ON THE MODE OF HYSTERECTOMY

WITH EMPHASIS ON RECOVERY AND WELL-BEING

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On the mode of hysterectomy
- with emphasis on recovery and well-being.
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‘I will never be an old man. To me, old age is always 15 years older than I am.’

Francis Bacon

To my beloved Joar
List of publications

This thesis is based on the following original articles, which are referred to in the text by their Roman numerals.


III. Persson P, Brynhildsen J, Kjølhede P. A one-year follow-up of psychological well-being after subtotal and total abdominal hysterectomy - a randomised study. Accepted for publication.

IV. Persson P, Brynhildsen J, Kjølhede P. Short term recovery after subtotal and total abdominal hysterectomy - a randomised clinical trial. Submitted to BJOG.

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### Abbreviations

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<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AH</td>
<td>Abdominal hysterectomy</td>
</tr>
<tr>
<td>BDI</td>
<td>Beck Depression Inventory</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CIN</td>
<td>Cervical intraepithelial neoplasia</td>
</tr>
<tr>
<td>FSH</td>
<td>Follicle-stimulating hormone</td>
</tr>
<tr>
<td>GnRH</td>
<td>Gonadotropin-releasing hormone</td>
</tr>
<tr>
<td>HT</td>
<td>Hormone therapy</td>
</tr>
<tr>
<td>LAVH</td>
<td>Laparoscopically assisted vaginal hysterectomy</td>
</tr>
<tr>
<td>LH</td>
<td>Laparoscopic hysterectomy</td>
</tr>
<tr>
<td>LSH</td>
<td>Laparoscopic supracervical hysterectomy</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PGWB</td>
<td>Psychological General Well-Being Inventory</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of life</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>RDD</td>
<td>Recommended daily dose</td>
</tr>
<tr>
<td>SCI</td>
<td>Stress Coping Inventory</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SH</td>
<td>Subtotal abdominal hysterectomy</td>
</tr>
<tr>
<td>SHBG</td>
<td>Sex hormone-binding globulin</td>
</tr>
<tr>
<td>STAI</td>
<td>State-Trait Anxiety Inventory</td>
</tr>
<tr>
<td>TH</td>
<td>Total abdominal hysterectomy</td>
</tr>
<tr>
<td>VH</td>
<td>Vaginal hysterectomy</td>
</tr>
<tr>
<td>WHQ</td>
<td>Women’s Health Questionnaire</td>
</tr>
<tr>
<td>WMD</td>
<td>Weighted mean difference</td>
</tr>
</tbody>
</table>
‘A more cruel, bloody and ill-judged operation is not, we think, recorded in the annals of surgery. We consider the extirpation of a uterus not previously protruded or inverted, one of the most cruel and unfeasible operations that ever was projected or executed by the head or hand of man.’

Foreword

Hysterectomy is the surgical removal of the uterus and it is the most common major gynaecological surgical procedure worldwide. It has a broad spectrum of indications ranging from malignant gynaecological disease to obstetrical indication. Regardless of mode, hysterectomy is most often performed for benign conditions such as irregular uterine bleeding with or without uterine fibroids, and the operation is done in order to improve the patient’s Quality of life (QoL). Hysterectomy is most often indicated when medical treatment or less invasive methods have failed [SKL 2008; NICE 2007; Lefebvre 2002].

Much research has been done in the field of hysterectomy. A PubMed search (8 March 2009) on “hysterectomy” gave 28,983 matches where the oldest reference was dated from 1892. In my training years as a registrar I worked at two different hospitals in the same region and found that the local policy regarding the choice of mode of hysterectomy varied. Local debate focused mainly on surgical methods [Dabrosin 1990]. During the same period, laparoscopic hysterectomy was introduced and as a gynaecologist with a surgical interest this technique seemed to me to be promising because of its less invasive character. It struck me that the decision for making a hysterectomy was not only to find a proper indication for surgery but also the challenge of finding an optimal approach. This makes hysterectomy unique and thus distinct from many other surgical procedures. Added to this, the strong mystical value of the uterus has as a ‘bearer of life’ made me interested in the patient’s psychological-well-being after hysterectomy. Reading the literature, I found that indications, surgical methods, complications, risks and benefits had been much debated during the past 75 years or more. In the 1950s when scientific and technological advances had made the procedure safe, work directed at the evaluation of the outcome of hysterectomy in such broader terms as social, psychological and sexual well-being was started. The early results were contradictory and there were no randomised studies that focused on psychological well-being in women after different modes of hysterectomy. From this, my thesis developed.
Introduction

Short history of hysterectomy

The origins of hysterectomy are unclear but removal of a prolapsed gangrenous uterus is mentioned by Soranus in a manuscript dated almost two thousand years ago [Temkin 1956]. Berengario from Bologna is given credit for the first authentic description of the removal of the uterus through the vagina, a procedure which is dated 1517 [Garrison 1929]. The first abdominal hysterectomy was a subtotal hysterectomy (SH) performed by Charles Clay in Manchester 1843. The procedure was indicated by an adnexal mass that in fact was a large fibroid and the corpus of the uterus was removed. Despite the successful operation the patient died on the 15th postoperative day [Clay 1863]. Since then, focus on the indications and methods for performing a hysterectomy has changed several times. From the beginning, abdominal hysterectomy was always performed as a subtotal hysterectomy and total abdominal hysterectomy (TH) was first described 1878 [Freund 1878). The technique of TH as we know it today was first introduced by Richardsson 1929. He advocated the total procedure in order to prevent the development of cervical carcinoma [Richardsson 1929]. Despite this, subtotal hysterectomy was by far the most common method until the 1950s. With the development and availability of antibiotics and blood transfusions the trend turned towards TH in order to prevent cervical carcinoma.

In 1984 Semm suggested the use of laparoscopic technique in hysterectomy but the first actual laparoscopic hysterectomy was reported by Reich in 1989 [Semm 1984; Reich 1989]. This was a total laparoscopic procedure. The laparoscopically assisted vaginal hysterectomy (LAVH), described by Kovacs in 1990, was soon adopted because of a less demanding surgical technique and shorter operating time [Kovacs 1990]. Various classifications of the laparoscopic hysterectomy technique followed leading to the currently accepted classification system where laparoscopic dissection including clamping of the uterine arteries is the border used to classify the hysterectomy as a laparoscopic hysterectomy (LH) or a laparoscopically assisted vaginal hysterectomy even though the specimen is removed through the vagina in both methods [Garry 1994].

After the introduction of the laparoscopic technique of removing the uterus, the method soon became popular among gynaecologists. Ironically, the emergence of laparoscopic assisted vaginal hysterectomy also resulted in a rebirth of vaginal hysterectomy.
Gynaecologists who had previously only been familiar with vaginal hysterectomy for prolapse began to realize that the vaginal portion of laparoscopic assisted vaginal hysterectomy was easier, safer and quicker than using the laparoscope alone.

**Hysterectomy in Sweden**

In Sweden 7,712 hysterectomies were performed in 2007 [Socialstyrelsen 2009]. The number of hysterectomies in relation to different modes of hysterectomy during the last decade is shown in Table 1. In Sweden as in most other Western countries TH has been the predominant mode of hysterectomy until today. In an international perspective the relative proportion of subtotal hysterectomies in Sweden has been high [Gimbel 2007].


