

Title	What is to blame for postnatal pelvic floor dysfunction in primiparous women — Pre-pregnancy or intrapartum risk factors?
Authors	Durnea, Constantin M.;Khashan, Ali S.;Kenny, Louise C.;Durnea, Uliana A.;Dornan, James C.;O'Sullivan, Suzanne M.;O'Reilly, Barry A.
Publication date	2017-04-23
Original Citation	Durnea, C. M., Khashan, A. S., Kenny, L. C., Durnea, U. A., Dornan, J. C., O'Sullivan, S. M. and O'Reilly, B. A. (2017) 'What is to blame for postnatal pelvic floor dysfunction in primiparous women— Pre-pregnancy or intrapartum risk factors?', <i>European Journal of Obstetrics & Gynecology and Reproductive Biology</i> , 214, pp. 36-43. doi:10.1016/j.ejogrb.2017.04.036
Type of publication	Article (peer-reviewed)
Link to publisher's version	10.1016/j.ejogrb.2017.04.036
Rights	© 2017 Elsevier B.V. This manuscript version is made available under the CC-BY-NC-ND 4.0 license - http://creativecommons.org/licenses/by-nc-nd/4.0/
Download date	2024-07-03 23:57:34
Item downloaded from	https://hdl.handle.net/10468/4067



UCC

University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Accepted Manuscript

Title: What is to blame for postnatal pelvic floor dysfunction in primiparous women—Pre-pregnancy or intrapartum risk factors?

Authors: Constantin M. Durnea, Ali S. Khashan, Louise C. Kenny, Uliana A. Durnea, James C. Dornan, Suzanne M. O’Sullivan, Barry A. O’Reilly



PII: S0301-2115(17)30209-9
DOI: <http://dx.doi.org/doi:10.1016/j.ejogrb.2017.04.036>
Reference: EURO 9879

To appear in: *EURO*

Received date: 19-12-2016
Revised date: 15-3-2017
Accepted date: 19-4-2017

Please cite this article as: Durnea Constantin M, Khashan Ali S, Kenny Louise C, Durnea Uliana A, Dornan James C, O’Sullivan Suzanne M, O’Reilly Barry A. What is to blame for postnatal pelvic floor dysfunction in primiparous women—Pre-pregnancy or intrapartum risk factors?. *European Journal of Obstetrics and Gynecology and Reproductive Biology* <http://dx.doi.org/10.1016/j.ejogrb.2017.04.036>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

What is to blame for postnatal pelvic floor dysfunction in primiparous women - pre-pregnancy or intrapartum risk factors?

Dr. Constantin M. Durnea^{1,2}, Dr. Ali S. Khashan^{1,3}, Prof. Louise C. Kenny¹, Dr. Uliana A. Durnea¹, Prof. James C. Dornan⁴, Dr. Suzanne M. O'Sullivan², Dr. Barry A. O'Reilly²

¹ The Irish Centre for Fetal and Neonatal Translational Research (INFANT), University College Cork, Cork, Ireland

² Department of Urogynaecology, Cork University Maternity Hospital (CUMH), Cork, Ireland

³ Department of Epidemiology and Public Health, University College Cork, Cork, Ireland

⁴ Queen's University Belfast, NI, UK

Corresponding author: Constantin M. Durnea

Address: INFANT Research Centre, Department of Obstetrics and Gynaecology, Cork University Maternity Hospital, Cork, Ireland. Email: costea.durnea@gmail.com Tel: +447462023323; Fax: +353214205025

Abstract

Background: The aetiology of pelvic floor dysfunction (PFD) is still poorly understood.

However childbearing is recognized as a major risk factor.

Objectives: To investigate the impact of the mode of delivery on postnatal pelvic floor dysfunction (PFD) in primiparas, when PFD existing before the first pregnancy is taken into consideration.

Study Design: 4P-study (Prevalence and Predictors of Pelvic floor dysfunction in Primips) is a prospective cohort study, nested within the Screening for Pregnancy Endpoints (SCOPE) study set in a tertiary referral teaching hospital with 9000 deliveries annually. Established and proposed risk factors for urinary, fecal, prolapse and sexual dysfunction and the severity of symptoms for each of these outcomes were assessed using the Australian Pelvic Floor Questionnaire in 1482 nulliparous women, who each completed the questionnaire in early pregnancy. Of these, 1060 (72%) repeated the questionnaire 12 months postpartum. Outcomes were analyzed using multivariate ordinal logistic regression.

Results: Significant ($p < 0.05$) risk factors for postpartum PFD were pre-pregnancy presence of similar symptoms Odds Ratio (OR) (5.0-30.0), smoking (OR 2.2-4.6), recurrent UTI (OR 2.2-17.3), high hip circumference (OR 1.4-1.6), vigorous exercising (OR 3.1-17.9), induction of labor (OR 1.5-2.3), forceps delivery (OR 1.8- 8.8), and 3rd degree perineal tear (OR 2.4-2.7). Cesarean section was protective for stress urinary incontinence (OR 0.3-0.5). Other common pre-pregnancy significant ($p < 0.05$) risk factors for various PFD types prior to the first pregnancy were: diagnosed depression - (OR 1.6-2.1), high BMI (OR 3.1), strenuous

exercising (OR 1.3-2.2), recurrent UTI (OR 1.5-2.5) and lower educational achievement (OR 1.5-1.6).

Conclusions: Pre-pregnancy PFD was common and was mainly associated with modifiable risk factors such as smoking and exercising. The main risk factor for postpartum PFD was the presence of similar symptoms prior to pregnancy, followed by anthropometric and intrapartum factors. Hip circumference seems to be a better predictor of PFD compared to BMI. When pre-pregnancy PFD was included in the analysis, Cesarean section was protective only for stress urinary incontinence, while delivery by forceps increased the risk of prolapse.

Keywords: Pelvic floor dysfunction, primiparous, pre-pregnancy, postpartum, childbirth, risk factors.

