

1 Title

2 Symptomatic pelvic organ prolapse at midlife, quality of life and risk factors in GAZEL cohort.

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27

28 **Précis**

29 In women in their 50s, symptoms of pelvic organ prolapse are associated with impaired quality of life,
30 body mass index and number of vaginal deliveries.

31

32 **Abstract**

33 Objective: To estimate quality of life (QoL), prevalence, and risk factors associated with symptomatic pelvic
34 organ prolapse (POP) among middle-aged women.

35 Methods: A questionnaire was mailed to 3114 women aged 50-61 years in the GAZEL cohort; 2640 (85%)
36 returned it. Symptomatic POP was defined by feeling a bulge from the vagina (sometimes, often, or all the time
37 versus never or rarely). QoL was determined with the Nottingham Health Profile (NHP) questionnaire. Multiple
38 linear regression was used to examine the association between frequency of POP symptoms and the QoL score.
39 Logistic regression was used to estimate the impact of risk factors on past or present symptomatic POP (current
40 symptoms or previous surgery for POP).

41 Results: The prevalence of symptomatic POP was 3.6% (96) and that of surgery for POP, 2.7% (70). POP
42 symptoms were associated with difficulty defecating, lower abdominal pain, and difficulty voiding. The
43 frequency of POP symptoms was associated with a poorer QoL score in each NHP domain (physical mobility,
44 pain, emotional reaction, social isolation, energy and sleep). Even when we took general characteristics, medical
45 history, and lifestyle associated with QoL into account, the global NHP score was significantly impaired by POP
46 symptoms. Factors significantly associated with past or present symptomatic POP were high body mass index
47 and the number of vaginal deliveries.

48 Conclusion: In our population of women in their 50s, POP symptoms are associated with impaired QoL, and the
49 number of vaginal deliveries is a risk factor for past or present symptomatic POP.

50

51 Key-words: Pelvic organ prolapse, Quality of life, Delivery

52

53 **Introduction**

54 The prevalence of pelvic organ prolapse (POP) increases with age and number of vaginal deliveries.¹ In
55 the 18th century, Madame du Coudray attributed the onset of a "falling womb" to childbirth.² Despite this
56 association, the mechanism of its onset remains obscure, and we do not know what organ is damaged, let alone
57 how. While numerous surgical techniques have been developed for POP, epidemiologic surveys on this topic are
58 rare. It is estimated that 15% of all hysterectomies are performed for POP and that the cumulative risk of surgery
59 for POP is approximately 7% at the age of 80 years.^{3,4} Mean age at this surgery is between 50 and 60 years of
60 age.⁵ Despite the frequency of recourse to surgery, the effect of POP on quality of life (QoL) is not well
61 understood. A Medline search using the terms "quality of life" and "pelvic organ prolapse" showed no studies
62 that examined the deterioration of general health-related QoL as a function of POP symptoms in a general
63 population, that is, a population not selected because of POP symptoms.

64 Our main purpose was to estimate the impact of symptomatic POP on QoL and its prevalence among
65 middle-aged women enrolled in a cohort study and to assess its obstetrical risk factors, while taking other
66 characteristics into account. This cohort of French women (GAZEL cohort) completed questionnaires to estimate
67 their general health-related QoL (NHP questionnaire) and the frequency of their POP symptoms.

68

69 **Methods**

70 Our population belongs to the French GAZEL cohort (www.gazel.inserm.fr), which began in 1989 with
71 more than 20,000 men and women employed by the French national power company (EDF-GDF) who
72 volunteered to participate in an epidemiological research program coordinated by INSERM (Institut National de
73 la Santé et de la Recherche Médicale, that is, the French National Institute for Health and Medical Research).⁶
74 Women of the GAZEL cohort aged 45-50 years between 1990 and 1996 (n = 3114) were included in a separate
75 prospective longitudinal survey, the “Women and their Health” study. Its principal objective is to study women's
76 health as they reach menopause and afterwards.⁷ These women receive a general health questionnaire each year
77 as part of the overall GAZEL survey and a separate questionnaire specific to women's health issues every three
78 years. In 2000, an additional questionnaire about incontinence and obstetrical history was mailed to all the
79 women in this survey. Except as otherwise specified, data come from both 2000 questionnaires. Three other
80 reports about incontinence based on the same questionnaires and database have previously been published.⁸⁻¹⁰