<table>
<thead>
<tr>
<th>Year</th>
<th>TH</th>
<th>SH</th>
<th>LSH</th>
<th>TLH</th>
<th>LH</th>
<th>LAVH</th>
<th>VH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>6027</td>
<td>1876</td>
<td>151</td>
<td>126</td>
<td>157</td>
<td>153</td>
<td>1043</td>
<td>9533</td>
</tr>
<tr>
<td>1999</td>
<td>6136</td>
<td>1879</td>
<td>141</td>
<td>162</td>
<td>63</td>
<td>152</td>
<td>1158</td>
<td>9691</td>
</tr>
<tr>
<td>2000</td>
<td>5676</td>
<td>1631</td>
<td>106</td>
<td>112</td>
<td>62</td>
<td>75</td>
<td>1421</td>
<td>9083</td>
</tr>
<tr>
<td>2001</td>
<td>5638</td>
<td>1489</td>
<td>82</td>
<td>67</td>
<td>18</td>
<td>92</td>
<td>1403</td>
<td>8789</td>
</tr>
<tr>
<td>2002</td>
<td>5556</td>
<td>1440</td>
<td>94</td>
<td>62</td>
<td>28</td>
<td>69</td>
<td>1489</td>
<td>8738</td>
</tr>
<tr>
<td>2003</td>
<td>5516</td>
<td>1428</td>
<td>87</td>
<td>58</td>
<td>31</td>
<td>84</td>
<td>1644</td>
<td>8848</td>
</tr>
<tr>
<td>2004</td>
<td>5427</td>
<td>1314</td>
<td>62</td>
<td>48</td>
<td>11</td>
<td>116</td>
<td>1693</td>
<td>8671</td>
</tr>
<tr>
<td>2005</td>
<td>5365</td>
<td>1228</td>
<td>45</td>
<td>48</td>
<td>9</td>
<td>110</td>
<td>1623</td>
<td>8437</td>
</tr>
<tr>
<td>2006</td>
<td>4844</td>
<td>1054</td>
<td>34</td>
<td>57</td>
<td>17</td>
<td>133</td>
<td>1401</td>
<td>7559</td>
</tr>
<tr>
<td>2007</td>
<td>4991</td>
<td>948</td>
<td>32</td>
<td>76</td>
<td>16</td>
<td>138</td>
<td>1523</td>
<td>7712</td>
</tr>
</tbody>
</table>


**Trends and attitudes to mode of hysterectomy**

Hysterectomy rates have decreased during the past two decades. In a Danish report, the number of total abdominal hysterectomies (TH) decreased 38% from 1988 to 1998. However, during the same period the number of subtotal abdominal hysterectomies (SH) increased by 458%. In 2001, abdominal hysterectomy still accounted for 80% of the hysterectomies in Denmark [Gimbel 2001]. The same trend has also been seen in the US [Farquhar 2002; Jacobson 2006]. In Sweden, the number of hysterectomy has decreased approximately 20% in the last 10 years. The relative proportion of TH has been stable during
the period but the proportion of VH has increased from 11 % to 20% at the cost of SH and LH. The reasons for the increased frequency of SH are unclear, but may be based on suppositions related to female sexual response supported by some Scandinavian studies as well as the facilitation of laparoscopic hysterectomy techniques [Kilkku 1983a,b; Helström 1994; Hasson 1993]. The increased popularity for VH in Sweden can partly be attributed to a single gynaecologist, who by dedicated programs with live hands-on teaching and training taught gynaecologists the technique of VH [Ottosen 1997]. In a recently published survey, the most preferred method of choice for hysterectomy on benign indication among Swedish gynaecologists was VH [Persson 2009]. Interestingly only 53% of the clinically active gynaecologists performed VH independently. Corresponding figures for TH/SH and LH were 90% and 20% respectively.

Quality of life and Psychological well-being

Quality of life (QoL) is a broad term that theoretically incorporates all aspects of an individual’s life. There is no universally accepted definition but according to the medical and nursing science literature QoL can be summarised in terms of physical, psychological, social and financial well-being [Padilla 1992; Sullivan 1992]. This corresponds well with the definition used by the World Health Organisation [WHOQOL group 1995]. Since hysterectomy is mostly performed for benign conditions, i.e. the goal is to improve QoL, assessing these aspects is important. Consequently, ‘better health’ and ‘going back to normal life’ have been reported as major expectations following hysterectomy [Bernhard 1992]. Measurement of psychological well-being includes general measures covering several parts of the general psychological well-being as well as specific measures that have been developed to detect changes in a specific domain of psychological well-being, or to be used as diagnostic tools. In the context of the present thesis measures are used to detect changes in the different states of psychological well-being and not as diagnostic tools for psychiatric illness. When the terms anxiety and depression are used they refer to feelings of anxiety, nervousness, tenseness, depressions, moodiness, downheartedness, i.e. anxiety and depressive states.
**Hysterectomy and Psychological well-being**

The results of previous studies on psychological well-being after hysterectomy are conflicting. A review of 21 studies from the 1960s and 70s found that 15 of the included studies showed undesirable psychological reactions to hysterectomy and some studies suggested that hysterectomy increased psychological problems and even caused psychiatric disorders [Meikle 1977]. These studies had severe methodological limitations. Most of them either lacked baseline measurement of the mental health or control groups and only a few used validated and standardised measures.

More recent prospective studies where women report their psychological well-being before and after surgery show improved psychological well-being after the hysterectomy for the vast majority of the women [Ryan 1989; Carlson 1994; Kjerulff 2000a,b]. In one of these studies complications, QoL, psychological and sexual functioning were evaluated. Significant improvements in depression and anxiety states were found after hysterectomy, although women who reported high levels in depressive state at baseline were more likely to have a poor outcome, defined as reporting more negative symptoms [Kjerulff 2000a]. Gath and co-workers found that women referred to hysterectomy had a higher psychiatric morbidity than women in the general population. The morbidity decreased after hysterectomy but was still higher than in the general population. This was explained by the preoperative morbidity and there was no evidence that the hysterectomy per se led to deterioration of psychiatric pathology [Gath 1982a,b]. Davies and Doyle showed that after surgery, the depressive state of the women in the hysterectomy group was similar to that of the women in the general population [Davies 2002].

The impact of the mode of hysterectomy on psychological well-being is poorly investigated. Twenty-five of the 27 studies included in the Cochrane review regarding hysterectomy on benign indication include the laparoscopic route. Psychological well-being was not included in any of the studies [Johnson 2006]. None of the previously published randomised studies on TH and SH has primarily focused on psychological well-being [Thakar 2002; Gimbel 2003; Learman 2003; Gorlero 2008].
**Hysterectomy and Short-term recovery**

Recovery after hysterectomy is, as reported in the literature, often measured as the time in hospital or the time to return to work and is considered a short-term outcome measure. This includes all Cochrane reviews regarding surgical methods of hysterectomy that have been published [Johnson 2006; Lethaby 2006; Lethaby 2009]. A well defined time for measuring recovery is lacking but five to six weeks postoperatively is usually used. Since time in hospital as well as time to return to work are influenced by several factors such as postoperative pain, occurrence of complications, local tradition and even the physician’s discretion it is important to assess the recovery properly. In the Cochrane review of hysterectomy on benign indication [Johnson 2006], 24 of the 27 trials included in the review assessed the length of post-operative hospital stay. Recovery time or the time needed to return to normal activities/work was assessed in 12 trials. None of these issues were listed as primary outcomes. Postoperative pain was assessed in 11 trials. All of the trials assessed the operation time and intra- or postoperative complications and the majority (22 trials) assessed blood loss or change in haemoglobin levels. In a recent up-date of this review (2009) the authors conclude that the selective reporting of ‘interesting’ results is a threat to the reliability of both the conclusions of the individual studies and the review. No studies regarding the actual speed of recovery after hysterectomy have been made.

