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Somatic outcome among patients hospitalised for Anorexia Nervosa in adolescence: disorders reported and links with global outcome

- Somatic outcome for Anorexia Nervosa

Hélène Roux^{1, 2}, Corinne Blanchet³, Chantal Stheneur^{2,4}, Emeline Chapelon⁵, Nathalie Godart^{1,2}

¹ Department of Psychiatry, Institut Mutualiste Montsouris, Paris, France ; School of Medicine, Paris Descartes University;

² INSERM U669, Paris Descartes University, Paris Sud

³ Maison de Solenn-Maison des Adolescents, Cochin Paris

⁴ Department of Pediatrics, Hospital Ambroise Paré, Paris, France

⁵ Department of Pediatrics, Hospital Victor Dupouy, Argenteuil, France

Institut Mutualiste Montsouris

42 boulevard Jourdan

75014 Paris France

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MD Nathalie Godart

Responsable de l'unité d'hospitalisation

Service de psychiatrie de l'adolescent du Pr Corcos

Institut Mutualiste Montsouris

42, Boulevard Jourdan

75014 Paris

tel: 01 56 61 69 35/29

fax: 01 56 61 69 34

nathalie.godart@imm.fr

Abstract

Aims: 1) to describe the frequency of somatic pathologies and depression among former Anorexia Nervosa patients, 2) to study links with subjects' clinical history and global outcomes.

Methods: 97 women hospitalised for Anorexia Nervosa during adolescence, 9.00 ± 1.92 years previously, were interviewed using structured questionnaires concerning somatic and psychiatric disorders that they had experienced.

Results: Iron deficiency, migraine, cystitis, upper digestive system disorders, fractures, osteoporosis, and dental problems were reported with a frequency greater than 20%. Depression was reported by 2/3 of the sample. Osteoporosis was 14 times more frequent in case of vitamin D deficiency. Fractures were three times more frequent in presence of osteoporosis and less frequent when the overall outcome was better.

Conclusion: Among women who had Anorexia Nervosa in adolescence, somatic comorbidities are frequent in adulthood. They are linked to the severity and the duration of Anorexia Nervosa, and to the overall outcome of the subject.

Introduction

Anorexia Nervosa (AN) involves considerable morbidity (1) and mortality (2) (AN).

The most severely ill patients require hospitalisation on account of immediately life-threatening states, or the fact that the disturbances have become chronic (3, 4). In care facility itineraries this selects the thinnest patients and those with the poorest prognosis (5), as well as patients more frequently presenting comorbid psychiatric disorders (6).

Outcome studies following up AN in adolescence (1) have most often focused on overall outcome indicators such as the Morgan-Russell score (7), which associates different groups of symptom – eating patterns, body image perceptions, evolution in weight, return of menstruation, mental state, and social involvement or via the return to normal of one of these core symptoms that are characteristic of AN, or via psychiatric diagnoses other than eating disorders (EDs) . Overall they conclude that only 47% of adolescents who receive care for AN are cured 4 to 10 years later (1).

There are very few studies that report outcomes in terms of global somatic condition. Those studies that do have often focused on one particular aspect, such as osteoporosis (8), fractures (9) or fertility (10). To our knowledge, few follow-up studies have provided information on general somatic outcome (11, 12), none has looked for risk factors for somatic complications in general, and none has linked global outcome or mental outcome and somatic problems.

For this reason, within the scope of an outcome study, we explored the somatic problems experienced in their lifetime by subjects hospitalised for AN in adolescence. In addition, we sought to study the link between these somatic complaints, the clinical history of the subjects' AN, and global outcome in adulthood.

Participants and methods

Participants (see figure 1) are 199 consecutive patients with DSM-IV criteria for AN, hospitalised in the psychiatric department in the Institut Mutuliste Montsouris (Pr. Jeammet), Paris, France from April 1996 to May 2004 (13-15). The moment of inclusion in the study (which is the start of follow-up) was defined as the first admission to the unit in that period. Six subjects who did not comply with these criteria were removed from the study, as were 13 men on account of their small number. Among the 180 women in the remaining sample, 146 were re-contacted (81.1%) for follow-up: 105 agreed to take part in the study, 37 refused, and

34 were lost to follow-up but were alive, and four had died. Exclusion criteria were patient refusal, inability to read or understand French or to complete forms and questionnaires.