81 At the time this study was initiated, there was no validated questionnaire for assessing pelvic floor
82 symptoms in women without known pelvic floor disorders. The prevalence and severity of symptomatic POP
83 was estimated from responses to the question: *In the past 4 weeks, have you experienced the sensation of a*
84 *bulging from your vagina? Never, Rarely, Sometimes, Often, or All the time.* The question was constructed with
85 the help of an expert and was modeled on the Bristol Female Low Urinary Tract Symptoms (BFLUTS)
86 questionnaire and the Urogenital Distress Inventory.^{11, 12} Understanding was not tested. Stress urinary
87 incontinence was assessed by responses to a question from the BFLUTS questionnaire: *Does urine leak when*
88 *you are physically active, cough or sneeze? Never, Rarely, Sometimes, Often, or All the time.* Women who
89 answered *Sometimes, Often* or *All the time* were considered to have stress urinary incontinence. Other pelvic
90 floor symptoms, i.e., urinary urge incontinence, voiding difficulties, constipation (fewer than 3 movements a
91 week), defecation difficulties, lower abdominal pain or heaviness, and pain at intercourse, were assessed by the
92 same method. Fecal incontinence was defined by involuntary loss of liquid or solid stool.

93 Other characteristics of the subjects considered in this analysis and recorded from the questionnaires are:
94 general characteristics (age at questionnaire, educational level, body mass index, and menopausal status),
95 medical history (diabetes mellitus, neurologic disease, cardiovascular disease, regular medical treatment, self-
96 reported nervous breakdown, self-reported depressed mood, anxiety or stress, hysterectomy, previous urinary
97 incontinence surgery, previous anal surgery, and previous POP surgery), lifestyle (household monthly income,

98 marital status, smoking habits, and regular physical exercise), and obstetrical history (parity, episiotomy, third-
99 degree perineal tear, birth weight of heaviest child, age at first delivery and mode of delivery). Previous POP
100 surgery was assessed by the questions: *Have you had a surgery? If yes, please specify the type of surgery* (a list
101 was provided): *pelvic organ prolapse (falling organs) repair? Yes, No*. Self-reported nervous breakdown, and
102 depressed mood, anxiety, or stress were defined by answers to a question presenting a list of health problems and
103 asking the subjects to indicate those they had had during the past 12 months. The list included: Nervous
104 breakdown as one answer, and depressed mood, anxiety or stress as another. We used logistic regression to
105 examine the association between POP symptoms and other pelvic floor symptoms.

106 We used the Nottingham Health Profile (NHP), a generic instrument widely used to estimate general
107 health-related QoL and validated in different populations, to determine whether symptomatic prolapse, like other
108 chronic conditions, interferes with everyday life activities.^{13, 14} The NHP questionnaire was included in the
109 general health questionnaire administered in 2000. It is a generic QoL questionnaire, applicable to a broad range
110 of populations and allowing comparisons between different clinical conditions. The NHP contains 38 items
111 covering 6 dimensions: physical mobility (8 items), pain (8 items), emotional reactions (9 items), social isolation
112 (5 items), energy (3 items), and sleep (5 items). The responses are dichotomous (yes/no) and concern the
113 subject's condition at the time she is completing the questionnaire. A weight is assigned to each response so that
114 a weighted score can be calculated for each of the six dimensions. The weighted scores for each dimension range
115 from 0 (high QoL) to 100 (low QoL). Each subject's profile is described by 6 scores. It is also possible to
116 construct a global score that is the mean of the 6 dimensions. We first used the Spearman rank test to analyze the
117 correlation between the QoL scores in each NHP dimension and the severity of POP symptoms. We then
118 examined the association between the global NHP score (mean of the scores for each dimension) and the severity
119 of the POP (defined by symptom frequency), using a linear regression to take into account the possible
120 confounding factors: general characteristics, medical history, lifestyle, and parity. We chose not to include in this
121 model other pelvic floor symptoms significantly associated with POP in the preceding analysis.

122 Past or present symptomatic POP was defined by the report of symptomatic POP or a history of surgery
123 for POP. Because this definition includes surgical history, we chose not to consider in the analysis other surgical
124 history (hysterectomy, surgery for urinary incontinence and anal surgery), all of which were statistically
125 associated with a history of surgery for prolapse. We compared the women with past or present POP to all the
126 others and conducted a multivariable analysis with a backward stepwise logistic regression. Candidate variables
127 for the multivariable model were those suspected to be risk factors for POP (age, BMI, occupation, menopausal

128 status, parity, and mode of delivery) or that could influence symptom reporting (educational level). A first model
129 was constructed for all women. A second model (not shown) was restricted to parous women; it included
130 obstetrical details (age at first delivery, birth weight of heaviest baby, episiotomy, and third-degree anal tears).
131 Variables remained in the final multivariable model only if the odds ratio was significant after backward
132 elimination; otherwise they were excluded.