**Personality and Preoperative psychological well-being**

Preoperative depression has been shown to be a predictor of a poor postoperative psychological outcome after hysterectomy. There is, however, no evidence that hysterectomy per se is a risk factor for development of depression [Gath 1982b, Gath 1995; Kjerulff 2000a,b]. How personality and coping abilities may influence the psychological outcome after hysterectomy is poorly investigated. There is some evidence that personality factors such as masculinity and hardiness may influence psychological outcome postoperatively [Ryan 1989; Thornton 1997], but how coping abilities and personality factors are associated with the short-term recovery process has not been investigated.
Complications of hysterectomy

Hysterectomy is usually carried out as elective surgery to cure a non life threatening condition. It is supposed to have a low mortality rate and a low risk of complications peroperatively and in the postoperative period. It should also have a high success rate in curing the symptom(s) on which the decision to operate was based without leaving the patient with any new problems. Today hysterectomy, regardless of surgical method, is a safe procedure with low risk of complications. Because of the relative short follow-up times in the randomised trials concerning hysterectomy, results from observational studies are an important complement. The largest prospective observational study of hysterectomy published so far (n = 37 295 cases) reported that complications occurred peri- and postoperatively in 3% and 1%, respectively. Hysterectomy for fibroids was associated with significantly more complications than hysterectomy for women with dysfunctional uterine bleeding (adjusted OR 1.34; 95% CI 1.14 to 1.56). LAVH doubled the risk of operative complications compared with abdominal hysterectomy (AH) (adjusted OR 1.92; 95% CI 1.48 to 2.50). Both VH and LAVH techniques had a significantly higher risk of complications than AH (adjusted OR 1.39; 95% CI 1.01 to 1.90 and adjusted OR 1.64; 95% CI 1.00 to 2.68, respectively). Fourteen deaths were reported within the 6-week period following surgery [McPherson 2004]. Complication rates from randomised controlled trials (RCTs) and observational studies are shown in Table 2 and 3.

Table 2. Hysterectomy complication rates reported in RCTs (n= 3,643) included in the Cochrane review [Johnson 2006]. Modified from NICE guideline “Heavy menstrual bleeding” CG44. 2007

<table>
<thead>
<tr>
<th>Complication</th>
<th>AH</th>
<th>VH</th>
<th>LH/LAVH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood transfusion (%)</td>
<td>3.33</td>
<td>3.87</td>
<td>4.23</td>
</tr>
<tr>
<td>Bowel injury (%)</td>
<td>0.67</td>
<td>0.00</td>
<td>0.20</td>
</tr>
<tr>
<td>Vascular injury (%)</td>
<td>0.77</td>
<td>0.94</td>
<td>1.81</td>
</tr>
<tr>
<td>Pelvic haematoma (%)</td>
<td>6.00</td>
<td>4.04</td>
<td>3.94</td>
</tr>
<tr>
<td>Vaginal cuff infection (%)</td>
<td>2.06</td>
<td>1.93</td>
<td>4.15</td>
</tr>
<tr>
<td>Wound abdominal wall infection (%)</td>
<td>7.38</td>
<td>0.00</td>
<td>1.92</td>
</tr>
<tr>
<td>Laparotomy (%)</td>
<td>---</td>
<td>2.66</td>
<td>4.17</td>
</tr>
<tr>
<td>Urinary tract injury (bladder or urethral) (%)</td>
<td>0.86</td>
<td>1.60</td>
<td>2.33</td>
</tr>
<tr>
<td>Urinary tract infection (%)</td>
<td>4.87</td>
<td>1.27</td>
<td>4.77</td>
</tr>
<tr>
<td>Infection unspecified (includes febrile morbidity) (%)</td>
<td>13.15</td>
<td>7.73</td>
<td>10.01</td>
</tr>
<tr>
<td>Thromboembolism (%)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.59</td>
</tr>
</tbody>
</table>
Table 3. Hysterectomy complication rates reported by long-term cohort studies.

<table>
<thead>
<tr>
<th>Complication</th>
<th>AH</th>
<th>VH</th>
<th>LH/LAVH/TLH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.38 per 1000 (95% CI: 0.25 - 0.64) (within 6 weeks; for all modes of hysterectomy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major perioperative complications (%)</td>
<td>3.6</td>
<td>3.1</td>
<td>6.1</td>
</tr>
<tr>
<td>Major postoperative complications (%)</td>
<td>0.9</td>
<td>1.2</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Major complications included deep venous thrombosis, pulmonary embolism, myocardial infarction, renal failure, cerebrovascular accident, septicaemia, necrotising fasciitis, secondary haemorrhage, fistula, ureteric obstruction and visceral damage.
Specific Background for the studies

The introduction of LH was also the starting point for several randomised studies where different modes of hysterectomy were compared. It was widely believed that the method would have less impact on the patient’s surgical and psychological outcome, i.e. operating trauma, time in hospital, recovery and sick-leave. Some authors stated that the laparoscopic technique was the future for hysterectomy and that it could replace both abdominal and vaginal hysterectomy [Liu 1992; Garcia-Padial 1992; Wood 1997]. In almost all of the randomised studies performed, the focus was placed on surgical outcome and this is reflected in the Cochrane review “Surgical approach to hysterectomy for benign gynaecological disease” where 25 of 27 studies include LH/LAVH [Johnson 2006]. The review does not however include psychological well-being as an outcome. When our first randomised trial (LH vs. AH) was started, there were no randomised studies comparing modes of hysterectomy published that focused on psychological well-being. Later, one Swedish study showed no difference in postoperative psychological well-being measured by Psychological General Well-Being Inventory (PGWB) in women undergoing LH and AH but the time in hospital and sick-leave was shorter in the laparoscopic group [Ellström 2003]. Where the explanation is to be found for the reported speedier recovery after laparoscopic hysterectomy is ambiguous. Since none of the randomised studies in this field are blinded and since measures of the day-by-day recovery are lacking, there is an obvious risk for bias in the results regarding both time in hospital and sick-leave.

Regarding SH, the operation was abandoned in favour of TH by most gynaecologists in the 1950s because of the possibility of treating infections and giving blood transfusions and thereby reducing serious postoperative complications. The focus of attention was paid to the reduction of the risk of cervical cancer in the remaining cervical stump. However, in Scandinavia SH became the object of renewed interest when Kilkku in 1983 published retrospective studies in which he concluded that some aspects of the woman’s sexuality, e.g. libido and orgasm, were better after SH compared with TH, and this was supported ten years later by a Swedish study by Helström who found favourable effects on orgasm and coital frequency. Unfortunately, the studies by Kilkku lacked a baseline measure and the study by Helström lacked a comparison group [Kilkku 1983a,b; Helström 1994].
The reappearance of an international interest in SH came after the introduction of the laparoscopic supracervical hysterectomy in the early 1990s which was accompanied by publications in which some researchers stated the advantages of the supracervical approach [Semm 1991; Hasson 1993; Lyons 1993]. Preservation of a normal organ, a reduced surgical risk and a more rapid recovery were all seen as reasons for the supracervical approach. With this debate came a need for randomised trials comparing SH with TH. Once again short-term surgical outcomes became the centre of attention, but there was also an increase in interest in evaluation outcomes regarding bladder, bowel and sexual function [Munro 1997; Scott 1997; Thakar 1997]. In Sweden a consensus conference in 1993 led to a request for randomised studies comparing SH and TH [Cullhed 1993]. Yet when our second randomised trial was started in 1998 there was still no randomised study that had been published on this issue.

Although some years have passed since these studies were initiated there is still a need for studies to aid clinicians in identifying individuals at risk of developing a poor quality of life or experiencing psychological disturbances after a hysterectomy [Rannestad 2005].

