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**University College Cork, Ireland**  
Coláiste na hOllscoile Corcaigh

1 **Health-related quality of life in women after colposcopy: Results from a longitudinal**  
2 **patient survey**

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13 **Running title:** Health-related quality of life in women after colposcopy

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23 **Abstract**

24 **Background:** Information concerning the health-related quality of life (HRQoL)  
25 consequences of colposcopy is limited, particularly over time. In a longitudinal study, we  
26 investigated women's HRQoL at 4, 8 and 12 months post-colposcopy and the factors  
27 associated with this.

28 **Methods:** Women attending colposcopy at two large hospitals affiliated with the national  
29 screening programme in Ireland were invited to complete questionnaires at 4, 8 and 12  
30 months post-colposcopy. HRQoL was measured using the EQ-5D-3L and compared across a  
31 range of socio-demographic, clinical and attitudinal variables. A mixed-effects logistic  
32 multivariable model was employed to investigate associations between these variables and  
33 low HRQoL.

34 **Results:** Of 584 women initially recruited, 429, 343 and 303 completed questionnaires at 4, 8  
35 and 12 months, respectively. The mean overall HRQoL score for the sample across all time  
36 points was 0.90 (sd=0.16). Approximately 18% of women experienced low HRQoL at each  
37 of the three time points. In multivariable testing, over the entire 12-month follow-up period,  
38 non-Irish nationals (OR=8.99, 95% CI 2.35-34.43) and women with high grade referral  
39 cytology (OR=2.78, 95% CI 1.08-7.13) were at higher odds of low HRQoL. Women who  
40 were past (OR=0.20, 95% CI 0.07-0.58) or never (OR=0.42, 95% CI 0.16-1.12) smokers  
41 were at lower odds of low HRQoL than current smokers. As women's satisfaction with their  
42 healthcare increased their odds of experiencing low HRQoL fell (OR per unit increase=0.51,  
43 95% CI 0.34-0.75).

44 **Conclusions:** Women's HRQoL did not change over the 12 months post-colposcopy, but  
45 some subgroups of women were at higher risk of experiencing low HRQoL. These subgroups  
46 may benefit from additional support.

47 **Keywords:** Health-related quality of life, colposcopy, cervical screening, longitudinal study  
48 design

49

## 50 **Introduction**

51 Cervical cancer screening is effective in reducing incidence and mortality from cervical  
52 cancer among target populations [1]. To ensure effectiveness of screening, women who  
53 receive positive cytology test results require follow-up investigation, usually a hospital-based  
54 colposcopy. Colposcopy is a very common procedure with 171,874 women undergoing  
55 colposcopy for the first time in England in 2018[2].

56

57 Colposcopy and its related interventions (e.g. biopsies of any areas of the cervical  
58 transformation zone that appear abnormal, or treatment to remove abnormal cervical cells)  
59 are associated with distress and anxiety in women before and during the procedure(s) [3].

60 Concerns around cancer, sex and fertility can also persist after coloscopy and  
61 relatedinterventions [4-8].While an extensive body of literature exists on these dimensions of  
62 quality of life, there is considerably less evidence on validated health-related quality-of-life  
63 (HRQoL) measures, particularly those that are typically used to impute quality-adjusted life  
64 years (QALYS) in health economic evaluations, such as the widely-used EuroQoL EQ-5D  
65 instrument [9]. Information is also limited on factors associated with HRQoL in women  
66 following colposcopy and related procedures and how colposcopy related HRQoL varies over  
67 time [10]. What evidence does exist, particularly from longitudinal studies, is often based on  
68 small samples [6, 11, 12] or includes only women with low-grade abnormal cytology [13].  
69 While it could be hypothesised, given the relationship between anxiety and undergoing  
70 colposcopy, that the procedure would negatively impact HRQoL, it is difficult to draw such  
71 conclusions from the existing literature with some studies finding little to no relationship  
72 between receipt of colposcopy and HRQoL [6, 11], others a modest positive relationship [13]  
73 and still others a negative relationship, albeit short-term [12].