133 Odds ratios and their 95% confidence intervals are reported for each association examined. All analyses
134 were performed with Statview (SAS Institute Inc., Cary, NC).

135 The GAZEL cohort scientific committee and the CNIL (Commission Nationale de l'Informatique et des
136 Libertés, that is, the French Data Protection Authority) approved this study, which received no external funding.

137

138 **Results**

139 Questionnaires were sent to 3114 women, 2640 (85%) of whom completed and returned them. Median
140 age was 54 (range 50-61) years and median parity 2 (0-6); 79% were postmenopausal. Respondents and
141 nonrespondents did not differ significantly for age (mean age 54.6 versus 54.9, $p=0.14$, t-test), while respondents
142 had a higher educational level than nonrespondents (20% had a high school diploma versus 15%, $p=0.012$, Chi²
143 test).

144 Data about POP symptoms were missing for 193 women (7.3%); 2296 (87.0%) reported no *sensation of a*
145 *bulge from their vagina* in the past 4 weeks, 69 *rarely* (2.6%), 70 *sometimes* (2.7%), 18 *often* (0.7%) and 8
146 (0.3%) *all the time*. Additionally, 70 women (2.7%) had previously undergone surgery for POP. POP symptoms
147 were associated with difficulty defecating, lower abdominal pain, and difficulty voiding (Table 2). Other pelvic
148 floor symptoms (stress urinary incontinence, urge urinary incontinence, fecal incontinence, painful intercourse,
149 urinary infection, and fewer than 3 bowel movements per week) were not significantly associated with POP
150 symptoms, after adjustment for difficulty in defecation or voiding and lower abdominal pain.

151 The NHP QoL questionnaire was completed by 2285 women (87%). As Figure I shows, the frequency of
152 POP symptoms was associated with increased (that is, poorer) QoL scores in all NHP dimensions: physical
153 mobility ($p<0.0001$), pain ($p<0.0001$), emotional reaction ($p=0.01$), social isolation ($p=0.03$), energy ($p=0.0002$),
154 and sleep ($p=0.008$). The correlation between the severity of POP symptoms and QoL impairment, measured by
155 the global NHP score, persisted even after adjustments (linear multiple regression) for other factors with a
156 significant effect on QoL: urinary incontinence, anal incontinence, diabetes, regular physical exercise, BMI
157 (continuous variable), self-reported nervous breakdown, self-reported depressed mood, anxiety or stress, living
158 with a partner, occupation, and household monthly income (Table 3).

159 Overall, 158 women (6.0%) were considered to have past or present symptomatic POP. Characteristics
160 associated with it were BMI, and the number of vaginal deliveries (Table 4). The one-variable model that used
161 mode of delivery to predict a history of symptomatic POP had an $R^2=0.008$ (data not shown). The multivariable
162 model for women with children, which also tested age at first delivery, episiotomy, a third-degree anal tear and
163 birth weight of the largest child, found no other obstetrical variable to be significant (data not shown).

164

Discussion

The principal limitation of our study was that POP was not clinically confirmed. Prolapse is a sign observed during clinical examinations, and epidemiologic surveys about this disease are difficult because of the indirectness of its study by questionnaires. Nonetheless what matters from a practical point of view is symptomatic prolapse that motivates the woman to seek care. That is, women see their doctors for a functional disease and not for an anatomical defect. Moreover, a study of QoL and the risk factors associated with POP symptoms requires the availability of a sample of women recruited outside of a medical practice. It thus seems useful from a public health perspective to look at the prevalence of prolapse symptoms in the general population.

