Nutritional status in nocturnal hemodialysis
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Publication date:
2016

Citation for published version (APA):

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A difference between day and night: protein intake improves after the transition from conventional to frequent nocturnal home hemodialysis

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Ralf Westerhuis
Ellen M. Duym
Casper F.M. Franssen

Abstract

Background: Malnutrition is an important cause of the excessive morbidity and mortality rate of dialysis patients. Frequent Nocturnal Home Hemodialysis (NHHD) has many benefits compared with conventional thrice-weekly hemodialysis (CHD), due to the virtual absence of dietary restrictions and a much higher overall dialysis efficiency. In this observational study, we investigated whether these benefits of NHHD translate into an improved nutritional intake, with a special emphasis on protein intake.

Methods: We prospectively assessed the effect of the transition of CHD to NHHD on nutritional intake (5-day dietary intake journal), normalized protein catabolic rate, and anthropometric parameters in 15 consecutive patients who started NHHD in our center between 2004 and 2009 and completed at least 8 months of follow-up. Data were collected before the transition from CHD to NHHD and 4 and 8 months after the transition.

Results: Protein intake, as measured by both dietary intake journal and normalized protein catabolic rate, increased significantly after the transition from CHD to NHHD. Accordingly, phosphate intake increased significantly; however, serum phosphate levels did not increase, despite negligible phosphate binder use during NHHD. Body mass index and upper arm muscle circumference did not change significantly.

Conclusion: The transition from CHD to NHHD has a positive effect on nutritional intake, in particular, protein intake. NHHD should be considered in malnourished patients on CHD.
Introduction

Malnutrition is one of the most important causes of the increased morbidity and mortality rate of dialysis patients\textsuperscript{1,2}. It is evidenced by a loss in fat mass as well as in fat-free mass\textsuperscript{3,4}. There are multiple causes of malnutrition, but a loss of appetite and a reduced nutritional intake play an important role\textsuperscript{2,3,5,6}. Dietary advice for protein and energy intake is established at 1.1 g/kg ideal body weight (IBW)/day and 30 to 40 kcal/kg IBW/day, respectively\textsuperscript{4}. However, in clinical practice, these advices are difficult to achieve, and many dialysis patients who are prescribed a high-protein diet have only modest increases in actual protein intake\textsuperscript{7}.

The transition from conventional hemodialysis (CHD) to frequent nocturnal home hemodialysis (NHHD) may have potential benefits with regard to nutrition. Patients on NHHD have virtually no dietary or fluid restrictions, use almost no medication to regulate phosphate levels, and experience an improvement of the quality of life\textsuperscript{8-11}. Some studies have suggested that the nutritional status might improve after the transition from CHD to NHHD\textsuperscript{9,11,12}. However, at the time of the start of this study, the effect of the transition from CHD to NHHD on nutritional status had not been studied in detail. Therefore, we performed this observational study to investigate whether the transition from CHD to NHHD is associated with a change in nutritional intake, with a special emphasis on protein intake.

Patients and methods

Study design and participants

We prospectively assessed the effect of the transition of CHD to NHHD on nutritional intake, biochemical results, and anthropometric parameters in 15 consecutive patients who started NHHD in our center between 2004 and 2009 and completed at least 8 months of follow-up. Data were collected before and 4 and 8 months after the transition from CHD to NHHD. Exclusion criteria were absence of informed consent and short life expectancy.

For all participants, we collected demographic data at the start of NHHD, the primary renal disease (according to codes of the European Renal Association-European Dialysis and Transplantation Association), dialysis vintage, and previous renal replacement therapy. The study was performed in accordance with the principles of the Declaration of Helsinki and Guidelines for Good Clinical Practice. Informed consent was obtained from all patients.
Dialysis regimen
The dialysis treatment of CHD patients consisted of 3 times a week 4 to 5 hours of hemodialysis (2 needles). The dialysis scheme during NHHD consisted of 5 or 6 nights a week 8 hours of hemodialysis during the night (1 needle). During both CHD and NHHD, low-flux polysulphon dialysers were used and low-molecular-weight heparin was used as anticoagulant. Dry weight was evaluated clinically (peripheral edema, signs of pulmonary congestion, intra- and interdialytic blood pressure course, muscle cramps in combination with the cardiothoracic ratio (CTR) on chest X-ray) by the nephrologist.