74

75 The discovery of the causal relationship between infection with certain high-risk strains of  
76 human papillomavirus (HPV) and cervical neoplasia [14]has transformed cervical cancer  
77 prevention. Many screening programmes have introduced (or intend to introduce) HPV  
78 testing as their primary screening tool instead of cytology-based testing and many countries  
79 offer vaccination against certain HPV types to young adolescents [15]. To determine how  
80 best to implement cervical cancer prevention in this changing context, the cost-effectiveness  
81 of these newer strategies are being assessed [16-18]. Consequently, new estimates of HRQoL  
82 for use in the calculation of QALYs would appear timely. Although primary HPV screening  
83 has been adopted by programmes, colposcopy is likely to remain a central pillar of follow-up  
84 of women with abnormal screening tests into the future.

85

86 The current study aimed to: (1) assess how women's HRQoL changes over the 12 months  
87 following colposcopy; (2) provide mean utility scores for different clinical and socio-  
88 demographic subgroups for use in (future) cost-effectiveness modelling; and (3) investigate  
89 the factors associated with low HRQoL in the year after colposcopy, as this may identify  
90 subgroups of women who could benefit from additional interventions or supports.

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## 98 **Methods**

### 99 *Setting*

100 The study setting was Ireland, which has a mixed public–private healthcare system. The  
101 national cervical screening programme (CervicalCheck) was introduced in 2008, offering free  
102 cervical cytology tests and follow-up, if needed, to women aged 25–60 years. Women with  
103 two or more low-grade abnormal cervical cytology test results, or one high-grade result, were  
104 referred for colposcopy in a clinic affiliated with the screening programme located in one of  
105 15 maternity hospitals throughout Ireland.

### 106 *Participants and procedures*

107 Women attending two large colposcopy clinics in Dublin, Ireland (The Coombe Women and  
108 Infants University Hospital and the National Maternity Hospital) were recruited to the study  
109 between September 2010–July 2011. Women were eligible if they were referred to  
110 colposcopy because of an abnormal cytology test result in the context of routine screening.  
111 They were eligible irrespective of the management they received at their initial clinic  
112 appointment (i.e. colposcopy only, loop excision, or another form of intervention or  
113 treatment) or subsequent follow-up. The exclusion criteria for the study were pregnancy at  
114 recruitment or treatment for previous cervical abnormalities. A member of the research team  
115 (CW) approached women at the clinics and invited them to participate in the study. For  
116 reasons relating to the clinical and operational circumstances prevailing in the two  
117 recruitment centres, it was not possible to consecutively approach all women attending  
118 clinics. The women were given a study information sheet with more details about the  
119 research. Interested women signed a consent form and returned it to the research team and  
120 were mailed questionnaire packs to complete at 4, 8 and 12 months after their clinic visit.

121

122 The women received no reward or payment for being recruited to the study, however, women  
123 who took part in the study and completed at least one of the questionnaires were offered the  
124 chance to enter into a prize draw to win one of two €150 high street shopping vouchers.  
125 Offering modest incentives such as these has been shown to be the most effective way of  
126 maximizing response rates [19]. Women were not be told about this incentive until they  
127 received their first (~4 month) questionnaire so that it did not affect their willingness to  
128 consent to the study. Ethical approval was obtained from the ethics committees of the  
129 Coombe Women and Infants University Hospital (ref:21-2006) and the National Maternity  
130 Hospital, Dublin (no reference number given).

131 *Assessment of health-related quality of life*

132 HRQoL was measured using the EuroQol EQ-5D 3L [9] included as part of the psychosocial  
133 questionnaire administered at 4,8 and 12 months after the women's initial colposcopy  
134 appointment. The EQ-5D is a widely used instrument for measuring HRQoL, particularly for  
135 health technology assessments (HTAs) and other economic evaluations. A broader  
136 description of the instrument can be found in the EuroQol Research Foundation's User Guide  
137 [20]. The EQ-5D consists of five dimensions: mobility; self-care; usual activities;  
138 pain/discomfort; and anxiety/depression. Each of these dimensions has three response levels  
139 consisting of 1 'no problems', 2 'some problems' and 3 'extreme problems'. These responses  
140 can be linked to utility values ranging from 0-1 (death-full health). No Irish value set is  
141 available, consequently health states were valued using value sets for the UK [21].

142 The distribution of the HRQoL index values was discrete and non-normal. For modelling  
143 purposes, therefore, we defined low HRQoL as a response of “3” in at least one dimension or  
144 an answer of “2” in at least two dimensions.