Condensation:

PFD prior to first pregnancy is the most significant risk factor for persistent PFD postnatally. Cesarean section appears to protect from stress urinary incontinence.

Introduction

Pelvic floor dysfunction (PFD) following childbirth has been the focus of attention over the last decades and the desire to avoid future PFD, is cited as indications for elective Cesarean section (CS). This issue of PFD in women has been highlighted recently in Europe and the USA as recently as December 2015[1, 2]. In order to identify women at a higher risk of PFD, multiple studies have investigated risk factors (RFs) for PFD and have identified the most significant as high BMI, age, parity, reduced quality of life scores, or features of childbearing such as vaginal delivery, oxytocin use and prolonged second stage of labor[3-8].

However, PFD is a common problem not only in parous women, but also in nulliparous women, and in the majority of them there is multi-compartment involvement[9]. There is limited knowledge about the RFs associated with PFD before the first pregnancy and in particular how they may correlate with intrapartum RFs leading to postnatal pelvic floor morbidity.

We hypothesized that pre-pregnancy RFs for PFD in nulliparous women may play an important role in the persistence of postnatal PFD, whereas perinatal RFs could be partially confounding, on background of a weak pelvic floor pre-pregnancy. In the present 4P-study (Prevalence and Predictors of Pelvic floor dysfunction in Primips) we aimed to define the group of patients at higher risk of PFD. In addition we wished to clarify the natural history of PFD, by investigating the role of pre-pregnancy and labor related RFs in the development of postnatal PFD in primiparous women.

Materials and Methods

The 4P is a prospective cohort study, nested within the parent SCOPE (Screening for Pregnancy Endpoints) Ireland study (www.scopestudy.net), described in detail elsewhere[9].

The Irish arm of this study was based at Cork University Maternity Hospital, a tertiary hospital with over 9000 deliveries annually. The Clinical Research Ethics Committee of the Cork Teaching Hospitals Ireland approved this study and all women gave informed written consent.

The study cohort consisted of nulliparous women, who were recruited between February 2008 and March 2011, and completed the Australian Pelvic Floor Questionnaire[10] in early pregnancy and one year postnatally (Figure 1). Inclusion criteria (reliant on the parent SCOPE study) required the participants to be nulliparous in their first ongoing pregnancy, having a singleton fetus being <12 weeks' pregnant. Exclusion criteria consisted of pre-pregnancy pre-existing complications such as diabetes, hypertension, three or more terminations or miscarriages and previous cervical cone biopsy.

The initial questionnaire was completed by 1472 participants (84% of those recruited for SCOPE). The postnatal questionnaire was answered by 1060 women (71% of those who completed the pre-pregnancy). However, a further 188 women (13%) were excluded from the final analysis as they had a second ongoing pregnancy at the time of the study (Figure 1).

At recruitment, all participants were specifically asked about pre-pregnancy PFD symptoms, the questionnaire clearly stating: "All these questions pertain to the period BEFORE you were pregnant". In addition, they were verbally instructed to ignore any new symptoms that

had developed in pregnancy. Postnatal questionnaires were completed at one year postnatally, to exclude short-term transitory postpartum PFD.

In this questionnaire all questions are graded from 0 to 3, where zero means no symptom present and 3 reflects the most frequent or severe symptom(Online Supplement - 1). The symptoms from each compartment section can be logically divided into primary - mandatory to diagnose a condition and secondary symptoms – giving extra information on the severity of primary symptoms e.g. reduced fluid intake, pad usage, laxative use etc. The primary symptoms constituted the main outcome measures and were selected according to the International Continence Society definitions for urinary and fecal dysfunction[11]. For the sexual dysfunction section, we used dyspareunia, vaginal laxity and tightness – as most frequently reported clinical symptoms by patients in clinics and commonly used in other questionnaires. All questions included in prolapse section were regarded as primary symptoms, as found in the pelvic floor distress inventory and used in other studies[12]. Besides individual symptom scores, the questionnaire contains a total section score for all types of dysfunction. This score is meant to better characterize the severity of primary symptoms rather than representing a scale score and is calculated by adding all individual symptom scores in each section[10]. We investigated the pre-pregnancy and postnatal association of primary symptoms with various anthropometric, social, professional, medical RFs, and with the mode of delivery (Online Supplement 2). The section score, being a composite score, had a larger number of observations than individual scores. Accordingly some RFs became significant here, while being non-significant or of borderline significance for individual primary symptoms. This helped to outline some common characteristics of women with the same type of PFD.

Statistical analysis

All statistical analyses were performed using IBM SPSS 19 and Stata 13.0. All statistical tests were two sided and a p-value < 0.05 was considered statistically significant. To investigate the effect of potential RFs on PFD, ordinal logistic regression was used to calculate the Odds Ratio (OR) and 95% Confidence Interval (CI). For each outcome measure, we performed a univariate ordinal logistic regression. Any RFs with a p-value < 0.1 was included in a stepwise ordinal logistic regression, where $p < 0.05$ was considered statistically significant.

Results

Demographic and intrapartum characteristics of study participants are presented in Tables 1 and 2 accordingly. Pre-pregnancy and postnatal RFs are presented in the Table 3 and Table 4 accordingly. In this section we describe significant results only ($p < 0.05$) from multivariate analysis, all others are included in Online Supplement 3.

Urinary Dysfunction

Pre-pregnancy

Diagnosed depression was the most universal pre-pregnancy RF associated in multivariate analysis with all symptoms of urinary dysfunction including stress urinary incontinence (SUI), urgency urinary incontinence (UUI), urinary urgency (UU) and total urinary section score (OR 1.6-2.1). Other important associations were: recurrent urinary tract infections (rUTI) with SUI and UU, smoking with UU, while vigorous exercising and lower educational level with UU and SUI. Stopping alcohol use decreased the risk of UUI (OR 0.5). Increasing weight was associated with SUI and UUI (Table 2).

Postnatally

The most important RF for postnatal urinary dysfunction was the presence of similar symptoms pre-pregnancy (Table 3), where more significant pre-pregnancy symptoms were associated with higher OR postnatally, compared to mild symptoms (Online Supplement 3).