A major advantage of our sample is that the women participating were not recruited because they had symptoms. Their status as volunteers probably explains the excellent response rate (85%). At the time we began this study, there were no questionnaires validated in a population at low risk for POP.¹⁵ Unfortunately, the question we used (*have you experienced a sensation of bulging from your vagina?*) could not be combined with clinical examination. Seeing or feeling a vaginal bulge is considered a specific symptom of POP, but the sensitivity of this symptom is mediocre in low-risk populations.¹⁶ Barber et al showed that the question *Do you usually have a bulge or something falling out that you can see or feel in your vaginal area?*¹⁷ had a specificity of 99% but a sensitivity of 35% for prolapse at or beyond the hymen (grades II and III) in a population at low risk. The question used by Rortveit et al in their study (*has there been a visible bulging or protrusion from your vagina?*) had a sensitivity of only 16% for grade II or III prolapse.¹⁸ Symptoms increased with the severity of prolapse; they were frequent for stages III and IV and usually absent at stages I or 0.¹⁹ Tan et al examined 1912 women who answered the question: *Do you ever feel a bulge or that something is falling out of the vagina?*²⁰ The response was positive in 79-85% of women who had a stage III or IV prolapse compared with 6-11% of women with a stage I or 0. It is therefore probable that those who responded positively in our survey were those with the most serious prolapse. In our study, the bulging symptom was correlated with pelvic pain and difficulties in voiding and defecation (Table 2), which serves as evidence supporting the clinical relevance of the question. Ellerkmann et al showed that POP documented by a standardized clinical examination is often associated with these symptoms.²¹ Finally, the more frequent the prolapse symptoms, according to this question, the greater the impairment of QoL in all NHP dimensions. This graded association between the frequency of prolapse symptoms and QoL is additional evidence of the question's clinical relevance.

193 The relatively rare character of this condition necessarily means that in a general population sample we
194 find few symptomatic women, thus statistical power is limited and significant risk factors more difficult to show.
195 Only 2.7% of our participants had a history of surgery for prolapse and 3.7% had symptoms suggestive of
196 prolapse. These figures are close to those of studies based on clinical examination, which have found only a 0-
197 2.1% prevalence of prolapse beyond the introitus (Stage III or IV) in women 50-59 years.^{22, 23} The cumulative
198 risk of surgery for POP or urinary incontinence is estimated at 4.7 to 5.1% for women in their 50s.^{3, 24}

199 Another limitation is that our population sample is not exactly representative of middle-aged French
200 women, because women enrolled in the GAZEL cohort were recruited from a work setting and volunteered to
201 participate in medical research. We know, for example, that the women who agreed to participate in GAZEL had
202 a higher education level and were in better health than nonparticipating employees.⁶⁻⁸ From our point of view,
203 that is not likely to affect the QoL impairment observed or the risk factors identified.

204 Few studies have examined the impact of POP on QoL with a generic QoL tool. We showed that the more
205 frequent the prolapse symptoms, the greater the impairment of QoL in all of the NHP dimensions. Even in
206 multivariable analysis taking numerous factors likely to be associated with QoL into account, the symptoms of
207 POP remained associated with a significant impairment in overall QoL. In the case-control study by Jelovsek et
208 al, the SF-12 (Short Form Health Survey) physical scale showed impairment in women with prolapse, while the
209 mental scale was similar in both groups; this study did not include multivariable analysis. We have previously
210 shown that impairment of QoL in the NHP dimensions of physical mobility and pain is proportional to the
211 severity of urinary incontinence.⁹ A similar result appears for POP symptoms (figure 1). This suggests that
212 symptomatic POP can have an important impact on general health-related quality of life and interfere as a
213 disability with physical mobility, pain, emotional reaction, social isolation, energy and sleep .

214 We still know very little about its causes. A congenital or acquired tissue factor is probable;²⁵⁻²⁷ the
215 position of the pelvis or the spine may play a role;^{28, 29} and physical effort, constipation, a chronic cough, and
216 obesity (BMI is a significant factor in our study) weighing on the pelvic floor may also be involved.³⁰⁻³³ The
217 most frequently suggested hypothesis is that of obstetrical trauma. Mant et al found a risk of hospitalization for
218 POP proportional to parity.³² Clinical examination shows that prolapse is more frequent in women with
219 children.^{22, 23} Several other cross-sectional surveys have shown that symptoms of POP are more frequent in
220 women with vaginal deliveries.^{1, 34, 35, 36} Nonetheless the role of vaginal delivery in the natural history of prolapse
221 must be slight, for in our population it explains less than 1% of the symptomatic prolapses. Other mechanisms
222 probably play a role in onset but we are limited by the cross-sectional nature of our study, which makes it

223 impossible to record the risk factor when it occurs. Only a longitudinal survey can identify traumatic events to
224 the perineum as they occur. In the same GAZEL population, severe stress incontinence (15% prevalence) and
225 fecal incontinence (9.5%) were not associated with mode of delivery.^{8, 10} It is therefore probable that even though
226 these pelvic floor disorders are often associated they do not share the same pathophysiologic mechanisms. This
227 is consistent with the work by DeLancey, who showed that stress urinary incontinence is linked more to an aging
228 sphincter than to the impairment of urethral support.³⁷

229 In conclusion, although their prevalence is relatively slight, POP symptoms have a significant impact on
230 the QoL of the women who have them. Even if it is probable that vaginal delivery plays a role in the genesis of
231 POP, it is an incidental factor that explains only a very small part.