145

#### 146 *Assessment of potential predictors of health-related quality of life*

147 Information on potential predictors of low HRQoL was obtained from the four-month  
148 questionnaire, which contained questions on a range of socio-demographic and lifestyle  
149 factors [4, 7]. Women’s satisfaction with life and general healthcare were assessed by means  
150 of items adapted from McCaffery et al [22]. Colposcopy clinic records were used to provide  
151 information on colposcopy referral cytology, initial colposcopic impression, initial  
152 management and histology result. Clinical data were extracted from women’s records at the  
153 four month timepoint.

154

#### 155 *Statistical Analyses*

156 Analyses were conducted in Stata 12. Mean HRQoL scores at each follow-up time point (i.e.  
157 4, 8 and 12 months were computed overall and for a range of key socio-demographic and  
158 clinical variables.

159 Because we had longitudinal data, a mixed-effects logistic multivariable regression model  
160 was used to explore associations between socio-demographic, clinical and attitudinal  
161 variables and low HRQoL. This allowed inclusion of all observations across all points [23].  
162 Variables that were significant at the 5% level in univariate logistic analysis were included in  
163 initial multivariable analysis and Wald tests used to determine which remained significant



164 once other independent variables were included. The final model only included variables that  
165 remained statistically significant. Time-point was included in all models, in order to test for a  
166 temporal trend in low HRQoL.

167 As sensitivity analyses, we re-ran the final model with utility scores as a continuous  
168 dependent variable in a mixed-effects linear model. We also changed the specification of  
169 “low” HRQoL so that it included women in the bottom three quartiles and re-ran the final  
170 model. These alternative analyses did not change the variables that attained statistical  
171 significance, nor the direction of their relationship with “low” HRQoL (data not shown).

172 Our study conformed with the Strengthening the Reporting of Observational Studies in  
173 Epidemiology (STROBE) statement [24]. A copy of the completed STROBE checklist for  
174 this study is available in supplementary file [Online Resource 1].

175

## 176 **Results**

### 177 *Characteristics of participants*

178 Of 584 women who consented to participate in the study: 429 (73%); 343 (59%) and 303  
179 (52%) completed questionnaires at 4, 8 and 12 months post-colposcopy respectively.

180 Women’s socio-demographic, clinical lifestyle and attitudinal characteristics at four months  
181 are summarised in Table 1.

### 182 *Temporal trends in HRQoL post-colposcopy*

183 Mean overall HRQoL was static at 0.90 across all three time points (standard deviation  
184 (SD)=0.16 at 4 and 8 months and 0.14 at 12 months). Table 2 details the mean HRQoL scores

185 over time by several key clinical and socio-demographic characteristics. While broadly  
186 HRQoL appeared similar across groups, those without tertiary education had lower mean  
187 HRQoL than those who had. Those who had undergone large loop excision of the  
188 transformation zone (LLETZ) had lower HRQoL than those who had not and those with a  
189 medical card (which is available to those with limited means and provides free healthcare in  
190 the public system) had lower HRQoL than those who did not.

191 75 (18%) women were classified as having “low” HRQoL at four months post colposcopy.  
192 This percentage was unchanged at 8 months (n=57;18%) and 12 months (n=50;18%) post-  
193 colposcopy.

#### 194 *Factors that influence HRQoL over 12 months post colposcopy*

195 The results of univariate analysis of associations between socio-demographic, clinical and  
196 attitudinal variables and low HRQoL testing are presented in Table 3. In the multivariable  
197 model (Table 4), nationality, the woman’s referral cytology, smoking status and satisfaction  
198 with healthcare were significantly related to low HRQoL. The odds of having low HRQoL in  
199 non-Irish women were almost nine times higher than for Irish women (adjusted OR=8.99,  
200 95% CI 2.35-34.43). Odds of low HRQoL was also more than two and half times higher for  
201 women referred for colposcopy on the basis of a high-grade cytology result (OR=2.78, 95%  
202 CI 1.08-7.13). Conversely, women who were either past smokers or who never smoked were  
203 at significantly lower odds of experiencing low HRQoL compared to current smokers (past vs  
204 current smoker: OR=0.20, 95% CI 0.07-0.58; never vs current smoker: OR=0.42, 95% CI  
205 0.16-1.12). Higher levels of satisfaction with general healthcare received were associated  
206 with a lower odds of low HRQoL; with every unit increase in satisfaction on a Likert scale of  
207 1-10 (where 10 indicated complete satisfaction), the odds of experiencing low HRQoL were  
208 reduced by approximately one half (OR=0.51, 95% CI 0.34-0.75).