This thesis deals with hysterectomy on benign, non-prolapse indication in perimenopausal women. Focus is set on recovery (short-term) and psychological well-being (long-term) outcome and different methods of hysterectomy are compared in two different randomised controlled trials. The factors associated with recovery and psychological well-being are analysed in these studies.
Theory and Hypotheses

It has been felt that the level of postoperative recovery, psychological and general well-being in women after hysterectomy depends on the surgical method used. LH and SH are both considered to be less invasive than TH. The less invasive a surgical method is, the better the outcomes in the domains of psychological and general well-being are thought to be.

On the basis on the considerations described above I developed a series of hypotheses.

- Laparoscopic hysterectomy provides better psychological well-being and a faster short-term recovery than abdominal hysterectomy.

- A high stress-coping ability is favourable for postoperative psychological well-being after hysterectomy.

- Subtotal abdominal hysterectomy leads to better psychological well-being than total abdominal hysterectomy.

- Subtotal hysterectomy is associated with a lower complication rate and thus gives a faster day-by-day recovery of general well-being than total hysterectomy.

- Psychological well-being is expected to improve after hysterectomy regardless of mode of surgery.

The aims of the study were then formulated on the basis of these hypotheses.
‘Considering the time man has inhabited this planet, the history of hysterectomy is comparatively short and we have undoubtedly come a long way. Our pioneering forefathers had to contend with a horrendous mortality rate and very high morbidity, but with technological advances made during this century, particularly with regard to antisepsis and antibiotic prophylaxis of infection, together with safe anaesthesia, intravenous fluids and blood transfusion, the procedure is now very safe with a mortality rate of approximately 12 per 10 000 (Bachmann, 1990) and is increasingly performed to improve quality of life, rather than to save life.’

Aims of the thesis

- to evaluate the influence of laparoscopic hysterectomy and abdominal total hysterectomy on postoperative psychological well-being and surgical measures.

- to study whether the day-by-day recovery of general well-being is faster in women undergoing laparoscopic hysterectomy compared with total abdominal hysterectomy.

- to analyse the association between stress-coping and the day-by-day recovery of general well-being and sick-leave in women undergoing laparoscopic hysterectomy compared with total abdominal hysterectomy.

- to determine whether long-term psychological well-being differs between women who have undergone subtotal hysterectomy and those who have had total abdominal hysterectomy.

- to analyse psychological well-being in women after subtotal and total abdominal hysterectomy taking into account the influence of postoperative complications and sex hormone levels.

- to establish whether the short-term recovery of general well-being differs between women undergoing subtotal and total abdominal hysterectomy.

- to analyse factors associated with the postoperative recovery in women after subtotal and total abdominal hysterectomy.
Material and Methods

Study designs and populations

This thesis is based on two separate randomised multicenter trials; Trial 1, laparoscopic hysterectomy (LH) versus abdominal hysterectomy (AH) and Trial 2, total abdominal hysterectomy (TH) versus subtotal abdominal hysterectomy (SH). The timeline and assessments in the trials are shown in Fig. 1. The flowcharts for each trial are shown in Fig. 2 and 3.

<table>
<thead>
<tr>
<th>Event</th>
<th>Trial 1</th>
<th>Trial 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of hysterectomy</td>
<td>LH vs. AH</td>
<td>SH vs. TH</td>
</tr>
<tr>
<td>Baseline 1 week prior to surgery</td>
<td>demographic data psychometric tests start of diary Stress Coping Inventory (SCI)</td>
<td>demographic data psychometric tests start of diary sex hormones</td>
</tr>
<tr>
<td>Surgery</td>
<td>peroperative data</td>
<td>peroperative data</td>
</tr>
<tr>
<td>5-weeks</td>
<td>clinical examination complications psychometric tests diary collected</td>
<td>clinical examination complications diary collected</td>
</tr>
<tr>
<td>6-months</td>
<td>clinical examination psychometric tests</td>
<td>psychometric tests</td>
</tr>
<tr>
<td>12-months</td>
<td>END OF TRIAL</td>
<td>clinical examination psychometric tests sex hormones END OF TRIAL</td>
</tr>
</tbody>
</table>

Figure 1. Time-line and assessments in trial 1 and 2. The psychometric tests include Psychological General Well-being (PGWB); Women’s Health Questionnaire (WHQ); State Trait Anxiety Inventory (STAI); Beck Depression Inventory (BDI).
In both trials a table of random numbers for randomisation and serially numbered sealed opaque envelopes for allocation of concealment were used [Lentner 1982]. The trials were approved by the ethics research committee of the Faculty of Health Sciences, Linköping University (trial 1 and 2) and Regional Hospital, Örebro (trial 2).

**Trial 1 (paper I and II)**

This was a randomised, multicenter study of laparoscopic hysterectomy versus abdominal hysterectomy. The Departments of Obstetrics and Gynaecology at five hospitals in the South-East Health Region of Sweden participated in the study. The hospitals were two county hospitals, two central hospitals and one university hospital. Women admitted to the departments for hysterectomy due to benign gynaecological conditions between October 1996 and May 2003 were eligible for the study. Only women in whom laparoscopic hysterectomy was considered possible by the surgeon were enrolled in the study. Women with hysterectomies carried out in association with operations for benign ovarian tumours or genital prolapse were not enrolled.

Medical inclusion criteria were meno-metrorrhagia, dysmenorrhoea, dysplasia (CIN I-III) of the cervix, endometrial hyperplasia without atypia, fibroids or other benign gynaecological diseases. At least one ovary was to be preserved at the operation. Exclusion criteria were genital tract malignancy, preoperative treatment with GnRH analogues, postmenopausal women without hormone therapy (HT), and severe psychiatric disorders. Patients with HT were allowed to participate in the study if the HT was continued until the last follow up six months postoperatively.
Randomised
(n = 125)

Allocated to laparoscopic hysterectomy
(n = 64)

Converted to abdominal hysterectomy due to complication or technical reason (n = 3)

Received allocated intervention
(n = 61)

Withdrew consent before 5-weeks follow-up. (n = 1)

Completed the study
(n = 60)

Intention-to-treat analysis:
Converted to abdominal hysterectomy.
(n = 3)

Analysed
(n = 63)

Did not complete diary (n = 1)

Analysed
(n = 62)

Allocated to abdominal hysterectomy
(n = 61)

One patient withdrew consent prior to surgery
(n = 1)

Withdrew consent before 5-weeks follow-up. (n = 4)

Completed the study
(n = 59)

Analysed
(n = 56)

Did not complete diary (n = 1)

Analysed
(n = 55)
Trial 2 (paper III and IV)

The Departments of Obstetrics and Gynaecology at seven hospitals and one private gynaecological clinic in the South-East Health Regions of Sweden participated in this randomised multicenter study of subtotal abdominal hysterectomy versus total abdominal hysterectomy. The hospitals comprised three county hospitals, three central hospitals, and one university hospital. Women admitted for hysterectomy due to benign gynaecological conditions, between March 1998 and April 2004, were eligible for the study. Not all of the departments were actively recruiting patients during the whole period.

Medical inclusion criteria were primarily uterine fibroids with bleeding disturbance or mechanical symptoms but other benign disorders where hysterectomy was recommended were also included. After the operation at least one ovary should be preserved. Exclusion criteria were malignancy in the genital organs, previous or present cervical dysplasia, rapidly growing fibroids where malignancy could not be ruled out preoperatively, preoperative treatment with GnRH analogues, postmenopausal women without hormone therapy (HT), and severe psychiatric disorders.
Figure 3. Flowchart of Trial 2.