Procedures

This work was approved in 2007 by the French *Direction Générale de la Santé* the French national committee for private freedoms. Written consent was completed by the subject and her parents for the outcome evaluations. .

At the start of inpatient treatment a structured chart collecting socio-demographic and clinical information is completed. This systematic questionnaire was set up in 1996 (16).

Follow-up assessment

Subjects were assessed 6 to 12 years after the end of their first hospitalisation. This evaluation was performed by structured interview with a clinician and a self-administered questionnaire. Morgan and Russell's Global Outcome Assessment Scale (GOAS) (7) was used to assess clinical status over the previous six months, across 5 sub-scales exploring eating and diet, menstruation, mental state, psycho-sexual functioning, and socio-economic status. The score varies from 0 (doing very badly) to 12 (doing very well). Outcome was defined as "good" for a score of ≥ 9 , "intermediate" outcome was recorded for a score of 6-8, and "poor" outcome was recorded for a score under 6.

The somatic questionnaire was specifically designed for the study. The pathologies that the researcher was to look for were as follows (for details see table 2): 1) cardio-vascular disorders; 2) deficiencies; 3) skin disorders; 4) digestive disorders; 5) endocrine disturbances; 6) neurological disturbances; 7) respiratory disorders; 8) rheumatological disorders; 9) urological diseases; 10) gynaecological other than those relating to procreation. In addition, for each type of pathology, the subject was asked if she had experienced other problems than those reported (shown under the heading "other" in table 1). All this data was self-reported.

For the diagnosis of depression (at least one lifetime depressive episode) a module from a structured diagnostic interview were used: the Mini International Neuropsychiatric Interview (MINI) validated in French (17). Version 4.1 of the MINI assesses DSM-IV Axis 1 psychiatric diagnosis criteria in standardised manner (3). All assessors in the study received training in MINI administration.

Statistical analyses

Analyses were performed under SPSS 17.0. All the somatic disturbances reported were described in terms of frequencies and numbers. Certain categories of disorders were grouped. For instance gastro-duodenal ulcers, gastritis and oesophagitis were grouped under the heading "upper digestive tract disorders". Likewise pressure sores and skin ulcers were considered conjointly.

Univariate analyses

Subjects lost to follow-up (n=75) were compared to subjects assessed in follow-up for inclusion data (χ^2 for qualitative data and Student's t-test for quantitative data).

We then sought clinical or prognostic factors associated with the presence of somatic complains. We first of all used univariate analyses to test these links. Proportions were compared using χ^2 or Fisher's exact test, depending on sample size (18). Means were compared using Student's t-test (for variables with a normal distribution) or the Mann-Whitney test.

We looked for links between the most frequently observed somatic problems (frequency of around 20%) and the following: the clinical characteristics of these former AN patients reflecting the clinical history and evolution of their AN, including elements classically described as prognostic factors for AN outcome (minimum lifetime BMI, age at onset of AN, pre-menarcheal anorexia) (1) and initial clinical factors that were potentially implicated for the most severe cases (duration of amenorrhoea at admission, initial and follow-up duration of anorexia, length of first hospitalisation, history of depression in follow-up, history of bulimic episodes).

We also tested the link between vitamin D deficiency and osteoporosis (19), that between osteoporosis and the presence of fractures (20, 21), and that described between osteoporosis and a history of antidepressant treatment (22).

Finally, we studied the link between global outcome of the subjects (scores on the Morgan and Russell scale), the most frequently observed somatic disorders (frequency close to 20%, see above) and the duration of the evolution of the ED.

All of these statistical tests were two-sided, the level of significance was $\alpha = 0.05$. No adjustments for multiple testing were made (23).