209 **Discussion**

210 In this longitudinal study we found no discernible change in women's HRQoL over the 12  
211 months post colposcopy; mean HRQoL values were identical at each time point as was the  
212 proportion of women with low HRQoL. In multivariable analysis, we identified two  
213 subgroups of women at higher odds of experiencing low HRQoL: (1) non-Irish women and  
214 (2) women with high-grade abnormal referral cytology. We also found that women who were  
215 not current smokers were less likely to experience low HRQoL and that as women's  
216 satisfaction with their healthcare increased, their odds of experiencing low HRQoL  
217 decreased.

218 *Temporal trends in HRQoL post-colposcopy*

219 Over the course of the three follow-up time points, mean HRQoL remained stable and high at  
220 0.90. It is likely that the high index score reflects the relatively young age distribution of our  
221 study population; EQ-5D Index scores have been shown to decrease with age and younger  
222 respondents report better health status [25]. The pattern of little change over time is in  
223 keeping with most of the (limited) literature in this area. Korfage et al [12] found that both  
224 EQ-5D and EQ-VAS (a visual analogue scale running from 1-100) scores were similar at 1, 3  
225 and 6 months post-colposcopy. Similarly, while Whynes et al [13] found some differences  
226 across time, none of these were greater than the minimum important difference for the EQ-  
227 VAS [26]. Heinonen et al [11] found that HRQoL was worse at 12 months than at baseline,  
228 but this may, in part, be because they used a more sensitive instrument to assess outcomes  
229 [27-29]. The issue of (lack of) sensitivity with respect to the EQ-5D-3L, has been  
230 documented before [28, 29]; this may also be an issue in the context of investigation and  
231 treatment of abnormal cervical cytology [30].

232

233 *Factors that influence HRQoL over 12 months post colposcopy*

234 Women whose referral cytology indicated moderate or severe dyskaryosis (i.e. “high-grade”)  
235 were more likely to be report responses on the EQ-5D consistent with low HRQoL than  
236 women referred to colposcopy with (multiple) low-grade results. This finding appears new to  
237 the literature. Neither Heinonen et al [11] nor Korfage et al [12] found evidence of a  
238 relationship between HRQoL and women’s original cytological abnormality. However, in  
239 both of these studies the numbers of women in the groups with different referral cytology  
240 were substantially smaller than those in our study. In a study of women with low-grade  
241 referral cytology, Whynes et al [13] found a relationship between colposcopy plus LLETZ  
242 management (compared to colposcopy only and colposcopy plus punch biopsies) and lower  
243 HRQoL at some follow-up time points. This association suggests that it is possible our  
244 finding reflects women with high-grade cytology being more likely, than those with low-  
245 grade cytology, to have underlying cervical intraepithelial neoplasia (CIN) grade 2/3 and  
246 undergo LLETZ. Women with high-grade cytology are also more likely to have undergone  
247 additional follow-up procedures. We did not have information on any interventions or  
248 procedures after the initial colposcopy appointment, and this is a limitation of the study.

249 We and others have shown that colposcopy itself, and attending for follow-up, can have an  
250 adverse psychological impact on women with high grade findings, causing significant  
251 anxiety, distress and worries which may be long lasting [31-33]. It is possible that these  
252 adverse psychological effects translate into decrements in HRQoL. For example, Whynes et  
253 al. [34] found the EQ-5D to be responsive to differing degrees of HADS-assessed anxiety and  
254 depression among a large sample (n=3119) of UK women with low grade cervical  
255 abnormalities detected through screening. In that study, a higher likelihood of HADS-  
256 identified anxiety and/or depression was associated with significantly lower EQ-5D index.

257 This suggests that our observed association between high grade dyskaryosis and low HRQoL  
258 may reflect more worries, distress or anxiety in that group.