232

233 **References**

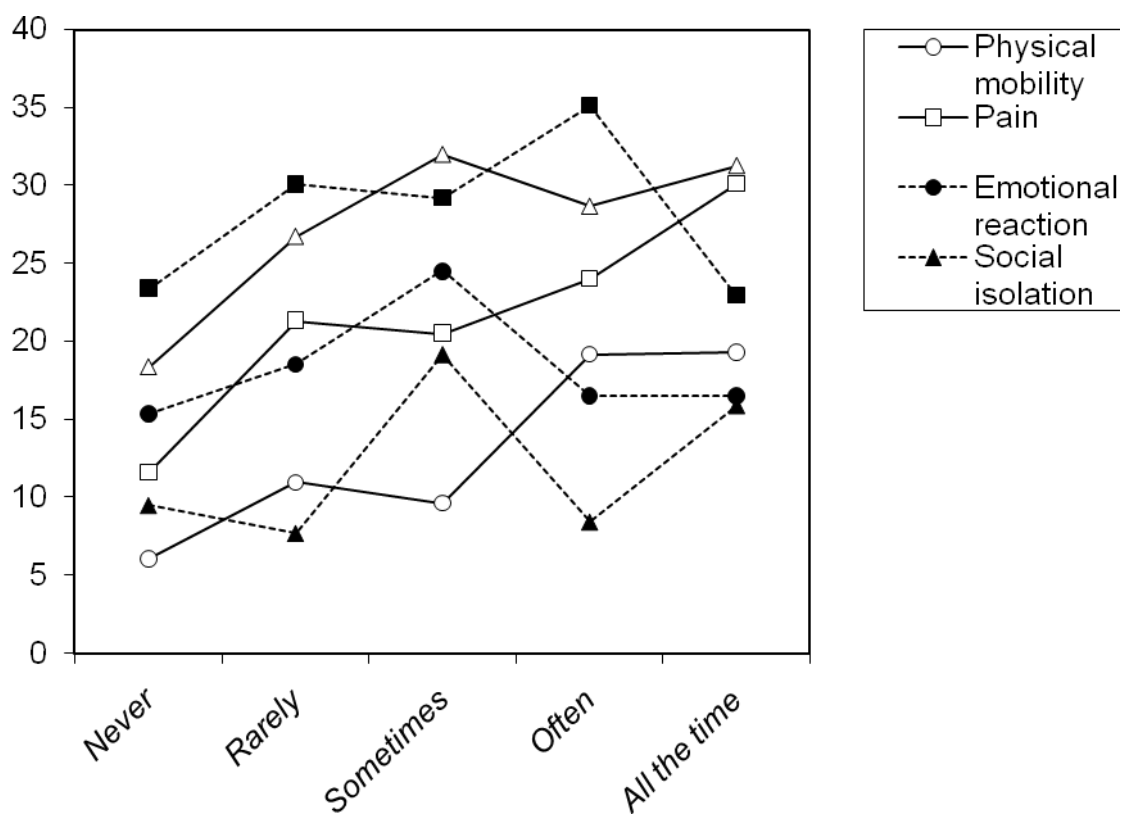
- 1 Rortveit G, Brown JS, Thom DH, van den Eeden SK, Creasman JM, Subak LL. Symptomatic pelvic organ prolapse, prevalence and risk factors in a population-based, racially diverse cohort. *Obstet Gynecol* 2007;109:1396-403.
- 2 DuCoudray AM. *Abrégé de l'art des accouchements*. Châlons-sur-Marne: Bouchard, 1773.
- 3 Carlson KJ, Nichols DH, Schiff I. Indications for hysterectomy. *New Engl J Med* 1993;328:85-60.
- 4 Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. *Obstet Gynecol* 1997;89:501-6.
- 5 Shah AD, Kohli N, Rajan SS, Hoyte L. The age distribution, rates, and types of surgery for pelvic organ prolapse in the USA. *Int Urogynecol J* 2008;19:421-8.
- 6 Goldberg M, Chastang JF, Leclerc A, Zins M, Bonenfant S, Bugel I, et al. Socioeconomic, demographic, occupational and health factors associated with participation in a long-term epidemiologic survey: a prospective study of the French GAZEL cohort and its target population. *Am J Epidemiol* 2001;154:373-84.
- 7 Ringa V, Ledésert B, Bréart G. Determinants of hormone replacement therapy among postmenopausal women enrolled in the French GAZEL cohort. *Osteoporosis Int* 1994;4:16-20.
- 8 Fritel X, Ringa V, Varnoux N, Fauconnier A, Piaux S, Bréart G. Mode of delivery and severe stress incontinence. A cross-sectional study among 2625 perimenopausal women. *BJOG* 2005;112:1646-51.
- 9 Saadoun K, Ringa V, Fritel X, Varnoux N, Zins M, Bréart G. Negative impact of urinary incontinence on quality of life, a cross-sectional study among women aged 49-61 years enrolled in the GAZEL cohort. *Neurourol Urodyn* 2006;25:696-702.
- 10 Fritel X, Ringa V, Varnoux N, Zins M, Bréart G. Mode of Delivery and Fecal Incontinence at Midlife: A Study of 2,640 Women in the GAZEL Cohort. *Obstet Gynecol* 2007;110:31-38.
- 11 Jackson S, Donovan J, Brookes S, Eckford S, Swithinbank L, Abrams P. The Bristol Female Lower Urinary Tract Symptoms questionnaire: development and psychometric testing. *Br J Urol* 1996;77:805-12.