Multivariate analyses

A forward stepwise logistic regression was then performed on the qualitative variables (somatic disorders with a frequency around 20%). Explanatory variables initially introduced in the regressions were selected from data from the literature and clinical pertinence (according to the present authors) that had a statistical significance (at the $p < 0.05$ level)—in the univariate tests comparing their value as a function of the variable to be explained (somatic disorder in two categories: present or absent).

The relationship between global outcome (Morgan and Russell score) and possible predictors (somatic disorders that were statistically significant at $p < 0.05$ in univariate analyses) was tested using stepwise multiple linear regression, adjusting for the duration of the disease.

Results

Sample representativeness: comparison of subjects assessed with the other subjects

No significant difference was evidenced on the different variables recorded at the time of hospitalisation in adolescence between the 180 subjects hospitalised and the 97 subjects assessed in the outcome study. Consequently, we can consider that the outcome sample was representative of the initial sample (see table 1).

Table n°1: Description of the initial sample and the outcome sample

Outcome study (follow-up of 97 young women)

Global outcome

The mean global outcome was "intermediate" (GOAS 8.44 ± 1.66). Among them, 45.4% ($n=44$) had a "good" outcome, 44.3% ($n=43$) an "intermediate" outcome, and 9.3% ($n=9$) a "poor" outcome. Their current BMI, with a mean of $19.38 \pm 2.71 \text{ kg/m}^2$, ranged widely from extreme thinness (10.94 kg/m^2) to overweight (27.01 kg/m^2). In 26.8% of cases ($n=26$) the subjects still presented amenorrhoea, among whom 5 presented primary amenorrhoea.

Somatic outcome

The somatic history of the 97 patients for whom follow-up was obtained is detailed in table 2.

Table n°2 : Description of somatic disorders

Iron deficiency for almost half the subjects and migraines for almost one third, cystitis and problems affecting the upper digestive tract (gastro-duodenal ulcers, gastritis, oesophagitis) were observed.

Almost one third of the subjects had at least one fracture in their lifetime; 18.5% (n=18) reported just one, 8.2% (n=8) reported two and 4.1% (n=4) reported three. These fractures were mostly located on the upper limbs (31/34: arm, fingers, wrist) and the rest on the lower limbs (10/46: ankle, tibia, foot, hip); there was also collar bone (n=1), ribs (n=1), pelvis (n=2) and skull (n=1).

In this population around one quarter of the subjects reported osteoporosis and dental problems.

Further to this the following problems were reported: allergies (n=3), and one case for each of the following: astigmatism, short sight, blindness in the left eye, strabismus, feverish convulsions, factor V Leiden deficiency, eardrum graft, cyst in the wrist, glandular fever, Osgood Schlatter disease, urethro-vesical reflux, heterozygote thalassaemia, and potomania.

Psychiatric outcome

There was a lifetime diagnosis of major depression for two thirds of the subjects.

Univariate analyses

The link between clinical history and somatic history

In presence of osteoporosis, mean minimum lifetime BMI values were significantly lower than when it was not present ($12.61 \pm 1.35 \text{ kg/m}^2$ vs 13.28 ± 1.08 , $p=0.022$), vitamin D deficiency was more frequent (66.7% vs 33.3%, $p=0.0002$), duration of AN was longer (5.70 ± 4.71 yrs vs 2.60 ± 2.38 , $p=0.007$), and the total number of hospitalisations (4.14 ± 2.51 vs

2.53±2.30, $p=0.006$); however depression tended to be less frequent (17.5% vs 82.5%, $p=0.061$).

In case of a history of fracture, osteoporosis was more frequently reported (54.5% vs 45.5%, $p=0.005$, and the total number of hospitalisations was greater (3.9 ± 3.5 vs 2.5 ± 1.7 , $p=0.042$).

In case of upper digestive tract disorders, the number of hospitalisations was likely to be greater (4.18 ± 3.63 vs 2.65 ± 2.04 , $p=0.019$).

Migraine was linked to lower lifetime occurrence of bulimia (45.5% vs 54.5%, $p=0.009$).

The presence of dental problems was linked to a larger number of hospitalisations (3.80 ± 3.36 vs 2.64 ± 1.97 , $p=0.043$).