Thus, SUI had an OR of 15.9, UUI (OR 6.0) and UU (OR 17.6). Additionally, some postnatal urinary dysfunction symptoms were associated with a different pre-pregnancy urinary symptom, such as the link between significant pre-pregnancy UU and postnatal UUI (OR 10). Increased body weight was associated with urinary dysfunction.: high waist to height ratio with SUI, high hip circumference with UU. Other important associations were: poor social support and rUTI with SUI, induction of labor (IOL) with SUI and UU. CS and vacuum delivery decreased the risk of SUI (OR 0.3-0.6), whereas forceps delivery increased the risk of UU (Table 3).

Fecal Dysfunction

The RFs associated with pre-pregnancy and postnatal fecal dysfunction, due to limited number of significant observations, are not be reported in the results section, but instead summarized in tables 2 and 3 and Online Supplement 3.

Sexual Dysfunction

Pre-pregnancy

The most common RF was poor social support associated with vaginal tightness/vaginismus, dyspareunia and sexual section score (OR 1.4-2.2). Other significant associations were between vigorous exercising with dyspareunia, low educational level with section score (Table 2).

Postnatally

The presence of pre-pregnancy symptoms was significantly associated with persistence of symptoms postpartum: vaginal laxity (OR 5.0) and dyspareunia (OR 5.7). Interestingly, postpartum dyspareunia was associated with high urinary section score, fecal urgency and flatus incontinence pre-pregnancy (OR 1.1-4.2). Increased body weight seemed to have a protective role for sexual dysfunction. High hip circumference was negatively associated with dyspareunia (OR 0.02). Other important associations were between smoking with vaginal tightness, dyspareunia and sexual section score, which correlated with number of smoked cigarettes. Third degree perineal tear was associated with vaginal laxity, dyspareunia and section score. Interestingly vigorous exercising was associated with vaginal tightness (OR 3.1). CS was associated with reduced sexual section score (OR 0.4) (Table 3).

Pelvic organ prolapse

Small numbers precluded a multivariate analysis for prolapse symptoms pre-pregnancy.

Postnatally

Various pre-pregnancy symptoms including prolapse, urinary and sexual dysfunction were associated with the postpartum sensation of vaginal pressure or heaviness (OR 3.3-9.9) (Table 3). Recurrent UTI was associated with sensation of pressure and prolapse sensation. Moderate exercising was associated with decreasing prolapse section score (OR 0.2), while vigorous exercising, conversely, with increasing score (OR 17.9). Vacuum and forceps delivery were associated with higher prolapse section score. Levator ani muscle (LAM) trauma was associated with prolapse sensation while LAM ballooning with vaginal pressure and heaviness (Table 3).

Comment

Previous studies investigating PFD in primiparous women have mainly focused on incontinence and prolapse with very few exploring the role of pre-pregnancy pathology in postnatal PFD [3, 6]. In the present study, besides outlining the group of patients who were at a higher risk of PFD before and after the first childbirth, we aimed to determine whether the mode of delivery had an impact, if preexisting PFD was taken in consideration.

Urinary dysfunction

The majority of our anthropometric, social and delivery related findings were in line with previous studies[3, 6, 13]. The link between urinary incontinence and depression has been reported previously and explained by altered serotonin function[14, 15]. Social circumstances have been demonstrated previously to impact on SUI[16]. Intensive exercising has also been demonstrated to be associated with UI more than with POP in young women[13, 17, 18]. However, in contrast to previous studies, we did not find an association with length of second stage of labor and fetal weight[19]. This could reflect different obstetric management strategies, with active management of labor being commonly used in Ireland.

Sexual dysfunction

Surprisingly, we found that higher maternal body weight decreased the risk of some sexual dysfunction symptoms. Additionally, for sexual dysfunction and POP, we tested the association with symptoms from other pelvic floor compartments, attempting to clarify the aetiology of possibly overlapping symptoms from different types of PFD. As seen from Table 3, there is a significant association between urinary fecal and sexual dysfunction symptoms, which stresses the need for careful clinical investigation. Postnatal findings were consistent with previous studies[20]. Similar to previous researches, the mode of delivery in our study did not affect any particular symptom, being associated with sexual section score only[21].

Pelvic Organ Prolapse

Instrumental delivery was associated with an increased prolapse score, while CS did not seem to offer protection. A possible explanation for this discrepancy could be the fact that pre-pregnancy symptoms were included in the analysis and this finding correlates with previous studies[22]. The association between LAM trauma and POP is also supported by recent evidence[23].

PFD - general overview

PFD in nulliparous women was associated with smoking, diagnosed depression, lower education level, poor social support, high BMI, rUTI and vigorous exercising. The impact of factors such as depression, lower education level and poor social support could possibly be explained by diet or other issues that warrant further investigation. Vigorous exercising may seem to be at odds with this phenotype but undoubtedly results in chronic increased intra-abdominal pressure which is line with previous studies [24].

However, the most important and universal RF for postnatal PFD was the presence of similar symptoms before the onset of pregnancy. It has been previously demonstrated that PFD with denovo onset during the pregnancy is more severe than PFD with postnatal onset [25, 26]. Other significant RF for various types of PFD were rUTI, smoking, poor social support, high body mass, IOL and 3rd degree perineal tear which is consistent with previous studies[3, 26, 27]. Similarly with previous data, we identified smoking being a significant RF for UU and sexual dysfunction[28, 29]. CS, in contrast to previous studies, proved to be protective against SUI only. Additionally, recent evidence has suggested that postnatal PFD is more severe in primiparous women when it is present pre-pregnancy. It would appear that CS may play a greater preventative role in the possibility of these symptoms worsening postnatally[30]. This could be due to congenital predisposition, which needs further investigation[31-33]. Moreover, the prevalence of all types of urinary incontinence and their severity at 20 years postpartum is higher in primiparous women who have delivered vaginally compared with those delivered by CS [34]. Our postnatal findings may slightly differ from previously reported RFs, possibly because we investigated relatively young, healthy primiparous women, in whom the magnitude of symptoms is not so striking. Additionally, many of previously reported RFs were statistically significant here only in univariate but not in multivariate analysis, probably due to the inclusion of pre-pregnancy symptoms in the analysis. The protective role of CS and the negative impact of instrumental delivery reported in previous studies could be confounded by lack of control over preexisting PFD during statistical analysis.