-
- 12 Uebersax JS, Wyman JF, Shumaker SA, McClish DK, Fantl JA. Short forms to assess life quality and symptom distress for urinary incontinence in women: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Continenence Program for Women Research Group. *Neurourol Urodyn* 1995;14:131-9.
- 13 Hunt SM, McEwen J, McKenna SP. Measuring health status: A new tool for clinicians and epidemiologists. *J R Coll Gen Pract* 1985;35:185-8.
- 14 Bucquet D, Condon S, Ritchie K. The French version of the Nottingham Health Profile. A comparison of items weights with those of the source version. *Soc Sci Med* 1990;30:829-35.
- 15 Baessler K, O'Neill SM, Maher CF, Battistutta D. An interviewer-administered validated female pelvic floor questionnaire for community-based research. *Menopause* 2008;15:973-7.
- 16 Doshani A, Teo REC, Mayne CJ, Tincello DG. Uterine prolapse. *BMJ* 2007;335:819-23.
- 17 Barber MD, Neubauer NL, Klein-Olarte V. Can we screen for pelvic organ prolapse without a physical examination in epidemiologic studies? *Am J Obstet Gynecol* 2006;195:942-8.
- 18 Bradley CS, Nygaard IE. Vaginal wall descensus and pelvic floor symptoms in older women. *Obstet Gynecol* 2005;106:759-66.
- 19 Ghetti C, Gregory WT, Edwards SR, Otto LN, Clark AL. Pelvic organ descent and symptoms of pelvic floor disorders. *Am J Obstet Gynecol* 2005;193:53-7.
- 20 Tan JS, Lukacz ES, Menefee SA, Powell CR, Nager CW. Predictive value of prolapse symptoms: a large database study. *Int Urogynecol J* 2005;16:203-9.
- 21 Ellerkmann RM, Cundiff GW, Melick CF, Nihira MA, Leffler K, Bent AE. Correlation of symptoms with location and severity of pelvic organ prolapse. *Am J Obstet Gynecol* 2001;185:1332-8.
- 22 Swift SE. The distribution of pelvic organ support in a population of female subjects seen for routine gynecologic health care. *Am J Obstet Gynecol* 2000;183:277-85.
- 23 Samuelsson EC, Victor FTA, Tibblin G, Svärdsudd KF. Signs of genital prolapse in a Swedish population of women 20 to 59 years of age and possible related factors. *Am J Obstet Gynecol* 1999;180:299-305.