The occurrence of sores or ulcers was linked to minimum lifetime BMI (12.60 ± 1.33 vs 13.27 ± 1.08 , $p=0.029$), to longer duration of the initial hospitalisation (5.49 ± 3.48 months vs 3.85 ± 2.55 months, $p=0.025$), and to a larger number of hospitalisations (3.89 ± 3.36 vs 2.62 ± 2.02 , $p=0.040$).

The occurrence of cardiac arrhythmia was associated with more numerous hospitalisations (4.47 ± 3.34 vs 2.55 ± 1.99 , $p=0.002$).

The persistence of amenorrhoea was linked to lower lifetime BMI (12.60 ± 1.16 kg/m² vs 13.33 ± 1.11 , $p=0.005$), to greater frequency of pre-menarcheal AN (55.6% vs 44.4%, $p=0.041$), to a larger number of hospitalisations (4.04 ± 3.50 vs 2.52 ± 1.74 , $p=0.043$), to longer AN duration (5.14 ± 4.81 yrs vs 2.74 ± 2.51 , $p=0.022$) and to a trend towards earlier age at AN onset (14.44 ± 2.15 yrs vs 15.37 ± 2.07 , $p=0.055$).

Cystitis and eczema were not linked to any factor.

Links between global outcome, somatic history and AN clinical history

Poorer global outcome was significantly linked to a history of osteoporosis (7.82 ± 1.65 vs 8.70 ± 1.60 , $p<0.001$), to a history of fractures (7.54 ± 2.02 vs 8.74 ± 1.42 , $p=0.016$) and to longer AN duration ($r=-0.452$, $p<0.0001$).

Greater weight concerns were linked to cardiac arrhythmia (3.80 ± 4.29 vs 6.48 ± 3.69 , $p=0.007$), to fractures (3.93 ± 3.61 vs 6.82 ± 3.77 , $p=0.001$), and to longer duration of AN ($r=-0.327$, $p=0.001$).

Poorer mental state was linked to bulimic episodes (7.86 ± 3.08 vs 9.32 ± 2.23 , $p=0.011$), to migraines (7.83 ± 2.46 vs 9.05 ± 2.79 , $p=0.042$) and to fractures (7.79 ± 2.96 vs 9.02 ± 2.57 , $p=0.041$). There was also a trend towards poorer mental status in case of osteoporosis (7.63 ± 2.64 vs 8.93 ± 2.64 , $p=0.053$) and in case of upper digestive tract disorders (7.59 ± 2.81 vs 8.99 ± 2.64 , $p=0.053$).

Poorer psycho-sexual functioning was linked to osteoporosis (8.72 ± 3.07 vs 10.57 ± 1.65 , $p=0.012$), amenorrhoea (8.62 ± 2.94 vs 10.65 ± 1.62 , $p=0.002$) and longer duration of AN ($r=-0.561$, $p<0.0001$).

Finally, poorer socio-economic function was linked to amenorrhoea (8.60 ± 1.90 vs 9.65 ± 1.71 , $p=0.011$) and longer duration of AN ($r=-0.211$, $p=0.037$).

Depression was not linked to either somatic disorders or outcome.

Multivariate analyses

The link between AN clinical history and somatic history

The risk of osteoporosis was 14 times greater ($p<0.0001$) for subjects having experienced vitamin D deficiency, independently from minimum lifetime BMI, total duration of AN and number of hospitalisations.

The risk of fracture was three times greater in case of osteoporosis ($p=0.038$) and this risk tended to increase with the number of hospitalisation ($p=0.056$).

The risk of skin ulcers or pressure sores was proportionally greater in relation to the duration of the initial hospitalisation ($p=0.039$) and tended to increase in case of low lifetime BMI ($p=0.058$) independently from the total number of hospitalisations.

The persistence of amenorrhoea was proportionally more frequent in relation to longer AN duration ($p=0.048$) independently from premenarcheal AN status, minimum lifetime BMI and number of hospitalisations.

