup> although some reported an association between good clinical response and mild symptomatology<sup>7,26</sup> or severe symptomatology.<sup>15</sup>

In addition to the predictive factors found in our study, agreement exists on several factors that seem to influence the outcome of physiotherapy treatment, such as patient-therapist interaction<sup>22</sup> and patient motivation.<sup>4</sup> Patients with severe neurological deficits, substantial co-morbidity or cognitive impairments are unlikely to benefit from physiotherapy treatment.<sup>30</sup>

## CONCLUSIONS

Identifying patients who are likely to benefit most from physiotherapy is crucial for clinical practice. Our study provides a small subset of factors that independently predict favorable outcome of physiotherapy treatment in patients with moderate to severe FI. Moreover, we considered various predictive factors that have never been considered before. These predictors may be relevant in patient counseling and targeting physiotherapy treatment more efficiently, especially as they are available early in the diagnostic process. However, careful interpretation of the results is warranted due to the small sample size, use of multiple imputation and marginally statistically significant predictors. Future research is warranted to find out if selecting patients for physiotherapy treatment based on the predictors found in this study may result in better outcomes. In addition, more studies are needed to confirm these predictors in other settings and in patients not represented in this study, such as mild symptomatology.

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