We would like to highlight other interesting RFs as a potential area for future research. It is possible that certain RFs did not reach significance in multivariate analysis due to the limited number of observations. Participants born SGA or preterm had higher section scores for urinary, fecal and sexual dysfunction. This area has not been investigated previously and

may well contribute to some specific PFD symptoms. In the present study high BMI, waist/hip ratio, waist and hip circumferences all were associated with PFD symptoms, similar to previous reports[35, 36]. However, in our study high BMI was significant mostly in univariate analyses, waist/hip ratio had large confidence intervals, whereas hip circumference was significant in most of the cases in multivariate analysis. It is likely that hip circumference could be the most specific weight related RF predictor for various PFD outcomes.

Strengths and Limitations

The main strength of our study is the comprehensive approach to our investigation, using a validated questionnaire covering all areas of PFD. In addition, the prospective design with inclusion of a large number of nulliparous participants followed up until one year postnatally, containing detailed medical, anthropometric and social characteristics adds strength. Finally, all women were delivered in the same hospital following similar obstetric approaches and protocols.

The main limitation of this study is that patients were not clinically examined to verify questionnaire findings. We recognize that in an attempt to comprehensively describe PFD before first childbearing and one year postnatally, we used many RFs and there is a possibility for some outcomes to become significant by chance.

In conclusion the majority of pre-pregnancy RFs are modifiable. The most important RF for postnatal PFD was the presence of similar symptoms pre-pregnancy. Their inclusion in the analysis alters the significance of potential protective effects of CS for prolapse but it is unchanged for SUI, especially in those affected pre-pregnancy. Hip circumference seems to

be a better predictor of PFD compared to BMI. Further research is required to confirm how efficient avoidance of vaginal delivery in the pre-pregnancy affected group is in preventing severe postnatal PFD. We hope to perform a model based on our data on nulliparous women, to create a risk scoring system predicting future PFD, to help counseling women about to embark on their first pregnancy.

Funding: SCOPE Ireland was funded by the Health Research Board of Ireland (Grant Reference CSA 2007/2). This study was supported and funded by Continence Foundation Ireland and Science Foundation Ireland. This work was supported in part by a Science Foundation Ireland Program Grant for INFANT (12/RC/2272).

Conflict of interest: None of the authors has anything to disclose or conflict of interest.

Previous presentation: These data has been presented in part at the International Urogynecology Annual meeting in Sydney, Australia, 2012 and at mixed research meeting of Royal College of Obstetricians and Gynaecologists/British Society of Urogynecology 2013.

Acknowledgments

We would like to thank all SCOPE Ireland participants, Continence Foundation Ireland and Irish Centre for Fetal and Neonatal Translational Research (INFANT) for their input into this research project.

References:

1. Bahrapour, T., *The hidden medical epidemic few women have been willing to talk about, until now*. The Washington Post, December 22, 2015(Social Issues).
2. Davies, P.D.S., *Chief Medical Officer calls for action on women's health*. Department of Health, UK, 11 December 2015.
3. MacLennan, A.H., et al., *The prevalence of pelvic floor disorders and their relationship to gender, age, parity and mode of delivery*. BJOG, 2000. **107**(12): p. 1460-70.
4. Dolan, L.M. and P. Hilton, *Obstetric risk factors and pelvic floor dysfunction 20 years after first delivery*. Int Urogynecol J, 2010. **21**(5): p. 535-44.
5. Uustal Fornell, E., G. Wingren, and P. Kjolhede, *Factors associated with pelvic floor dysfunction with emphasis on urinary and fecal incontinence and genital prolapse: an epidemiological study*. Acta Obstet Gynecol Scand, 2004. **83**(4): p. 383-9.
6. Torrisi, G., et al., *A prospective study of pelvic floor dysfunctions related to delivery*. Eur J Obstet Gynecol Reprod Biol, 2012. **160**(1): p. 110-5.
7. Svare, J.A., B.B. Hansen, and G. Lose, *Risk factors for urinary incontinence 1 year after the first vaginal delivery in a cohort of primiparous Danish women*. Int Urogynecol J, 2013.
8. Devore, E.E., V.A. Minassian, and F. Grodstein, *Factors associated with persistent urinary incontinence*. Am J Obstet Gynecol, 2013. **209**(2): p. 145 e1-6.
9. Durnea, C.M., et al., *An insight into pelvic floor status in nulliparous women*. Int Urogynecol J, 2014. **25**(3): p. 337-45.
10. Baessler, K., et al., *Australian pelvic floor questionnaire: a validated interviewer-administered pelvic floor questionnaire for routine clinic and research*. Int Urogynecol J Pelvic Floor Dysfunct, 2009. **20**(2): p. 149-58.
11. Abrams, P., et al., *The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society*. Urology, 2003. **61**(1): p. 37-49.
12. Hendrix, S.L., et al., *Pelvic organ prolapse in the Women's Health Initiative: gravity and gravidity*. Am J Obstet Gynecol, 2002. **186**(6): p. 1160-6.
13. Brown, S.J., et al., *Urinary incontinence in nulliparous women before and during pregnancy: prevalence, incidence, and associated risk factors*. Int Urogynecol J, 2010. **21**(2): p. 193-202.
14. Zorn, B.H., et al., *Urinary incontinence and depression*. J Urol, 1999. **162**(1): p. 82-4.
15. Melville, J.L., et al., *Major depression and urinary incontinence in women: temporal associations in an epidemiologic sample*. Am J Obstet Gynecol, 2009. **201**(5): p. 490 e1-7.
16. Yip, S.O., et al., *The association between urinary and fecal incontinence and social isolation in older women*. Am J Obstet Gynecol, 2013. **208**(2): p. 146 e1-7.
17. Eliasson, K., A. Edner, and E. Mattsson, *Urinary incontinence in very young and mostly nulliparous women with a history of regular organised high-impact trampoline training: occurrence and risk factors*. Int Urogynecol J Pelvic Floor Dysfunct, 2008. **19**(5): p. 687-96.
18. Nygaard, I.E. and J.M. Shaw, *Physical activity and the pelvic floor*. Am J Obstet Gynecol, 2015.
19. Casey, B.M., et al., *Obstetric antecedents for postpartum pelvic floor dysfunction*. Am J Obstet Gynecol, 2005. **192**(5): p. 1655-62.
20. van Brummen, H.J., et al., *Which factors determine the sexual function 1 year after childbirth?* BJOG, 2006. **113**(8): p. 914-8.
21. R., K.K.W.C.W., *Does the mode of delivery influence sexual function after childbirth?* J Womens Health (Larchmt). 2009 Aug. **18**(8): **1227-31**. doi:101089/jwh.2008.1198.
22. Glazener, C., et al., *Childbirth and prolapse: long-term associations with the symptoms and objective measurement of pelvic organ prolapse*. BJOG, 2013. **120**(2): p. 161-8.
23. Heilbrun, M.E., et al., *Correlation between levator ani muscle injuries on magnetic resonance imaging and fecal incontinence, pelvic organ prolapse, and urinary incontinence in primiparous women*. Am J Obstet Gynecol, 2010. **202**(5): p. 488 e1-6.
24. Goldstick, O. and N. Constantini, *Urinary incontinence in physically active women and female athletes*. Br J Sports Med, 2014. **48**(4): p. 296-8.