Links between global outcome and somatic history

Better global outcome was linked to fewer fractures ($\beta=-0.219$, $p=0.016$) independently from AN duration ($p<0.0001$). However no link was found with osteoporosis ($\beta=-0.158$, $p=0.121$).

Weight concerns were more likely in presence of fractures ($\beta=-0.320$, $p=0.001$) and cardiac arrhythmia ($\beta=-0.268$, $p=0.005$) independently from AN duration ($p=0.001$).

Mental state was likely to be poorer in case of bulimia ($\beta=-0.263$, $p=0.009$), fractures ($\beta=-0.201$, $p=0.048$) and migraine ($\beta=-0.207$, $p=0.041$), independently from AN duration for all these sub-scores ($p<0.2$).

Psycho-sexual functioning was likely to be less good in case of current amenorrhoea ($\beta=0.252$, $p=0.004$) and longer AN duration ($p<0.001$).

Finally, poorer socio-economic functioning was linked to current amenorrhoea ($\beta=0.208$, $p=0.048$) independently from AN duration ($p=0.124$).

Discussion

In this sample of past adolescence AN subjects 6 and 12 years after discharge from hospital, somatic comorbidities were however frequent, with 70% reporting at least one lifetime somatic problem. Psychiatric comorbidities were likewise very frequent, with 67% of the subjects reporting at least one lifetime major depressive episode.

Among these subjects, iron deficiency was frequently reported (45%). This deficiency is also frequent in the general population. However it does appear particularly frequent in our sample, in comparison with a percentage of 19.3% reported among women students aged 21.4 yrs (2.4) (24).

In this study, the prevalence of migraine was over 30%. Among American women aged 18 to 29, prevalence assessed from self-report was estimated to be 20.4% (25, 26). An increase of the frequency of migraine in ED has been suggested (25), but is still in debate (27).

The prevalence of osteoporosis was 25% in our sample in which the mean age was 25.53 yrs (2.96). This is close to the frequency observed in a comparable clinical sample (21.24%) of young French anorexic women followed in psychiatric unit, aged 25 ± 8 yrs, who were assessed using osteodensitometry (28). It is however far higher than the expected prevalence for this age group, which is 1% (29).

The prevalence of fractures was high, with half of our population reporting fractures. This type of event reaches 30% in the general population among young subjects (15 ± 4.2 yrs) (30). It is not possible from our data to distinguish between traumatic origin and osteoporotic origin. The prevalence may also have been underestimated in the absence of systematic radiography of the rachis, since vertebral collapse can be virtually non-symptomatic. Our results suggest however that the underlying brittleness of bone is not the sole determinant of fractures, since established osteoporosis was not observed to be more frequent among subjects reporting fractures. It is possible that the frequency of fractures could be explained by more frequent falls (not studied here) in the course of risk-related behaviours. However it is also possible that osteoporosis had not been assessed by osteodensitometry in all patients, which led to it being underestimated.

We found certain expected associations between two parameters and report of osteoporosis: low BMI and AN duration, which probably reflect the damaging effects on bone of nutritional and hormone deficiencies. But according to our multivariate analysis, it is vitamin D deficiency, independently from minimum lifetime BMI, total AN duration and number of hospitalisations, that is the strongest explicative factor for osteoporosis. Vitamin D deficiency probably reflects poor overall health status, as suggested in other studies on chronic diseases (31). This deficiency has well-established negative effects on bone tissue and muscle function (19), and can therefore have an effect on the overall musculo-skeletal condition of these patients. The treatment of this deficiency is worth evaluating in the setting of the appropriate care strategies for AN complications.

Our results require confirmation by studies providing for systematic evaluation of the status of bone mass by osteodensitometry, and vitamin D titration, among AN patients. Present recommendations are in favour of vitamin D supplementation, although its impact is not known (3).

Gastro-oesophageal reflux (22%) did not appear more frequent in our sample than in the general population, where the pathology is common: 10% of the population have the symptom frequently, and 38% report it occasionally (32).

The cardiac arrhythmia reported (20%) is probably nutrition-related bradycardia, observed in cases of severe denutrition (33).