259 In a previous study analysing this population, non-Irish women were found to be at increased  
260 risk of anxiety after colposcopy [4] and our analysis here finds the same pattern with HRQoL  
261 (i.e. non-Irish women were significantly more likely to be considered to have low HRQoL in  
262 the 12 months after colposcopy than Irish women). To the best of our knowledge, our study is  
263 the first to show this relationship with HRQoL after colposcopy. Disparities in cervical  
264 screening participation among immigrants compared with general population women (e.g. in  
265 Finland and England) have been well documented [35-37], but less is known about the  
266 impacts of screening participation in migrants compared to native populations. The previous  
267 cervical screening history of the women included in our study (both Irish and non-Irish) was  
268 not available. However, it seems unlikely that lack of previous access to screening among  
269 non-Irish women would explain our findings, as all but seven of the thirty-nine non-Irish  
270 women were from another OECD country, and would likely have had some access to smear  
271 tests. Referral cytology was not associated with nationality ( $p=0.581$ ), and the model was  
272 adjusted for this, so this cannot explain the finding either. The number of non-Irish women in  
273 our study population was broadly in line with the number expected based on the nationality  
274 of people resident in Ireland [38]. Historically, the largest group of non-Irish nationals were  
275 UK citizens, but more diverse migration patterns mean that increasingly, non-Irish women  
276 may not speak good English. This may impede them in navigating the healthcare system and  
277 limit their understanding of information about their colposcopy. The Irish cervical screening  
278 programme has produced information leaflets in 11 languages, but these do not include  
279 information about colposcopy and follow-up, nor is information in a suitable language likely  
280 to be the only thing needed to enable a migrant to understand and navigate, and feel confident  
281 within, an unfamiliar healthcare system. More culturally appropriate screening and follow-up

282 literature for non-Irish women is needed for women who have limited English. In addition,  
283 more support, and assistance with patient navigation, for non-Irish women, could help reduce  
284 the risk of low HRQoL in such women following colposcopy.

285 Satisfaction with healthcare also determined whether women reported EQ-5D responses  
286 considered to indicate low HRQoL in the 12 months post colposcopy. While evidence on the  
287 relationship between satisfaction with healthcare and HRQoL is comparatively sparse, a  
288 review by Bamm et al. [39] and colleagues of people living with chronic conditions found a  
289 generally positive relationship between HRQoL and satisfaction with care, consistent with  
290 our findings.

291 In terms of our final predictor of HRQoL, the observed association between current smoking  
292 and low HRQoL measured by the EQ-5D is consistent with relationships in the general  
293 population [40-42], though it is possible that this finding reflects uncontrolled confounding  
294 by comorbidities; smokers have higher prevalence of comorbidities than non-smokers [43].  
295 However, given the young age profile of participants (approximately 70% of participants  
296 were aged forty or younger) and the exclusion of women managed for previous cervical  
297 abnormalities, it is likely that the number of women with significant comorbidities would be  
298 small. There was a greater proportion of current smokers among women with high-grade  
299 disease compared to those with low-grade disease in our study (44% vs 29%) and smoking  
300 status and referral cytology result were significantly associated ( $p=0.018$ ). Previous studies  
301 have observed an association between being a current smoker and low HRQoL [41,42].  
302 However, in our model the effect of smoking was adjusted for referral cytology, so this  
303 cannot account for the observed association with smoking. The likelihood of regression of  
304 cervical precancerous lesions is significantly lower among women who smoke than in never-  
305 smokers [44] and women who smoke are more likely to require follow-up visits to

306 colposcopy clinics and require further treatments to remove cervical abnormalities compared  
307 to non-smokers [45]. This may explain our findings.

308 *HRQoL, colposcopy and the implications for cost-effectiveness modelling*

309 Many healthcare systems are re-evaluating the cost-effectiveness of cervical cancer screening  
310 protocols. Accurate estimates of HRQoL are of great importance to this process. The  
311 numbers of women involved in screening and follow-up are large, meaning that it is arguably  
312 more important to have robust HRQoL data for these health states than for states for which  
313 HRQoL might be lower, but which affect fewer women (e.g. cancer). To the best of our  
314 knowledge, our study represents one of the very few longitudinal studies on HRQoL of  
315 follow-up and which provides QALY weights for use in economic analyses. We have  
316 reported weights both by treatment received and also by histological finding. Ours is one of  
317 the few studies to do both. With respect to treatment received results are largely in keeping  
318 with the available literature. Whynes et al [13], for example, found mean QALY weights for  
319 women who had received a colposcopy (0.906), a colposcopy with biopsy (0.912) and  
320 LLETZ (0.919). These values are close to our own (0.92-0.89, 0.91 and 0.86-0.89  
321 respectively). Our QALY weights by histology are also similar to those found in other studies  
322 [12, 46]. While there were not a sufficient number of women in our sample who had  
323 developed a cancer to report reliable weights for cervical cancer, we feel that these weights  
324 will be of use to cost-effectiveness modellers.