25. Gartland, D., et al., *The onset, recurrence and associated obstetric risk factors for urinary incontinence in the first 18 months after a first birth: an Australian nulliparous cohort study*. BJOG, 2012. **119**(11): p. 1361-9.
26. Chan, S.S., et al., *Prevalence of urinary and fecal incontinence in Chinese women during and after their first pregnancy*. Int Urogynecol J, 2013. **24**(9): p. 1473-9.
27. Parazzini, F., et al., *Risk factors for stress, urge or mixed urinary incontinence in Italy*. BJOG, 2003. **110**(10): p. 927-33.
28. Hsieh, C.H., et al., *Risk factors of urinary frequency among women aged 60 and older in Taiwan*. Taiwan J Obstet Gynecol, 2010. **49**(3): p. 260-5.
29. Zhang, A.X., et al., *[Multivariate analysis of dyspareunia in women]*. Zhonghua Nan Ke Xue, 2011. **17**(12): p. 1073-7.
30. Durnea, C.M., et al., *The role of prepregnancy pelvic floor dysfunction in postnatal pelvic morbidity in primiparous women*. Int Urogynecol J, 2014.
31. Wu, J.M., et al., *Phenotyping clinical disorders: lessons learned from pelvic organ prolapse*. Am J Obstet Gynecol, 2013. **208**(5): p. 360-5.
32. Allen-Brady, K., et al., *Evidence for pelvic organ prolapse predisposition genes on chromosomes 10 and 17*. Am J Obstet Gynecol, 2015. **212**(6): p. 771 e1-7.
33. Durnea, C.M., et al., *Prevalence, etiology and risk factors of pelvic organ prolapse in premenopausal primiparous women*. Int Urogynecol J, 2014. **25**(11): p. 1463-70.
34. Gyhagen, M., et al., *A comparison of the long-term consequences of vaginal delivery versus caesarean section on the prevalence, severity and bothersomeness of urinary incontinence subtypes: a national cohort study in primiparous women*. BJOG, 2013. **120**(12): p. 1548-55.
35. Qiu, J., et al., *Body mass index, recreational physical activity and female urinary incontinence in Gansu, China*. Eur J Obstet Gynecol Reprod Biol, 2011. **159**(1): p. 224-9.
36. Townsend, M.K., et al., *BMI, waist circumference, and incident urinary incontinence in older women*. Obesity (Silver Spring), 2008. **16**(4): p. 881-6.