In the study sample, pressure sore and skin ulcers were reported by more than 20%, and this probably reflects their nutritional state. These conditions are rare among young subjects. Lifetime prevalence of pressure sores and skin ulcers reported in the literature for hospitalised patients is 8.6% in France for a population with a mean age of 74 yrs. For leg ulcers, the prevalence in the general population is 1%, and 3% among the over 65s (34). The occurrence of pressure sores is often linked to being bed-ridden for long periods and/or to poor nutritional status (35). This was conformed in our sample, since the risk of ulcers or sores was proportionally greater where initial hospitalisation was long, and in case of low lifetime BMI, independently from the total number of hospitalisations.

Eczema affected 20% of our sample compared to under 10% in the general population (36),.

A less favourable global outcome among subjects who have suffered from AN in adolescence was associated with more frequent fractures, independently from AN duration.

Mental state was likely to be poorer among subjects reporting episodes of bulimia during their illness, independently from its duration. This observation confirms earlier findings that linked the occurrence of bulimia to a less favourable outcome among anorexic subjects (1), and greater suicide risk (37). It is interesting to note that poorer mental state was associated with greater risk of fractures and migraine.

Psycho-sexual functioning was likely to be not as good in case of current amenorrhoea which is associated with lower BMI. The existence of multifactorial sexual dysfunction among ED subjects has been reported in the literature (38). (39). Somatic and neuro-hormonal factors (gonadotrope dysfunction, neurotransmitter modifications, physical sequelae of AN etc) and psychosocial factors inherent in the ED (depression, social isolation) are certainly closely interwoven.

Finally, socio-economic functioning was likely to be poorer in case of current amenorrhoea, which is linked to longer AN duration, and more marked withdrawal from the social sphere.

The main limitation of this study is that the data used is derived from self-report, and that it is not based on any medical assessment of the disorders reported. In addition, the data does not enable differentiation of problems that appeared before AN, from those occurring concomitantly with AN or afterwards. Nor did we have a matched control group, which restricts our conclusions.

Nevertheless it does appear that somatic problems are frequent. They are related to AN severity and duration. The frequency of fractures is greater in case of poorer global outcome and poorer mental health status. These elements should encourage practitioners to provide for long-term pluri-disciplinary follow-up of AN patients, involving somatic and mental health professionals.

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Table n°1: Description of the initial sample and the outcome sample

Characteristics	Total initial sample N=180*	Sample inclusion (N=97)*	at Follow-up sample after 6-12 years (N=97)
Age at onset of disorder, m (SD), years	15.2 (1.7)	15.1 (2.2)	-
Age, m (SD), years	16.9 (2.1)	16.7 (2.1)	25,53 (2,96)
Duration of AN before admission, m (SD), months	21.2 (20.4)	19.5 (17.9)	-
Minimum BMI, m (SD),kg/m ²	12.9 (1.3)	13.2 (1.2)	
BMI at admission, m (SD),kg/m ²	13.2 (1.3)	13.3 (1.2)	-
BMI at discharge or follow up, m (SD),kg/m ²	17.4 (1.5)	17.4 (1.3)	19.3 (2.7)
Duration of hospitalization, m (SD), months	4.3 (3.3)	4.1 (2.9)	-
Duration of AN, m (SD), years	-	-	2.9 (3.6)
Duration of past AN m (SD), years	-	-	2.4 (2.9)
Duration of current AN, m (SD), years	-	-	12 (1.6)
Duration of follow-up, m (SD), years	-	-	9.3 (1.9)
Socio-professional status of the family head, N (%)			
- Upper class	43 (59.7)	74 (77,9)	
- Middle class	14 (19.5)	12 (12.6)	
- Manual Worker employee	15 (20.8)	9 (9.5)	
At least one lifetime depressive episode, N (%)	-	-	65 (67%)
Vomiting, N (%)	-	-	20 (20, 6%)
Premenarcheal AN, N (%)	105 (58, 3%)	9 (9, 3%)	-

m = mean; SD = Standard Deviation. *: non significant differences

Description of the initial sample (180 girls / young women)