Dietary consultation
During both the CHD and the NHHD period, patients had regular contact with the dietician every 4 to 6 weeks. During these visits, the nutritional status was evaluated and changes in weight, laboratory results, and appetite were monitored. Before the start of NHHD, patients received additional information on the diet after the transition to NHHD. The advice on energy and protein intake was unchanged: 30 to 40 kcal/kg IBW/day for energy and 1.1 g/kg IBW/day for protein. Sodium restriction was unchanged at 2,000 to 2,300 mg sodium. The potassium restriction was stopped after the transition to NHHD. Use of phosphate binders was discontinued by the nephrologist at the day of the transition to NHHD. The advice on fluid intake was less strict after the transition to NHHD, and we advised the patients to ultrafiltrate their daily fluid intake during the dialysis session.

Nutritional intake
Patients were asked to fill out a 5-day food diary. The diary had to include at least one weekend day. The diaries were filled out on regular days only, that is, not during holidays or during disease periods. Nutritional items were written down as part of domestic measures, for example, 1 cup of coffee (125 mL) or 2 slices of bread brown/white/wholemeal. The diaries were used to calculate energy, macronutrient (protein, fat, carbohydrates), and dialysis-related micronutrient (sodium, potassium, phosphate) content using a food measurement program based on the Dutch food table (Nederlands Voedingsstoffenbestand).

Biochemical measurement
Equilibrated Kt/V was calculated from pre- and postdialysis plasma urea concentration, using the Daugirdas second-generation logarithmic equation. In this formula, K denotes dialyzer clearance of urea, t denotes dialysis time, an V denotes volume of distribution of urea. The protein catabolic rate (PCR) and the normalized protein catabolic rate (nPCR) were calculated from the increase in urea plasma concentration during the interdialytic interval.

In the nutritional diary week, we measured predialysis plasma levels of urea, sodium, potassium, calcium, phosphate, albumin, total cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, and hemoglobin. To
interpret (changes in) plasma phosphate and cholesterol levels and hemoglobin concentrations, we also recorded the use of phosphate binders (type and dose) and the dose of erythropoiesis-stimulating agents (ESA).

**Anthropometric measurements**

Body mass index (BMI) was calculated as follows: post-dialysis weight (kg)/length (m)$^2$. The interdialytic weight change during CHD and NHHD was measured during the same week as the 5-day food diary was recorded by the patient and normalized to the weight gain per 24 hours. The mid-upper arm muscle circumference was measured according to previously published data$^{15,16}$ at the first dialysis session in the diary week. At baseline and at 8 months of NHHD, a standing chest X-ray was performed for the measurement of the CTR as an estimate of (the change in) hydration status. These measurements were done by one of the authors (C.F.M.F.) who was blinded to the order of the chest X-rays.

**Statistical analysis**

All data were analyzed using SPSS 16.0 for Windows (IBM Corp, New York, NY). Data are presented as mean (SD), unless otherwise stated. A repeated-measures analysis with post-hoc Bonferroni adjustments for multiple comparisons was conducted to assess differences between baseline (0 months) and 4 and 8 months after the transition to NHHD. If sphericity could not be assumed, Greenhouse-Geisser analyses were used. A paired Student $t$ test was used to compare CTR at baseline (0 months) and at 8 months of NHHD. Correlations were assessed by the Pearson correlation coefficient. A significance level of 0.05 was used for all analyses.