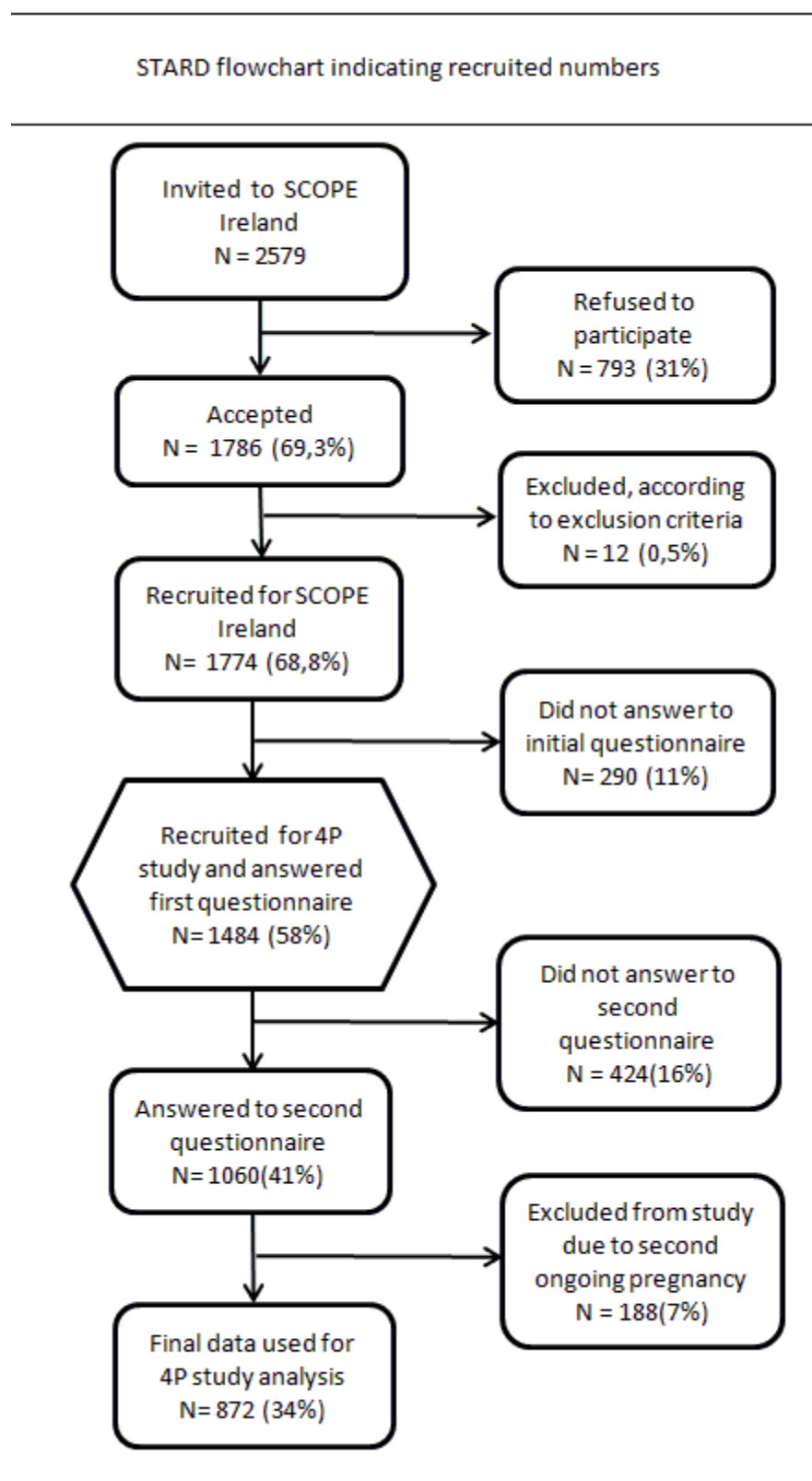
Figure 1. STARD flowchart indicating recruited numbers

Table 1: Demographic characteristics of the population in the 4P-Study (n=872)

Caucasians	858(98.4%) ^A
Age in years	
17-24	73(8.4%)
25-29	251(28.8%)
30-34	415(47.6%)
35-45	133(15.3%)
BMI	
Underweight	12(1.4%)
Normal	489(56.1%)
Overweight	259(29.7%)
Obese	112(12.8%)
Education	
≤12 years	101(12%)
>12 years	771(88%)
Smoking	
Non smokers	661(75.8%)
Smokers	211(24.2%)
Alcohol consumption	
No	176(20.2%)
Yes	696(79.8%)
Mean values ^B	
Age in years	30.5 0(4.2)
BMI	25.0(4.1)
Weight in kg.	67.8(11.8)

^A All values presented as number of cases and (%) of total

^B Data presented as mean value and Standard Deviation (SD)

Table 2. Risk factors associated with PFD in nulliparous women (n=1472)

Risk factors ^A	Univariate analysis			Multivariate analysis		
	OR	[95% CI]	P=	OR	[95% CI]	P=
Urinary dysfunction						
Stress Urinary Incontinence						
Recurrent UTI	1.6	(1.08-2.24)	0.018	1.6	(1.08-2.3)	0.018
High waist/height ratio	638.2	(76.0-5380.0)	<0.001	832.9	(96.21-7211.11)	<0.001
Moderate exercising > 4 times/week	1.5	(1.06-2.2)	0.025	1.8	(1.29-2.38)	<0.001
Diagnosed depression	2.2	(1.41-3.38)	<0.001	2.1	(1.33-3.28)	0.001
Social support (seldom)	1.9	(1.07-3.38)	0.029	1.8	(1.1-3.22)	0.049
Urgency Urinary Incontinence						
Participant's birth weight 1.5 - 2.5kg	19.6	(2.11-182.48)	0.009	13.2	(1.55-111.76)	0.018
Alcohol use (former - stopped previously)	0.4	(0.2-0.95)	0.037	0.5	(0.27-0.96)	0.036
High waist circumference (> 90 centile)	1.01	(1.001-1.04)	0.002	84.4	(6.62-1075.44)	0.001
Diagnosed depression	2.1	(1.24-3.42)	0.005	1.8	(1.09-3.1)	0.022
Urinary Urgency						
Education < 12 years of schooling	1.5	(1.09-1.99)	0.011	1.5	(1.09-2.01)	0.012
Recurrent UTI	1.4	(1.03-1.93)	0.030	1.5	(1.09-2.04)	0.013
Smoker (current: 1-5 cig/day)	2.1	(1.42-3.17)	<0.001	2.1	(1.37-3.08)	<0.001
Vigorous exercising once / week	1.3	(1.04-1.65)	0.022	1.4	(1.08-1.71)	0.012
Diagnosed depression	1.7	(1.17-2.58)	0.006	1.6	(1.08-2.41)	0.019
Bladder section score						
Stable relationship / not married	0.6	(0.41-0.75)	<0.001	0.8	(0.62-0.93)	0.009
Education < 12 years of schooling	1.6	(1.23-2.11)	0.001	1.6	(1.18-2.05)	0.002
Trade workers	1.2	(0.59-0.23)	0.675	5.3	(1.25-22.65)	0.024
Recurrent UTI	2.4	(1.83-3.18)	<0.001	2.5	(1.92-3.36)	<0.001
Smoker (current: 1-5 cig/day)	1.8	(1.01-3.03)	0.047	1.3	(1.01-1.77)	0.042
Diagnosed depression	2.0	(1.36-2.81)	<0.001	1.8	(1.27-2.66)	0.001
Fecal dysfunction						
Flatus incontinence						
Student	0.3	(0.15-0.76)	0.009	37	(1.97-695.56)	0.016
Fecal urgency						
Income \$50-74K / year	1.5	(1.003-2.18)	0.049	1.3	(1.03-1.56)	0.024
High BMI	1.4	(1.08-	0.01	1.3	(1.05-1.66)	0.016