325

326

327

328

329 *Strengths and limitations*

330 Our study is one of only a handful to examine the predictors of low HRQoL in the year after  
331 colposcopy employing a longitudinal study design. With the exception of one UK trial [47],  
332 which only included women with low-grade cytology, our study is also the largest to have  
333 investigated HRQoL after-effects of colposcopy and related interventions. As a generic  
334 questionnaire, the comparative lack of sensitivity of the EQ-5D-3L (and potential  
335 ceiling/floor effects) [48] might mean some factors that concern women following  
336 colposcopy, such as worries about fertility, sex and cancer [4, 49, 50], are not adequately  
337 captured by the instrument. In terms of the explanatory variables considered in the study,  
338 women's clinical data (e.g. initial management received) was extracted from colposcopy  
339 clinic records at 4 months and we lacked information on any procedures that happened  
340 between then and 12 months. The other variables explored for associations with HRQoL also  
341 related to the 4-month time point; if these changed during follow-up the results may be  
342 impacted by some non-differential misclassification. Related to this, although life events have  
343 been shown to have a modest impact on HRQoL [51], we did not collect information on these  
344 or some other variables that influence HRQoL (such as social support) [52], meaning there is  
345 a possibility of some uncontrolled confounding.

346 Women were recruited from only two colposcopy clinics, both were part of the  
347 CervicalCheck screening programme. However, the hospitals in which they were located  
348 serve large numbers of patients from diverse backgrounds. For logistical reasons related to  
349 running a research study within busy hospital clinics, we were not able to systematically  
350 approach every woman in every clinic. It is possible that some particular groups of women  
351 were not approached (e.g. those visibly upset). While the way the women who took part in  
352 the study were recruited may affect overall estimates of HRQoL (i.e. we may have  
353 overestimated this), internal comparisons within the study population will not necessarily be



354 impacted. Women who completed and returned at least one of the three questionnaires were  
355 offered the chance to enter into a prize draw to win one of two high street shopping vouchers.  
356 While modest incentives such as these are effective in improving questionnaire response rates  
357 [19], we cannot entirely preclude the possibility that they influenced (directly or indirectly)  
358 HRQoL as measured in the study participants. However, the authors are unaware of any  
359 empirical evidence to support this; indeed most studies show that incentives have no effect on  
360 quality of response, sample composition or response distributions [53].

361

## 362 **Conclusion**

363 While mean HRQoL the proportion of the sample considered to have low HRQoL, remained  
364 static over 12 months following colposcopy, some subgroups of women were at greater risk  
365 of low HRQoL. In particular non-Irish women and women whose referral cytology was high-  
366 grade had a significantly greater chance of low HRQoL. As well as providing information to  
367 inform cost-effectiveness analyses, our findings may aid policymakers, service providers and  
368 patient advocacy groups to better target supports and advice for women who have received a  
369 colposcopy thereby minimising the risk of them experiencing low health-related quality of  
370 life.

## **Declarations**

## **Acknowledgements**

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## **Author contributions**

AÓC analysed the data and wrote the paper. MOC conducted the survey, analysed the data and wrote the paper. KOB analysed the data and wrote the paper. JOL, CM, TD and GF conceived and designed the experiments and wrote the paper. JM conducted the survey and wrote the paper. WP and CR conceived and designed the experiments and wrote the paper. CW conducted the survey and wrote the paper. LP conceived and designed the experiments and wrote the paper. LS conceived and designed the experiments, analysed the data and wrote the paper. All authors read and approved the manuscript

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## **Compliance with ethical standards**

## **Conflict of interest**

The authors have no conflicts of interest relevant to this manuscript.

## **Ethical approval**

Ethical approval was obtained from the ethics committees of the Coombe Women and Infants University Hospital (ref:21-2006; approval granted 27 April 2010) and the National Maternity Hospital, Dublin (no ref. number given; approval granted 26<sup>th</sup> October 2010).

### **Informed consent**

Written informed consent was obtained from women interested in partaking in the study.

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