**Results**

**Patient characteristics**

Between April 2004 and September 2009, 23 patients started NHHD in our center, and all agreed to participate in the study. A total of 7 patients did not complete the 8 months of follow-up on NHHD because of renal transplantation (n=3), intercurrent illness (n=3), or death (n=1). One other patient was excluded because of participation in a weight loss program after gaining 5 kg (to a BMI of 38.5 kg/m$^2$) within the first 5 months after the transition from CHD to NHHD. The study population for this study consisted of 15 patients. Table 1 summarizes the characteristics of these patients at the time of the transition from CHD to NHHD.
Table 1. **Demographic characteristics at the time of transition from CHD to NHHD.**

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Male/Female)</td>
<td>11/ 4</td>
</tr>
<tr>
<td>Age (years), mean (range)</td>
<td>53.4 (28-71)</td>
</tr>
<tr>
<td>Dialysis vintage (years), mean (range)</td>
<td>4 (1-11)</td>
</tr>
<tr>
<td>Previous peritoneal dialysis, nr of patients (%)</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Previous renal transplantation, nr of patients (%)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Primary renal disease, nr of patients (%)</td>
<td></td>
</tr>
<tr>
<td>Adult polycystic kidney disease</td>
<td>5 (33)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>4 (27)</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Primary hyperoxaluria type 1</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Nephrosclerosis</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Chronic renal failure, etiology unknown</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>none</td>
</tr>
</tbody>
</table>

**Nutritional intake**

Table 2 shows the results of the 5-day food intake diaries. Energy intake showed a non-significant increasing trend. Protein intake increased significantly from baseline to 4 months of NHHD. The individual change in protein intake is shown in Figure 1. The change in protein intake varied between patients, but most patients showed an increase in protein intake. Carbohydrate intake was stable over time and fat intake increased non-significantly (Table 2). Sodium intake did not change, but potassium and phosphate intake increased significantly after the transition from CHD to NHHD. At the same time, the daily doses of phosphate binders decreased significantly (P=0.003) from baseline (5.1±5.6 tablets) to 4 months (0.1±0.5 tablets), and to 8 months (0.3±1.3 tablets). Phosphate supplementation during hemodialysis was needed in 8 of the 15 patients while on NHHD.
Table 2. Nutritional intake calculated from the 5-day food diaries.

<table>
<thead>
<tr>
<th>N=15</th>
<th>Baseline CHD</th>
<th>4 months NHHD</th>
<th>8 months NHHD</th>
<th>P*</th>
<th>Effect size (95% CI for difference with baseline CHD)(^5)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Energy (kcal)</strong></td>
<td>2003±287</td>
<td>2166±298</td>
<td>2183±388</td>
<td>0.088</td>
<td>0-4 months 0.2 - 22.8 g/day* 0-8 months -4.3 - 21.0 g/day</td>
</tr>
<tr>
<td><strong>Protein (g/day)</strong></td>
<td>80±11</td>
<td>92±19</td>
<td>89±19</td>
<td>0.023*</td>
<td>0-4 months 0-4 months 78.1 - 311.6 mg/day* 0-8 months -44.9 - 313.6 mg/day</td>
</tr>
<tr>
<td><strong>Carbohydrate (g/day)</strong></td>
<td>236±44</td>
<td>237±36</td>
<td>252±46</td>
<td>0.369</td>
<td>0-4 months 0-4 months 78.1 - 311.6 mg/day* 0-8 months -44.9 - 313.6 mg/day</td>
</tr>
<tr>
<td><strong>Fat (g/day)</strong></td>
<td>82±17</td>
<td>91±24</td>
<td>91±29</td>
<td>0.103</td>
<td>0-4 months 78.1 - 311.6 mg/day* 0-8 months -44.9 - 313.6 mg/day</td>
</tr>
<tr>
<td><strong>Sodium (mg/day)</strong></td>
<td>2799±633</td>
<td>3141±869</td>
<td>3066±601</td>
<td>0.136</td>
<td>0-4 months 0-4 months 78.1 - 311.6 mg/day* 0-8 months -44.9 - 313.6 mg/day</td>
</tr>
<tr>
<td><strong>Potassium (mg/day)</strong></td>
<td>2822±262</td>
<td>3241±525</td>
<td>3227±634</td>
<td>0.006*</td>
<td>0-4 months 0-4 months 78.1 - 311.6 mg/day* 0-8 months -44.9 - 313.6 mg/day</td>
</tr>
<tr>
<td><strong>Phosphate (mg/day)</strong></td>
<td>1401±182</td>
<td>1564±245</td>
<td>1536±299</td>
<td>0.012*</td>
<td>0-4 months 0-4 months 78.1 - 311.6 mg/day* 0-8 months -44.9 - 313.6 mg/day</td>
</tr>
</tbody>
</table>

Abbreviations: CI: confidence interval; CHD: Conventional Hemodialysis; NHHD: Nocturnal Home Hemodialysis. Mean±SD.