		1.71)	0			
Diagnosed depression	1.9	(1.29-2.92)	0.001	2.1	(1.39-3.22)	<0.001
Social support (Seldom)	1.9	(1.1-3.22)	0.021	2	(1.14-3.42)	0.015
Smoker (current: > 10 cig/day)	0.3	(0.08-0.99)	0.050	0.2	(0.06-0.81)	0.023
Recreational drugs user (current)	1.2	(0.99-1.52)	0.050	1.3	(1.02-1.56)	0.029
Bowel section score						
High waist/height ratio	7.6	(1.6-35.82)	0.011	6.3	(1.31-30.02)	0.022
Diagnosed depression	2.1	(1.45-2.96)	<0.001	2	(1.42-2.93)	<0.001
Social support (never)	1.4	(1.05-1.78)	0.020	1.6	(1.01-2.56)	0.047
Sexual dysfunction						
Vaginal tightness						
Social support (Never)	2.2	(1.22-3.81)	0.008	2	(1.11-3.46)	0.021
Dyspareunia						
Recurrent UTI	1.5	(1.07-2.08)	0.017	1.5	(1.1-2.15)	0.012
Vigorous exercising 2-3 times/week	1.9	(0.95-3.75)	0.069	2.2	(1.08-4.3)	0.029
Diagnosed depression	1.7	(1.09-2.52)	0.018	1.6	(1.06-2.5)	0.025
Social support (Seldom)	1.9	(1.1-3.36)	0.022	2.2	(1.27-3.71)	0.004
Sexual section score						
Education < 12 years of schooling	1.8	(1.35-2.35)	<0.001	1.6	(1.17-2.07)	0.003
Vigorous exercising 2-3 times/week	2.1	(1.12-3.91)	0.020	2.2	(1.19-4.12)	0.013
Social support (Never)	2.4	(1.39-4.02)	0.001	2.2	(1.28-3.65)	0.004

^ARisk factors with $p < 0.05$ only, considered statistically significant, were included in the table.

Risk factors with $p > 0.05$ were included in the table only if univariate result became significant in multivariate analysis

Table 3. Risk factors associated with PFD at 1 year postnatally (n=872)

Risk factors	Univariate analysis			Multivariate analysis		
	OR	[95% CI]	P=	OR	[95% CI]	P=
Urinary dysfunction						
Stress urinary incontinence						
Recurrent UTIs ^A	2.1	(1.41-3.12)	<0.001	2.2	(1.43-3.32)	<0.001
High waist/height ratio	324.5	(32.45-3244.84)	<0.001	168.4	(12.86-2205.8)	<0.001
Poor social support	1.4	(1.01-1.94)	0.045	1.5	(1.03-2.06)	0.032
Stress urinary incontinence pre-pregn.	18.8	(7.3-48.33)	<0.001	15.9	(5.67-44.59)	<0.001
Vacuum delivery	0.7	(0.53-1.04)	0.080	0.6	(0.43-0.87)	0.006
Elective Cesarean Section	0.6	(0.38-0.9)	0.015	0.5	(0.27-0.87)	0.015
Emergency Cesarean Section	0.4	(0.29-0.66)	<0.001	0.3	(0.19-0.6)	<0.001
IOL with prostaglandins + Oxytocin	1.5	(1.04-2.16)	0.032	1.5	(1.02-2.21)	0.037
Urgency urinary incontinence						
Urinary urgency pre-pregn.	11.2	(6.33-19.83)	0.000	10	(2.54-39.12)	0.001
Stress urinary incontinence pre-pregn.	2.8	(1.92-3.96)	0.000	1.6	(1.04-2.55)	0.034
Urgency urinary incontinence pre-pregn.	14.4	(5.09-40.93)	<0.001	6	(1.62-22.04)	0.007
Fetal head circumference	1.1	(1.04-1.26)	0.005	1.2	(1.01-1.3)	0.030
Urinary urgency						
High hip circumference (>95 cm)	1.8	(1.16-2.83)	0.009	1.6	(1.04-2.54)	0.034
Urgency urinary incontinence pre-pregn.	7.4	(2.52-21.86)	0.000	3.2	(1.04-9.95)	0.043
Stress urinary incontinence pre-pregn.	3.4	(2.34-4.81)	0.000	2	(1.4-2.99)	<0.001
Urinary urgency pre-pregn.	23.4	(12.78-42.67)	0.000	17.6	(5.05-61.57)	<0.001
Forceps delivery	1.6	(1-2.48)	0.049	1.8	(1.15-2.91)	0.010
IOL with prostaglandins	1.4	(0.97-2.05)	0.072	1.6	(1.05-2.3)	0.029
Increasing number of terminations of pregnancy	2.2	(0.94-4.93)	0.069	3.8	(1.54-9.36)	0.004
Bladder section score postnatally						
Smoker (current: 6-10 cig/day)	3.6	(0.81-16.33)	0.091	3.2	(1.17-8.84)	0.024
Stress urinary incontinence pre-pregn.	14.3	(1.9-107.51)	0.010	2.8	(1.07-7.34)	0.036
Urinary urgency pre-pregn. (significant)	16.5	(5.09-53.62)	0.000	4.8	(2.44-9.38)	<0.001
High hip circumference (>95 cm)	1.9	(1.16-3.17)	0.011	1.5	(1.05-2.28)	0.028
Poor social support	3.5	(1.18-10.31)	0.024	2.3	(1.13-4.84)	0.023
High urinary dysfunction section score pre-pregn.	8.1	(5.54-11.78)	<0.001	1.1	(1.06-1.2)	<0.001
Perineal tear grade 2	1.7	(1.05-2.64)	0.029	1.9	(1.48-2.43)	<0.001
Fecal dysfunction						
Flatus incontinence						
High hip circumference (>95 cm)	1.4	(1.03-1.94)	0.031	1.4	(1.03-2.03)	0.031
Flatus incontinence pre-pregn.	5.6	(3.19-9.87)	<0.001	7.3	(3.69-14.28)	<0.001
IOL with amniotomy + Oxytocin	2	(0.99-4.06)	0.053	2.3	(1.03-4.91)	0.041
Fecal urgency						
High waist/height ratio	21.9	(2.27-210.83)	0.008	22.6	(2.02-254.26)	0.011
Fecal urgency pre-pregn.	37.1	(18.51-74.34)	<0.001	30	(5.7-157.59)	<0.001
Flatus incontinence pre-pregn.	4.2	(2.39-7.48)	0.000	6.4	(2.05-19.83)	0.001
Bowel section score postnatally						
Participant born small for gestation age	0.6	(0.4-0.96)	0.031	0.5	(0.35-0.81)	0.003
High hip circumference (>95 cm)	1.6	(1.04-2.57)	0.033	1.4	(1.02-1.85)	0.039
Waist circumference (>90 centile)	1.02	(1.01-1.04)	0.011	1.01	(1.001-1.03)	0.036