Table n°2: Description of somatic disorders

Somatic history	n/N	%	Somatic history	n/N	%
Deficiencies			Cardio-vascular		
Iron	44/93	45,4	Cardiac arrhythmia	19/97	19,6
Vitamin D	24/95	24,7	Varicose veins	6/97	6,2
Vitamin K	14/93	14,4	Heart failure	0/97	0,0
Vitamin B12	9/94	9,3	Myocardial infarction	0/97	0,0
Folates	1/93	1,1	Other (cardiac arrest)	1/97	1,0
Other (magnesium)	9/97	9,3	Other (1 hypotension)	1/97	1,0
Other (calcium)	6/97	6,2	Other (oedema)	1/97	1,0
Other (Vitamin B6)	1/97	1,0	Dermatology		
Neurology			Eczema	20/96	20,6
Migraines	31/97	32,0	Sores and ulcers	21/95	20,6
Epilepsy	1/97	1,0	Psoriasis	97/97	3,1
Rheumatology			Urticaria	3/95	3,1
Fractures	30/97	30,9	Other(Acne)	9/97	9,3
Osteoporosis, Osteopenia	22/95	22,7	Other(Allergy)	2/97	2,1
Other (Raynaud Syndrome)	3/97	3,1	Other (Herpes)	2/97	2,1
Other (Arthrosis)	2/97	2,1	Other (underarm cysts)	2/97	2,1
Other (Vascularity)	2/97	2,1	Other (stress rash)	1/97	1,0
Other (Kyphosis)	1/92	1,0	Other (chillblains)	1/97	1,0
Other (Sciatica)	1/97	1,0	Other (chapped hands)	1/97	1,0
Urology			Other (Impetigo)	1/97	1,0
Cystitis	29/97	29,9	Other (hair loss)	1/97	1,0
Lithiasis (bladder)	2/97	2,1	Other (purpura)	1/97	1,0
Pyelonephritis	1/97	1,0	Other (warts)	1/97	1,0
Renal failure	0/97	0,0	Dental		
Other (kidney stones)	1/97	1,0	Other (tooth decay)	10/97	10,3

Gastro-enterology			Other (Abscess)	4/97	4,1
Gastro-oesophageal reflux	22/96	22,7	Other (Bruxism)	3/97	3,1
Gastritis	11/96	11,3	Other (tooth extraction)	2/97	2,1
Functional colopathy	7/97	7,2	Other (devitalisation molar teeth)	2/97	2,1
Gastro-duodenal ulcer	6/96	6,2	Other (gum graft)	1/97	1,0
Oesophagitis	6/95	6,2	Other (Robin syndrome)	1/97	1,0
Rectocolitis	1/97	1,0	Respiratory		
Crohn's disease	0/97	0,0	Asthma	10/97	10,3
Other (Colitis)	3/97	3,1	Pneumopathy	5/97	5,2
Other (Constipation)	2/97	2,1	Cystic fibrosis	0/97	0,0
Other (Appendicitis)	1/97	1,0	Respiratory failure	0/07	0,0
Other (bowel stoppage)	1/97	1,0	Other (asthma-like bronchitis)	1/97	1,0
Other (Amoebiasis)	1/97	1,0	Endocrine		
Other (Merycism)	1/97	1,0	Pituitary disorder	4/96	4,1
Other (Haemorrhoids)	1/97	1,0	Hyperthyroidy	2/96	2,1
Gynaecology					
(other than reproduction)			Hypothyroidy	1/97	0,0
Problems \neq procreation					
(mycosis)	26/97	26,8	Thyroiditis	1/97	0,0
Current amenorrhoea	26/97	26,8	Other (Retarded growth)	4/97	4,1
Other (ovarian cyst)	4/97	4,1			
Other (Mycosis)	3/97	3,1			
Other (Infections)	1/97	1,0			
Other (Chlamydia)	1/97	1,0			
Other (Papilloma virus)	1/97	1,0			
Other (polycystic ovary)	1/97	1,0			