\(*\)Repeated measurements analysis comparing baseline CHD with 4 and 8 months of NHHD.

\(^5\)The effect size is shown only for parameters that changed significantly in the repeated measurements analysis.

\(^{*}\)P<0.05.
Biochemical results
As shown in Table 3, both PCR and nPCR increased significantly after conversion to NHHD. The individual change in PCR is shown in Figure 2. Although the change in PCR varied considerably between patients, PCR increased in the vast majority of patients. As expected, Kt/V increased significantly after the transition to NHHD. Likewise, predialysis urea plasma levels decreased significantly. As expected, we found a significant correlation between PCR and protein intake, as assessed by the 5-day food diaries (r=0.51, P=0.000).
### Table 3. Biochemical results.

<table>
<thead>
<tr>
<th>N=15</th>
<th>Baseline CHD</th>
<th>4 months NHHD</th>
<th>8 months NHHD</th>
<th>P*</th>
<th>Effect size (95% CI for difference with baseline CHD)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCR (g/day)</strong></td>
<td>80±27</td>
<td>94±22</td>
<td>96±20</td>
<td>0.001*</td>
<td>0-4 months (4.7 - 24.7 g/day)<em>&lt;br&gt;0-8 months (5.3 - 27.0 g/day)</em></td>
</tr>
<tr>
<td><strong>nPCR (g/kg/day)</strong></td>
<td>1.07±0.27</td>
<td>1.29±0.22</td>
<td>1.30±0.19</td>
<td>0.001*</td>
<td>0-4 months (0.04 - 0.4 g/kg/day)<em>&lt;br&gt;0-8 months (0.4 - 4.14 g/kg/day)</em></td>
</tr>
<tr>
<td><strong>Kt/V</strong></td>
<td>3.93±1.30</td>
<td>9.24±2.25</td>
<td>8.84±1.59</td>
<td>0.000*</td>
<td>0-4 months (3.8 - 6.8)<em>&lt;br&gt;0-8 months (3.5 - 6.3)</em></td>
</tr>
<tr>
<td><strong>Predialysis urea (mmol/l)</strong></td>
<td>24.5±4.4</td>
<td>11.1±3.3</td>
<td>13.3±3.8</td>
<td>0.000*</td>
<td>0-4 months (-17.4 - -9.4 mmol/l)<em>&lt;br&gt;0-8 months (-15.4 - -6.9 mmol/l)</em></td>
</tr>
<tr>
<td><strong>Sodium (mmol/l)</strong></td>
<td>139.3±3.1</td>
<td>139.6±2.6</td>
<td>139.7±3.2</td>
<td>0.919</td>
<td></td>
</tr>
<tr>
<td><strong>Potassium (mmol/l)</strong></td>
<td>5.16±0.78</td>
<td>4.93±0.34</td>
<td>5.32±0.67</td>
<td>0.113</td>
<td></td>
</tr>
<tr>
<td><strong>Calcium (mmol/l)</strong></td>
<td>2.47±0.19</td>
<td>2.49±0.15</td>
<td>2.48±0.11</td>
<td>0.911</td>
<td></td>
</tr>
<tr>
<td><strong>Phosphate (mmol/l)</strong></td>
<td>1.64±0.39</td>
<td>1.52±0.32</td>
<td>1.61±0.40</td>
<td>0.565</td>
<td></td>
</tr>
<tr>
<td><strong>PTH (pmol/l)</strong></td>
<td>34.0±31.6</td>
<td>25.3±27.2</td>
<td>33.7±48.0</td>
<td>0.358</td>
<td></td>
</tr>
<tr>
<td><strong>Albumin (g/l)</strong></td>
<td>38±4.0</td>
<td>40±3.4</td>
<td>40±4.1</td>
<td>0.232</td>
<td></td>
</tr>
<tr>
<td><strong>Cholesterol (mmol/l)</strong></td>
<td>3.4±0.95</td>
<td>4.4±0.91</td>
<td>4.0±0.28</td>
<td>0.050*</td>
<td>0-4 months (0.1 - 1.9 mmol/l)<em>&lt;br&gt;0-8 months (-0.2 - 1.3 mmol/l)</em></td>
</tr>
</tbody>
</table>