High fecal dysfunction section score pre-pregn.	3.4	(1.93-6.04)	<0.001	1.5	(1.38-1.54)	<0.001
Fecal urgency pre-pregn.	2.9	(2.06-4.15)	0.000	1.4	(1.04-1.86)	0.026
Sexual dysfunction						
Vaginal laxity						
Poor social support	5.1	(2.16-11.89)	<0.001	3.8	(1.58-8.99)	0.003
Vaginal laxity pre-pregn.	4.7	(2.59-8.37)	<0.001	5	(2.51-9.79)	<0.001
Perineal tear grade 3	3	(1.28-7.08)	0.012	2.4	(1.01-5.64)	0.049
Vaginal tightness / vaginismus						
Smoker (current)	2.5	(1.38-4.42)	0.002	2.2	(1.08-4.68)	0.031
High waist/height ratio	0.02	(0.001-0.38)	0.008	0.003	(0.0001-0.15)	0.003
High sexual dysfunction section score pre-pregn.	1.8	(1.21-2.66)	0.004	1.4	(1.29-1.61)	<0.001
Vigorous exercising	2.3	(0.99-5.46)	0.051	3.1	(1.19-7.84)	0.020
Dyspareunia						
Smoker (current)	3.9	(1.38-11.16)	0.010	4.6	(1.41-14.8)	0.011
High hip circumference (>95 cm)	0.7	(0.47-0.91)	0.011	0.02	(0.001-0.42)	0.012
Dyspareunia pre-pregn.	17.3	(6.72-44.72)	<0.001	5.7	(1.42-22.92)	0.014
Flatus incontinence pre-pregn.	1.6	(0.92-2.8)	0.095	4.2	(1.19-14.87)	0.025
Fecal urgency pre-pregn.	1.8	(1.34-2.33)	<0.001	1.7	(1.20-2.38)	0.003
Perineal tear grade 3	2.1	(0.88-5.04)	0.095	2.6	(1.03-6.57)	0.044
Sexual section score postnatally						
Smoker (current)	2.8	(1.05-7.33)	0.039	3.3	(1.18-9.17)	0.023
High urinary dysfunction section score pre-pregn.	2.1	(1.55-2.84)	0.000	1.1	(1.03-1.12)	0.002
Fecal urgency pre-pregn.	1.6	(1.27-2.09)	0.000	1.5	(1.12-2.03)	0.006
High sexual dysfunction section score pre-pregn.	11.8	(6.8-20.4)	<0.001	1.4	(1.27-1.49)	<0.001
Emergency Cesarean Section	0.7	(0.46-0.94)	0.022	0.4	(0.22-0.84)	0.014
Perineal tear grade 3	2.7	(1.28-5.72)	0.009	2.7	(1.22-5.78)	0.013
Pelvic Organ Prolapse						
Vaginal pressure or heaviness						
Recurrent UTIs	2.1	(1.27-3.52)	0.004	4.4	(1.2-16.47)	0.026
Waist circumference (>90 centile)	1.02	(1.01-1.08)	0.041	1.1	(1.04-1.15)	0.001
Urinary urgency pre-pregn.	1.6	(1.09-2.43)	0.015	3.3	(1.23-8.57)	0.017
Dyspareunia pre-pregn.	2.2	(1.49-3.33)	<0.001	9.9	(1.33-73.25)	0.025
Episiotomy	1.7	(1.14-2.46)	0.009	4	(1.38-11.32)	0.010
LAM ² ballooning	1.1	(1.02-1.12)	0.006	3.1	(1.16-8.21)	0.024
Prolapse sensation						
Recurrent UTIs	2	(1.01-4.04)	0.048	17.3	(3.85-77.45)	<0.001
High prolapse section score pre-pregn.	2.7	(1.1-6.85)	0.030	2.1	(1.24-3.41)	0.005
LAM trauma ^B	6.01	(2.17-16.69)	0.001	15.6	(4.09-59.28)	<0.001
Prolapse section score postnatally						
Recurrent UTIs	1.9	(1.09-3.44)	0.024	4.6	(1.52-13.75)	0.007
Vigorous exercising	3.1	(1.1-8.81)	0.032	17.9	(2.89-110.62)	0.002
High prolapse section score pre-pregn.	4.8	(2.37-9.55)	<0.001	2.3	(1.46-3.68)	<0.001
Dyspareunia pre-pregn.	2.1	(1.35-3.3)	0.001	4.6	(1.93-10.99)	0.001
Urinary urgency pre-pregn.	1.5	(0.99-2.39)	0.053	3.7	(1.57-8.6)	0.003
Vacuum delivery	0.8	(0.46-1.34)	0.383	6.4	(2.23-18.16)	0.001
Forceps delivery	1.8	(0.96-3.25)	0.069	8.8	(3.05-25.23)	<0.001

^AUTI – urinary tract infections

^BLAM – Levator Ani Muscle