Randomised (n = 200)

Allocated to subtotal hysterectomy (n = 104)

- Withdrew consent prior to surgery (n = 5)

- Received allocated intervention (n = 99)

  - Ovarian cancer surgery, 10 months after hysterectomy (n = 1)

  - Withdrew consent during the study period. (n = 4)

  - Completed the study (n = 95)

  - Intention-to-treat analysis

  - Converted to subtotal hysterectomy for surgical technical reasons (n = 1)

  - Analysed (n = 94)

- Withdrew consent during the study period. (n = 3)

  - Intraoperative finding of cancer (n = 2)

  - Converted to subtotal hysterectomy for surgical technical reasons (n = 1)

  - Received allocated intervention (n = 90)

  - Protocol violation: Concomitant BSO (n = 1)

  - Withdrew consent during the study period. (n = 5)

  - Completed the study (n = 84)

  - Analysed (n = 85)

Allocated to total hysterectomy (n = 96)

- Withdrew consent prior to surgery (n = 5)

- Received allocated intervention (n = 90)

  - Ovarian cancer surgery, 10 months after hysterectomy (n = 1)

  - Protocol violation: Concomitant BSO (n = 1)

  - Withdrew consent during the study period. (n = 5)

  - Completed the study (n = 84)

  - Analysed (n = 85)

- Received allocated intervention (n = 90)

  - Protocol violation: Concomitant BSO (n = 1)

  - Withdrew consent during the study period. (n = 5)

  - Completed the study (n = 84)

  - Analysed (n = 85)

- Withdrew consent during the study period. (n = 4)

  - Completed the study (n = 95)

  - Intention-to-treat analysis

  - Converted to subtotal hysterectomy for surgical technical reasons (n = 1)

  - Analysed (n = 94)

- Diary missing (n = 1)

- Analysed (n = 94)

- Diary missing (n = 1)

- Analysed (n = 84)

- Diary missing (n = 1)

- Analysed (n = 84)
**Collection of clinical data**

Base line data were obtained one week preoperatively. The intra- and postoperative data were recorded continuously in the case report form. Data on complications/complaints, sick-leave and medication were collected at the follow-up visits according to the study protocols. Time and number of included participants in the two trials are shown in Fig. 4.
**Surgery**

All operations were conducted under general anaesthesia. The surgical technique of the three different methods of hysterectomy in the two trials was restricted as follows: In the laparoscopic procedure a three port technique was used and the uterine vessels were to be resected laparoscopically. Use of endoscopic stapler or bipolar coagulation for resection of the parametrium and uterine vessels was left to the surgeon’s freedom of action. The remaining parts of the cardinal ligaments and the uterosacral ligaments were resected through the vaginal part of the operation. The specimen was removed through the vagina. The uterosacral ligaments were attached to the vaginal cuff, which was closed from the vagina with the front-to-back closure technique. No pelvic peritonealisation was carried out. All total abdominal hysterectomies in the two trials were performed with the extrafascially technique. In trial 1 abdominal hysterectomy was performed through a Pfannenstiel skin incision and in trial 2 the surgeon decided about midline or low transverse skin incision depending on the size of the uterus, occurrence of previous laparotomy scar and the woman’s preference for all hysterectomies. In the subtotal hysterectomies the endocervical canal was treated according to local tradition or at the surgeon’s discretion.

**Measurements of psychological well-being (paper I,III, IV)**

The Psychological General Well-Being Inventory (PGWB) consists of 22 questions referring to anxiety, depression, well-being, self-control, health and vitality [Dupuy 1984]. Each question is rated on a six point scale from 1 to 6. The sum score ranges from 22 to 132. The higher the sum score, the higher the degree of well being. The PGWB has been tested for validity against various validated mental health scales and it has been shown sensitive to small changes in intrapsychic well-being. The Swedish version of PGWB has been validated [Wiklund 1992].

The Women’s Health Questionnaire (WHQ) is a questionnaire providing a detailed examination of minor psychological and somatic symptoms experienced by peri- and postmenopausal women [Hunter 1992; Hunter 2000]. It consists of 36 questions grouped in nine sections describing somatic symptoms, depressive mood, cognitive difficulties, anxiety, sexual function, vasomotor symptoms, sleep problems, menstrual symptoms and attraction. Each question is rated from 1 to 4 and the sum score ranges from 36 to 144. A higher sum
score indicates more distress and dysfunction. The Swedish translation of the WHQ has been validated [Wiklund 1993].

State-Trait Anxiety Inventory (STAI) is a questionnaire that assesses anxiety in two different forms representing state and trait anxiety. In this study the trait form is used. The trait form (Y-2) consists of 20 statements that evaluate anxiety proneness in the individual and it is found to be very stable over time with a test–retest reliability range from 0.73 to 0.86 in a normative sample. State and trait anxiety are strongly correlated \( r = 0.70 \) [Spielberger 1970; Spielberger 1983]. Individuals respond to each item of the form on a four-point Likert scale, indicating the frequency with which each strategy is used. The sum score ranges from 20 to 80 and the sum score increases in response to physical danger and psychological stress. The STAI has been widely used in assessing general anxiety in medical, surgical and psychiatric patients and has been translated to Swedish. Normative values for Swedish women are described [Hellsten 2007].

The Beck Depression Inventory (BDI) is a quantitative self-report scale for measuring the presence and severity of depression in clinical and normal populations of adults and adolescents [Beck 1961; Beck 1996]. It is made up of 21 items. Each item is rated on a four-point scale (0 – 3) in increasing severity, adding up to a total score range from 0 to 63. A high sum score indicates a more depressive state. BDI has been translated to Swedish and has been widely used and considered a well accepted instrument. However, to our knowledge it has only been validated for adolescents in Sweden [Larsson 1991].

For the dichotomisation of the psychometric measures in paper IV we estimated that median preoperative sum scores in PGWB, WHQ, and STAI (101, 61 and 33, respectively) could be discriminatory for high and low capability of postoperative recovery. These values are in the range of preoperative mean values in previously published papers on women undergoing benign hysterectomy or women who are perimenopausal [Spielberger 1983; Oldman 2004]. For BDI we used the 75-percentile value of our study group i.e. 9, which is equivalent to the discriminatory value of BDI for normal and mild depressive states [Beck 1984].
**Measurement of general well-being (paper II and IV)**

A Visual Analogue Scale (VAS) was used to assess the general wellbeing overall in both trials (paper II, paper IV). The women completed a diary concerning their general wellbeing starting one week before surgery, continuing daily until day 35 postoperatively and then one week before the 6-months visit in trial 1. The women were asked to record their state every evening before bedtime, using a visual analogue scale ranging from 0 – 100 to indicate their overall general well-being on average during the preceding 24 hours. The figure 0 represented extremely poor well-being and 100 represented feeling extremely well.

**Measurement of stress-coping (paper II)**

One week preoperatively the women in trial 1 completed the Stress Coping Inventory (SCI), which is a measure developed to study the individual’s appraisal of adaptive resources for dealing with stressful situations [Ryding 1998]. It consists of descriptions of 41 stressful situations that the woman is instructed to rate on a six-point Likert scale indicating how often she is able to cope with each situation. The minimum sum score is 41 and the maximum 246. The higher the sum score, the greater is the stress-coping capacity. The SCI has previously been found to have good internal consistency reliability [Ryding 1998; Söderquist 2006]. No clinical categorization of the SCI sum score has been established. On an empirical basis we categorised the SCI sum score ≤ 160 as low stress coping ability and > 160 as high [Ryding 1998].