Abbreviations: CI: confidence interval; CHD: Conventional Hemodialysis; NHHD: Nocturnal Home Hemodialysis. Mean±SD.

*Repeated measurements analysis comparing baseline CHD with 4 and 8 months of NHHD.

*The effect size is shown only for parameters that changed significantly in the repeated measurements analysis. *P<0.05.
Plasma sodium, potassium, calcium, phosphate, albumin, and parathyroid hormone levels did not change during the observation period. Total cholesterol increased from baseline to 4 months. Because sevelamer has a cholesterol-lowering effect\textsuperscript{17,18}, we studied the correlation between plasma cholesterol levels and sevelamer dose. We found a negative correlation ($r=-0.302$) of borderline statistical significance ($P=0.052$).

Hemoglobin levels increased nonsignificantly ($P=0.336$) from baseline (7.4±0.68) to 4 months (7.7±0.83), and to 8 months (7.9±1.39). In contrast, at the same time, the weekly darbepoetin dose fell ($P=0.053$) from baseline (39.3±24.9) to 4 months (30.1±20.6), and to 8 months (27.1±20.2).

Figure 2. \textit{Individual change in PCR.}
Anthropometric measurements

As shown in Table 4, post-dialysis weight and BMI did not change significantly in the first 8 months after the transition to NHHD. The course of body weight showed considerable interindividual variation, as shown in Figure 3. The mid-upper arm muscle circumference did not change significantly (Table 4). The interdialytic weight change per 24 hours increased significantly from baseline to 8 months of NHHD. The CTR decreased significantly (P=0.042) from baseline (0.50±0.063) to 8 months of NHHD (0.48±0.064).

Table 4. Anthropometric measurements.

| N=15 | Baseline CHD | 4 months NHHD | 8 months NHHD | P* | Effect size (95% CI for difference with baseline CHD)  

<table>
<thead>
<tr>
<th></th>
<th>BMI</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Post-dialysis weight (kg)</td>
<td>83.4±16.8</td>
<td>83.6±17.1</td>
<td>84.8±17.8</td>
<td>0.183</td>
<td></td>
</tr>
<tr>
<td>MUAMC (cm)</td>
<td>27.0±4.2</td>
<td>27.4±4.4</td>
<td>27.4±4.1</td>
<td>0.392</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interdialytic weight change (kg/24h)</td>
<td>1.2±0.7</td>
<td>1.5±0.6</td>
<td>1.7±0.6</td>
<td>0.034*</td>
<td>0-4 months (-0.3 - 0.9 kg/24h)</td>
<td>0-8 months (0.02 - 1.1 kg/24h)</td>
</tr>
</tbody>
</table>

Abbreviations: CI: confidence interval; CHD: Conventional Hemodialysis; NHHD: Nocturnal Home Hemodialysis, MUAMC: mid upper arm muscle circumference. Mean±SD.

*Repeated measurements analysis comparing baseline CHD with 4 and 8 months of NHHD.

5The effect size is shown only for parameters that changed significantly in the repeated measurements analysis.

*P<0.05.
Figure 3. **Individual change in post-dialysis body weight.**
Discussion

This study shows that protein intake increases after the transition from CHD to NHHD. This was consistently shown by 5-day dietary journals and the nPCR. Other changes in nutritional intake included significant increases in potassium and phosphate intake and a nonsignificant increase in fat intake. The increase in protein intake was not accompanied by significant increases in postdialysis body weight, BMI, or upper arm circumference over an eight-month period.