-
- 24 Fialkow MF, Newton KM, Lentz GM, Weiss NS. Lifetime risk of surgical management for pelvic organ prolapse or urinary incontinence. *Int Urogynecol J* 2008;19:437-440.
- 25 Carley ME, Schaffer J. Urinary incontinence and pelvic organ prolapse in women with Marfan or Ehlers Danlos syndrome. *Am J Obstet Gynecol* 2000;182:1021-23.
- 26 Chiaffarino F, Chatenoud L, Dindelli M, et al. Reproductive factors, family history, occupation and risk of urogenital prolapse. *Eur J Obstet Gynecol Reprod Biol* 1999;82:63-67.
- 27 Jackson SR, Avery NC, Tarlton JF, Eckford SD, Abrams P, Bailey AJ. Changes in metabolism of collagen in genitourinary prolapse. *Lancet* 1996;347:1658-61.
- 28 Lazarevski MB. Pelvic morpho-topography and pathogenesis of genital prolapse. *Neurourol Urodyn* 1999;18:332-333.
- 29 Mattox TF, Lucente V, McIntyre P, Miklos JR, Tomezsko J. Abnormal spinal curvature and its relationship to pelvic organ prolapse. *Am J Obstet Gynecol* 2000;183:1381-4.
- 30 Rinne KM, Kirkinen PP. What predisposes young women to genital prolapse? *Eur J Obstet Gynecol Reprod Biol* 1999;84:23-25
- 31 Jorgensen S, Hein HO, Gyntelberg F. Heavy lifting at work and risk of genital prolapse and herniated lumbar disc in assistant nurses. *Occup Med (Lond)* 1994; 44: 47-49.
- 32 Mant J, Painter R, Vessey M. Epidemiology of genital prolapse: observations from the Oxford family planning association study. *Br J Obstet Gynaecol* 1997;104:579-585.
- 33 Spence-Jones C, Kamm MA, Henry MM, Hudson CN. Bowel dysfunction: a pathogenic factor in uterovaginal prolapse and urinary stress incontinence. *Br J Obstet Gynaecol* 1994;101:147-152.
- 34 Lukacz ES, Lawrence JM, Contreras R, Nager CW, Luber KM. Parity, mode of delivery, and pelvic floor disorders. *Obstet Gynecol* 2006;107:1253-60.
- 35 Progetto Menopausa Italia Study Group. Risk factors for genital prolapse in non-hysterectomized women around menopause: results from a large cross-sectional study in menopausal clinics in Italy. *Eur J Obstet Gynecol Reprod Biol* 2000;93:135-40.
- 36 Hendrix SL, Clark A, Nygaard I, Aragaki A, Barnabei V, McTiernan A. Pelvic organ prolapse in the Women's Health Initiative: gravity and gravidity. *Am J Obstet Gynecol* 2002;186:1160-6.

-
- 37 DeLancey JO, Trowbridge ER, Miller JM, Morgan DM, Guire K, Fenner DE, Weadock WJ, Ashton-Miller JA. Stress urinary incontinence: relative importance of urethral support and urethral closure pressure. *J Urol* 2008;179:2286-90

Figure I



Mean quality of life score, in each NHP dimension, associated with POP symptoms frequency.

Table 1

Association between pelvic floor disorders and POP symptoms. Univariable and multivariable analysis using logistic regression.

Women's pelvic floor symptoms		N	POP symptoms % (n)	Univariable analysis crude OR (95%CI)	Multivariable analysis adjusted OR (95%CI) R ² =0.54
Difficult defecation	No	1735	2.5 (44)	1	1
	Yes	730	7.0 (51)	2.98 (1.97-4.51)	1.62 (1.04-2.53)
Bowel movement <3/week	No	1998	3.4 (68)	1	<i>Excluded</i>
	Yes	454	5.9 (27)	1.85 (1.17-2.92)	
Fecal incontinence	No	2243	3.3 (74)	1	<i>Excluded</i>
	Yes	250	8.0 (20)	2.55 (1.53-4.36)	
Lower abdominal pain or heaviness	No	1960	1.8 (36)	1	1
	Yes	494	12.1 (60)	7.80 (5.09-11.95)	4.79 (2.98-7.71)
Painful intercourse	No	1566	3.1 (49)	1	<i>Excluded</i>
	Yes	350	7.7 (27)	2.66 (1.64-4.33)	
Stress urinary incontinence	No	1557	2.3 (36)	1	<i>Excluded</i>
	Yes	1072	5.6 (60)	2.43 (1.60-3.71)	
Urge urinary incontinence	No	2186	2.9 (63)	1	<i>Excluded</i>
	Yes	445	7.4 (33)	2.65 (1.72-4.10)	
Urinary infection during the past 12 months	No	2265	3.2 (72)	1	<i>Excluded</i>
	Yes	329	7.3 (24)	2.41 (1.50-3.90)	
Difficult voiding	No	2106	2.2 (46)	1	1
	Yes	433	10.9 (47)	5.5 (3.61-8.39)	2.70 (1.69-4.29)

Variables remained in the final multivariable model only if the OR was significant (p value < 0.05) after backward stepwise elimination.