**Analgesics**

Intraoperative analgesia consisted of fentanyl and morphine intravenously. All patients received paracetamol 1g orally or rectally either preoperatively or intraoperatively. Oral paracetamol (1 g (q6h)) was administered regularly during the hospital stay and at discharge the patient was recommended to continue on demand as long as necessary. Additional postoperative pain relief was supplied on demand by intermittent injections of morphine, ketobemidone, pethidine or ketorolac or orally or rectally administered NSAID, tramadol, codeine or dextropropoxyphene. Calculation of equipotent dosage of narcotic analgesics was performed on the basis of the equipotent dosage factors shown in Table 4 [Foley 1985; FASS 2006]. The dose was calculated as equipotent intravenous morphine. The recommended
daily dosage (RDD) according to Fass® (the Pharmaceutical Specialities in Sweden) [FASS 2006] for orally and rectally administered analgesics was set to 1.0. For combination products, the RDD was calculated for each active ingredient. The proportions of RDD of all orally and rectally administered analgesics were added up. The daily use of analgesics after discharge from the hospital was noted in the diary with the trade name of the analgesic and the total daily dosage.

Table 4. Narcotic analgesics and equipotent dosage of morphine [Foley 1985; FASS 2006].

<table>
<thead>
<tr>
<th></th>
<th>Intravenous or intramuscular administration</th>
<th>Per oral administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10 mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Ketobemidone</td>
<td>10 mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Pethidine</td>
<td>75 mg</td>
<td>---</td>
</tr>
<tr>
<td>Codeine</td>
<td>130 mg</td>
<td>200 mg</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1 mg</td>
<td>---</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>25 mg</td>
<td>---</td>
</tr>
<tr>
<td>Tramadol</td>
<td>---</td>
<td>240 mg</td>
</tr>
<tr>
<td>Dextropropoxyphene</td>
<td>---</td>
<td>300 mg</td>
</tr>
</tbody>
</table>

**Biochemical measurements**

**FSH, Testosterone, SHBG (paper IV)**

Serum levels of follicle stimulating hormone (FSH), testosterone and sex hormone-binding globulin (SHBG) were measured preoperatively and at 12 months postoperatively. The analyses were centralized to one laboratory, using a uniform fluoroimmunometric assay method during the study period. (DELFIA®, Wallac Sweden AB).

**Haemoglobin, erythrocyte volume fraction (paper III and IV)**

Venous blood samples measuring haemoglobin (Hb) and erythrocyte volume fraction (EVF) were collected and analyzed locally at each hospital preoperatively and on day 2 postoperatively. If the patient received a blood transfusion prior to the second postoperative day, the pre-transfusion value of Hb and EVF was registered.
Statistics

In paper I-IV Student’s t-test was applied for comparison of groups of continuous data with normal distribution and Yates-corrected $\chi^2$ and Fisher’s exact test were used for nominal data. Analysis of variance (ANOVA) for repeated measurements were used to compare the results of the psychological measurements between the two groups from baseline to six months or one year follow up in paper I and III and for comparing the results of the diary and the consumption of analgesics between the two groups from baseline to follow-up in paper II. In paper III analysis of covariance (ANCOVA) was used to analyse differences in effect variables between the two groups at baseline and at 12 months follow-up. Adjustments were carried out for age, smoking habits, nulliparity, sex hormone levels, and use of antidepressants and HT for climacteric symptoms simultaneously. Subsequent post hoc testing was done with Fisher’s PLSD test. In paper IV analysis of variance (ANOVA) for repeated measurements was used to compare the results of general well-being and psychological measurements between the two groups.
Statistical significance was set at the 5% level.
All analyses were on an intention-to-treat basis. Statistical analyses with ANOVA for repeated measurements adjusted for confounding factors were made in the software SPSS v15.0, SPSS Inc, Chicago, Ill, USA. All other statistical analyses were carried out in StatView® for Windows, Copyright©, 1992-1998, Version 5.0.1 (SAS Institute Inc., SAS Campus Drive, Cary, NC 27513, USA).
'However, when we consider hysterectomy for benign conditions there remains some controversy about the indications for surgery, its frequency, the differences in incidence between countries, geographical regions and social classes and, most importantly, about its outcome for women's social and psychosexual wellbeing.'

Results and discussion

Psychological well-being (paper I and III)

No statistically significant differences were found in the sum scores of the four psychometric tests between the women in the two operating groups, either between those in LH and AH (paper I), or between those in TH and SH (paper III) as shown in Table 5 and 6. In both trials all psychometric measurements showed statistically significant improvement over time (p < 0.0001) irrespective of surgical method and no interaction effects were observed. Women with obvious severe psychiatric disorders were excluded in both trials. No patient met the BDI criteria for a severe depressive state with a score above 28 at baseline. Nevertheless we found a significant decline in the mean BDI score in the women after hysterectomy, indicating a reduction in depressive state.

Table 5. Questionnaire scores in women before and after laparoscopic- and abdominal hysterectomy.

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Occasion of measurement</th>
<th>Abdominal hysterectomy (n=56)</th>
<th>Laparoscopic hysterectomy (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean sum score (SD)</td>
<td>Mean sum score (SD)</td>
</tr>
<tr>
<td>PGWB</td>
<td>Baseline</td>
<td>96.5 (16.5)</td>
<td>96.7 (17.9)</td>
</tr>
<tr>
<td></td>
<td>5 – weeks</td>
<td>102.1 (16.4)</td>
<td>100.4 (16.7)</td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>106.1 (16.0)</td>
<td>104.7 (18.5)</td>
</tr>
<tr>
<td>WHQ</td>
<td>Baseline</td>
<td>63.9 (18.2)</td>
<td>64.9 (13.9)</td>
</tr>
<tr>
<td></td>
<td>5 – weeks</td>
<td>54.3 (17.1)</td>
<td>54.6 (12.8)</td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>54.2 (17.2)</td>
<td>55.0 (14.4)</td>
</tr>
<tr>
<td>STAI</td>
<td>Baseline</td>
<td>34.7 (10.1)</td>
<td>35.6 (9.1)</td>
</tr>
<tr>
<td></td>
<td>5 – weeks</td>
<td>31.7 (10.6)</td>
<td>32.7 (8.7)</td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>31.7 (9.2)</td>
<td>33.6 (10.2)</td>
</tr>
<tr>
<td>BDI</td>
<td>Baseline</td>
<td>6.9 (6.1)</td>
<td>6.6 (5.8)</td>
</tr>
<tr>
<td></td>
<td>5 – weeks</td>
<td>5.0 (6.5)</td>
<td>4.6 (5.5)</td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>4.0 (5.2)</td>
<td>5.3 (6.8)</td>
</tr>
</tbody>
</table>
Table 6. Questionnaire scores in women before and after subtotal and total abdominal hysterectomy

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Occasion of measurement</th>
<th>Subtotal hysterectomy (n=94) Mean sum score (SD)</th>
<th>Total hysterectomy (n=85) Mean sum score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGWB</td>
<td>Baseline</td>
<td>98.8 (15.6)</td>
<td>98.7 (16.2)</td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>107.7 (12.8)</td>
<td>107.2 (13.3)</td>
</tr>
<tr>
<td></td>
<td>12 - months</td>
<td>105.7 (14.1)</td>
<td>105.0 (16.0)</td>
</tr>
<tr>
<td>WHQ</td>
<td>Baseline</td>
<td>62.3 (15.0)</td>
<td>63.6 (15.4)</td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>52.0 (12.5)</td>
<td>53.5 (13.3)</td>
</tr>
<tr>
<td></td>
<td>12 - months</td>
<td>53.0 (13.3)</td>
<td>54.0 (13.4)</td>
</tr>
<tr>
<td>STAI</td>
<td>Baseline</td>
<td>36.0 (9.8)</td>
<td>34.9 (10.0)</td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>33.2 (9.0)</td>
<td>32.5 (8.8)</td>
</tr>
<tr>
<td></td>
<td>12 - months</td>
<td>32.6 (9.1)</td>
<td>32.4 (10.4)</td>
</tr>
<tr>
<td>BDI</td>
<td>Baseline</td>
<td>6.2 (6.0)</td>
<td>6.7 (6.3)</td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>4.2 (4.8)</td>
<td>4.2 (5.2)</td>
</tr>
<tr>
<td></td>
<td>12 - months</td>
<td>4.0 (5.6)</td>
<td>4.5 (6.1)</td>
</tr>
</tbody>
</table>

It must be kept in mind that this might be of no clinical importance since the scores of most of the women both before and after the hysterectomy, were within the limits of normality. The number of women on antidepressants or mood enhancing medication was low in both trials and did not change significantly between the time of the operation and the occasions of follow-up. Thus the improvement in depressive and anxiety states does not seem to be caused by medication.