Other studies have shown that it is difficult to increase the energy and protein intake in dialysis patients. Kloppenburg et al. found that prescribing a high-protein diet in patients on CHD resulted in only modest increases in actual protein intake. The patients who started NHHD in our center were mostly in a reasonable nutritional state. As we were aware of the preliminary results from another Dutch dialysis center, we advised our patients to monitor their food intake and try not to gain too much weight after the conversion to NHHD. We gave no explicit precautionary advices but informed our patients that appetite could improve after the transition to NHHD. Notably, the patients in that Dutch NHHD project gained, on average, 5 kg in the first year of NHHD. The increase in protein intake in that study was comparable with that in our study and even after 1 year after the conversion to NHHD, protein intake was higher compared with the CHD period. They found no significant increase in the nPCR of the whole group, but patients with a low nPCR (<1.0 g/kg/day) at baseline had a significant increase in nPCR at 1 year after the transition.

In a recent study of 12 patients, Schorr et al. found a modest, although not significant, increase in protein intake, assessed by 3-day dietary intake journal, during the first 6 months after the transition to NHHD. The increase in protein intake was not accompanied by a significant increase in body weight and BMI. This may be due to the relatively short observation period. Alternatively, changes in hydration status in the first months after the conversion from CHD to NHHD may have camouflaged increases in lean body mass. In other words, it is possible that in the first months after the conversion from CHD to NHHD, lean body mass increased, whereas post-dialysis weight did not increase, as a result of better extracellular volume control. The observation that the CTR decreased significantly during the first 8 months of NHHD suggests that this was indeed the case in our patients. Notably, the much higher total hemodialysis duration per week with NHHD enables a much better control of extracellular volume.

Patients on NHHD have almost no diet restrictions. The only restriction we advised our patients was sodium restriction, as it is useful for blood pressure regulation and is still advised after renal transplantation. In line with the increased protein intake, phosphate intake increased significantly. Plasma phosphate levels, however, did not rise, despite the discontinuation of phosphate binders in almost all patients, and 8 of the 15 patients even needed intravenous phosphate
supplementation during hemodialysis while on NHHD. It is possible that the cessation of phosphate binders improved appetite and food intake.

We found a nonsignificant increase in hemoglobin levels in this study, whereas at the same time the ESA dose decreased. Although this is not a uniform finding, a few other studies have documented reduced ESA dosages during NHHD in comparison with CHD\textsuperscript{21,22}. The higher hemoglobin level/ESA dose ratio may be explained by a lower concentration of uremic toxins as a result of a higher overall clearance with NHHD\textsuperscript{23}.

In this study, we used a 5-day food diary to measure food intake. Results from self-reported food intake should be interpreted with caution because of bias and imprecision, unless independent methods of assessing their validity are included\textsuperscript{24}. In our study, nPCR was the independent method that yielded identical results. We found a significant correlation between the nPCR and the protein intake, as measured by the 5-day dairy, indicating that the diaries were filled out adequately. In line with the results from other studies, the changes in protein intake measured with the diaries were lower than that by PCR. This is probably due to underestimation of dietary intake from self-reported food diaries, as has been previously been shown in another study in hemodialysis patients\textsuperscript{25}.

In conclusion, protein intake increased significantly in the first 4 months after the transition from CHD to NHHD. The improved protein intake was maintained during the remainder of the observation period from 4 months to 8 months after the transition. The transition to NHHD has a positive effect on the nutritional status of hemodialysis patients and should be considered in malnourished patients on CHD.

**Practical application**

This study may have important implications for clinical practice. Patients on CHD who are malnourished may benefit from the transition to frequent NHHD. Patients on frequent NHHD have almost no dietary restrictions, and this study showed that protein intake and nPCR increase significantly.

**Acknowledgements**

Dialysis nurses, dieticians, and nephrologists of the Dialysis Center Groningen are greatly acknowledged for their help in data collection. The authors also thank Wim Krijnen for the assistance in the statistical analyses.
References