Table 2

Multiple regression analysis of the association between overall quality of life, measured by the NHP global score, and the frequency of pelvic prolapse symptoms, self-reported nervous breakdown, self reported depressed mood anxiety or stress, back pain, urge urinary incontinence, fewer than 3 bowel movements a week, regular physical exercise, hysterectomy, neurologic disease, regular medical treatment, BMI, living with someone, occupation, monthly income. The other variables tested (age, high school diploma, smoking, menopausal status, parity, previous urinary incontinence surgery, previous POP surgery, previous anal surgery, stress urinary incontinence, fecal incontinence, urinary infection, diabetes, and cardiovascular disease) were not significant and were excluded from the final model.

NHP global score versus 16 independent variables, R ² =0.32, F=48.0, p<0.0001		Coefficient (CI 95%)	p
POP symptoms (sometimes, often, or all the time)		4.15 (0.93-7.38)	0.012
Self-reported nervous breakdown		10.31 (7.03-13.58)	<0.0001
Self-reported depressed mood, anxiety, or stress		8.70 (7.29-10.11)	<0.0001
Back pain		5.42 (4.19-6.65)	<0.0001
Urge urinary incontinence		3.11 (1.52-4.70)	0.0001
Bowel movement < 3/week		3.95 (2.33-5.57)	<0.0001
Regular physical exercise (at least 1/week)		-3.03 (-4.25-1.80)	<0.0001
Hysterectomy		1.63 (0.07-3.19)	0.040
Neurologic disease		6.39 (3.93-8.86)	<0.0001
Regular medical treatment		2.14 (0.88-3.40)	0.0009
Body Mass Index (kg/m ²)		0.20 (0.05-0.36)	0.011
Living as couple		-2.61 (-4.36-0.86)	0.0035
Occupation	Blue-collar, clerical staff	1.54 (0.12-2.96)	0.034
	Management or training	0.29 (-1.86-2.43)	0.80
Household monthly incomes,	< 1982 €	0.07 (-1.75-1.89)	0.94
	> 3810 €	-1.73 (-3.30-0.17)	0.030

Table 3

Association between women's characteristics and pelvic organ prolapse history (POP symptoms or previous POP surgery). Univariable and multivariable analysis with logistic regression.

Women's characteristics		POP history % (n)	Univariable analysis crude OR (95%CI)	Multivariable analysis adjusted OR (95%CI) R ² =0.013
Age at questionnaire	< 55	5.6 (83)	1	<i>excluded</i>
	≥ 55	6.4 (75)	1.19 (0.80-1.77)	
Body mass index (kg/m ²)	< 25	5.2 (87)	1	1
	≥ 25	7.2 (65)	1.41 (1.01-1.96)	1.41 (1.01-1.97)
Occupation	Blue-collar, clerical staff	6.9 (46)	1	<i>excluded</i>
	Supervisors, sales representatives	6.1 (103)	0.88 (0.61-1.26)	
	Management or training	2.8 (6)	0.38 (0.16-0.91)	
High school diploma	No	6.2 (128)	1	<i>excluded</i>
	Yes	4.3 (22)	0.68 (0.43-1.09)	
Menopausal status	Pre	5.1 (27)	1	<i>excluded</i>
	Post with HRT	6.1 (80)	1.20 (0.77-1.89)	
	Post without HRT	6.2 (49)	1.20 (0.74-1.95)	
Mode of delivery	None	2.9 (9)	1	1
	1 vaginal	5.2 (40)	1.89 (0.91-3.96)	1.91 (0.91-3.98)
	2 vaginal	6.8 (76)	2.49 (1.23-5.03)	2.49 (1.23-5.04)
	3 or more vaginal	9.6 (30)	3.61 (1.68-7.76)	3.55 (1.65-7.62)
	Cesarean only	2.2 (3)	0.75 (0.20-2.81)	0.73 (0.19-2.73)