Only a few studies regarding laparoscopic and abdominal hysterectomy deal with psychological outcome. In a previously published Swedish randomised study using PGWB as outcome measure, no significant difference was found in PGWB sum score between women undergoing abdominal and laparoscopic hysterectomy [Ellström 2003]. Another large multicenter study that used QoL as a secondary outcome measurement assessed by a brief questionnaire also failed to show a difference in QoL between abdominal and laparoscopic hysterectomy [Garry 2004a,b]. In both these studies the samples comprised women with or without bilateral oophorectomy performed concomitant to the hysterectomy. This makes the results more difficult to interpret since the changes in oestrogen levels may influence
psychological well-being [Nathorst-Böös 1993; Kastgir 1998; Taylor 2001]. Besides, the use of HT in the study by Garry et al. was not specified pre- or postoperatively. In the present trials the use of HT was specified and at least one ovary was preserved in order to retain the ovarian function postoperatively. In that way we intended to avoid an endocrine effect that could interfere with psychological functioning. Although one study has shown impaired ovarian function in women after unilateral oophorectomy concomitant with abdominal hysterectomy [Bukovsky 1995], there is no reason to believe that such an effect would be unevenly distributed in the present material. Only a few postmenopausal women were included in the present trials. According to the inclusion criteria the HT should be kept during the study period in these women.

None of the previously published randomised studies comparing SH and TH, have primarily focused on psychological well-being [Thakar 2002; Gimbel 2003; Learman 2003] and in these studies adjustments for bilateral oophorectomy or hormone levels have not been made. The rates of bilateral oophorectomy in these studies vary between 14-55%. In a recently published randomised study of SH and TH Gorlero et al. found a significantly better QoL outcome using Euro QoL (EQ-5D) at one year postoperatively in the SH group compared with TH [Gorlero 2008]. In that study 80% of the women were premenopausal. Although the groups did not differ significantly in age preoperatively, the mean age in the SH group was 49 years and in the TH group 46 years, which indicates that at the follow-up one year later there is a possibility that a larger proportion of women in the older group had become menopausal. Also, this study [Gorlero 2008] does not present the number of women having bilateral oophorectomy inducing surgical menopause, hormonal status or therapy, which can bias the interpretation of the results. Compared with the study by Gorlero, the women in trial 2 were younger. The material was more homogenous and therefore it seems less likely that women undergoing menopausal transition during the time of the trial should have affected our results. This was further supported by the fact that no significant associations were found between mode of hysterectomy and any of the four psychometric measures preoperatively or at 12 months in the ANCOVA models when adjusted for, sex hormone levels. Women who had concomitant bilateral oophorectomy have shown a poorer outcome in psychological well-being but the results are not unanimous [Rowe 1999; Kjerulf 2000a,b; Aziz 2005; Farquhar 2006], probably because of different designs of the studies and differences in concomitant hormone therapy. When looking at the four previously published
randomised studies on SH vs. TH addressing psychological well-being as secondary outcome, none of these made adjustments for bilateral oophorectomy or sex hormone levels [Thakar 2002; Gimbel 2003; Learman 2003; Gorlero 2008]. In the present study the results were adjusted for known or potential confounding factors of psychological well-being, i.e. age, parity, smoking habits, sex hormone levels and use of antidepressants and HT for climacteric symptoms and none of the women had had surgical menopause due to removal of the ovaries.

**Short-term recovery in general well-being (paper II and paper IV)**

The day-by-day recovery of general well-being did not differ significantly between women operated on by either method in any of the two studies, i.e. neither between LH and AH, nor between SH and TH. The graphic illustration of the day-by-day recovery of general well-being is presented in Fig. 5 and 6. To the very best of my knowledge no previous reports have been published on this issue and the results presented here can therefore not be compared with others. This information is pivotal. The women had regained their self-rated general well-being equivalent to the mean general well-being score at 7 days preoperatively after 17 (LH) vs. 20 (AH) days in trial 1 and 19 (TH) vs. 22 (SH) in trial 2. Considering these results one can argue that according to the self rated general well-being, there is a difference of only three days between LH and AH and SH and TH, respectively in recovery time. This difference does not seem to support the belief that LH and SH are methods of less invasive character that benefit recovery after hysterectomy. Return to normal activities is often reported in studies comparing surgical methods and it is perhaps the concept closest to recovery of self rated general well-being used here. In the Cochrane review regarding LH and TH, the mean time in days to return to normal activities was 24 days in LH and 43 days in AH [Johnson 2006]. Corresponding figures in SH and TH were 4.2 weeks and 4.1 weeks respectively [Learman 2003]. As these results may not represent the same outcome measure, conclusions cannot be drawn, but the results from the present trials strongly indicate the need for further studies regarding recovery where clear definitions of the outcome measures are presented.
Figure 5. Illustration of the recovery of the day-by-day general well-being after laparoscopic and abdominal hysterectomy. Plots and error bars indicate mean ±1SD.
Figure 6. Illustration of the recovery of the day-by-day general well-being after subtotal and total hysterectomy. Plots and error bars indicate mean ±1SD.
**Per- and postoperative data (paper I-IV)**

**Surgical measures (paper I-IV)**

The median operating time was significantly longer for LH (99 minutes (50-190)) compared with AH (64 minutes (35-150)), but there were no significant difference in estimated blood loss and the need for transfusions between the groups. These results correspond with those of previous studies concerning LH and AH. In the Cochrane review, the weighted mean difference (WMD) in operating time was 30.6 minutes (95% CI 25.6-35.6 minutes) in advantage to AH. Regarding blood loss a WMD of 45.3 ml (95% CI 17.9-72.7 ml) in favour of LH was found in the review but this did not influence the need for blood transfusions, which was similar in the two groups [Johnson 2006].

In trial 2 the operating time was significantly longer for TH (median 77, range 35-173 minutes) compared with SH (median 65, range 35-140 minutes). This is comparable to that reported in the meta analysis by Gimbel, who found a 13 minutes shorter operating time for SH compared with TH [Gimbel 2007]. This small difference in operating time probably lacks clinical importance.

The contradictory results about estimated blood loss between this study and the Cochrane review concerning LH and AH and the meta analysis by Gimbel concerning SH and TH, respectively may simply be explained by the fact that the mean estimated blood loss was relatively higher in all modes of hysterectomy in the Cochrane review (LH: 308 ml and AH: 345 ml) and in Gimbel’s meta analysis (SH: 351 ml and TH 452 ml) compared with this study (LH: 225 ml; AH: 257 ml; SH: 221 ml and TH 242 ml). These differences can be a result of different ways of assessing the blood loss, but they may also reflect a difference in surgical technique. The latter explanation might be the more plausible since the range of estimated blood loss and the need for blood transfusions were quite similar. Besides the drop in haemoglobin was almost identical in the two modes of hysterectomy in this trial, which may provide additional support for the concept of good surgical technique.

In trial 1, the hospital stay was significantly shorter for LH than for AH (median 2.0 days, range 1-11 vs. 3.0 days, range 2-7; (p=0.0006)). No such significant difference was seen in trial 2. These results correspond with previous studies [Johnson 2006; Lethaby 2006].

**Consumption of analgesics (paper II and IV)**

The consumption of analgesics on day 0 to day 3 postoperatively in trial 1 is presented in Table 7. There was a significantly lower consumption of opioids in the laparoscopic group
day 0 to day 3 (p = 0.0049), but no difference regarding other analgesics. No woman needed parenterally administered opioids after the third postoperative day in trial 1 (paper II). From postoperative day 4, no statistically significant differences between the two groups regarding use of analgesics could be found. Thus the findings indicate that within three days of the hysterectomy postoperative pain is sufficiently controlled with oral/rectal analgesics in both laparoscopic and abdominal hysterectomy. These results are in accordance with previous reports that the demand of opioids and analgesics in women undergoing LH is lower than after abdominal hysterectomy [Falcone 1999; Ferrari 2000; Garry 2004a,b]. Despite 30 minutes longer operation time of women with LH compared with AH the consumption of fentanyl during anaesthesia did not differ significantly between the two methods.

In trial 2 (paper IV) no significant differences were observed between the groups in the use of parenterally or enterally administered analgesics, even when adjusted for use of epidural analgesia. None of the women received opioids parenterally after postoperative day 4. None of the four previously published randomised studies on SH and TH present data on the use of analgesics in the postoperative period. The results of this study indicate that there is no difference in demand for, and consumption of, analgesics after subtotal and total abdominal hysterectomy. This may imply that the surgical trauma and pain stimulating effects are equal after SH and TH.

Table 7. Equi potent morphine day 0 to day 3 and sum of RDD of orally or rectally administered analgesics after laparoscopic and abdominal hysterectomy. Fentanyl given during anaesthesia is not included in the equipotent dosage of morphine.

<table>
<thead>
<tr>
<th>Day of measure</th>
<th>Equipotent dosage of morphine</th>
<th>Sum of RDD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Laparoscopic hysterectomy</td>
<td>Abdominal hysterectomy</td>
</tr>
<tr>
<td></td>
<td>(mean ± SD)</td>
<td>(mean ± SD)</td>
</tr>
<tr>
<td>Day of surgery (Day 0)</td>
<td>20.7 mg ± 12.9</td>
<td>25.2 mg ± 14.3</td>
</tr>
<tr>
<td>Postoperative Day 1</td>
<td>6.9 mg ± 9.1</td>
<td>14.5 mg ± 14.2</td>
</tr>
<tr>
<td>Postoperative Day 2</td>
<td>4.9 mg ± 9.4</td>
<td>8.7 mg ± 13.6</td>
</tr>
<tr>
<td>Postoperative Day 3</td>
<td>1.6 mg ± 4.3</td>
<td>3.5 mg ± 5.6</td>
</tr>
</tbody>
</table>

RDD = recommended daily dose
Complications and complaints

Complications frequencies in both trials are shown in Table 8. Basically the complications and complication frequencies correspond with those described in previous studies of LH and AH [Johnson 2006] and SH and TH [Lethaby 2006]. There were no significant differences in occurrence of minor or major complications between the groups. However, regarding the complication frequencies the present study is too small and thus under-powered to draw conclusions about comparisons of complications between different modes of hysterectomy. In trial 2 the women undergoing SH had significantly more complaints at the 12 month follow-up compared with women who had had TH (36% [32/90] vs. 20% [17/85]; p = 0.0337). This was mainly due to occurrence of regularly occurring vaginal discharge/bleeding. In the present study 20% (18/90) reported regular vaginal bleeding in the SH group compared with 1.2% (1/85) in the TH group (p < 0.0001). Corresponding figures reported in other studies are 5-22% [Gimbel 2007].

Table 8. Complications in trial 1 and 2 divided into minor and major complications.

<table>
<thead>
<tr>
<th></th>
<th>No complications</th>
<th>Minor</th>
<th>Major</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n/N)</td>
<td>% (n/N)</td>
<td>% (n/N)</td>
</tr>
<tr>
<td>**Trial 1 ***</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LH</td>
<td>66% (41/62)</td>
<td>21% (13/62)</td>
<td>12.9% (8/62)</td>
</tr>
<tr>
<td>AH</td>
<td>76% (42/55)</td>
<td>20% (11/55)</td>
<td>3.6% (2/55)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>71% (83/117)</td>
<td>20.5% (24/117)</td>
<td>8.5% (10/117)</td>
</tr>
<tr>
<td>**Trial 2 ***</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SH</td>
<td>72% (68/94)</td>
<td>20% (19/94)</td>
<td>7.4% (7/94)</td>
</tr>
<tr>
<td>TH</td>
<td>76% (64/84)</td>
<td>20% (17/84)</td>
<td>4.8% (4/178)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>74% (132/178)</td>
<td>20% (36/178)</td>
<td>6.1% (11/178)</td>
</tr>
</tbody>
</table>

*Figures extracted from paper II and paper IV.

Factors associated with postoperative recovery

Stress-coping (paper II)

There was a strong correlation between SCI sum score and all psychometric measures preoperatively (Table 9). Women with a high stress-coping ability (SCI sum score >160) had a statistically significant faster recovery of the general well-being after hysterectomy regardless of the surgical method used (LH vs. AH) compared with women with a low stress-
coping ability (Fig. 7). Even psychological well-being in general as well as depressive and anxiety states was better in the women with high stress-coping ability (Table 10). Multiple factors may potentially influence postoperative psychological outcome after hysterectomy due to the complex nature of the background for the hysterectomy. Personality factors have been shown to be predictive for psychological outcome after hysterectomy [Ryan 1989; Thornton 1997]. No previous studies have analysed the role of stress-coping ability in women referred to hysterectomy. The present study indicates that the woman's stress-coping ability plays an important role in determining both general and psychological wellbeing after hysterectomy.

Table 9. Correlations between SCI scores and the scores of the four psychometric tests.

<table>
<thead>
<tr>
<th>Comparison of sum scores:</th>
<th>Linear Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pearson's correlation coefficient</td>
</tr>
<tr>
<td>SCI and PGWB</td>
<td>0.57</td>
</tr>
<tr>
<td>SCI and WHQ</td>
<td>- 0.55</td>
</tr>
<tr>
<td>SCI and STAI</td>
<td>- 0.71</td>
</tr>
<tr>
<td>SCI and BDI</td>
<td>- 0.53</td>
</tr>
</tbody>
</table>
Figure 7. Illustration of general well-being pre- and post operatively after laparoscopic and abdominal hysterectomy in relation to high/low SCI sum score. Plots and error bars indicate mean ± 1SD.
Table 10. General psychological well-being (PGWB and WHQ), general anxiety (STAI) and depression (BDI) in women preoperatively (baseline), 5-weeks and 6 months after laparoscopic and abdominal hysterectomy in relation to low and high stress-coping (SCI) sum scores.

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Occasion of measurement</th>
<th>Women with low SCI sum score (n = 23)</th>
<th>Women with high SCI sum score (n = 94)</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean sum score (SD)</td>
<td>Mean sum score (SD)</td>
<td>Main effect between groups</td>
</tr>
<tr>
<td>PGWB</td>
<td>Baseline</td>
<td>81.1 (17.5)</td>
<td>100.5 (14.7)</td>
<td><strong>p &lt;0.001</strong></td>
</tr>
<tr>
<td></td>
<td>5 – weeks</td>
<td>93.9 (16.8)</td>
<td>103.1 (16.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>99.5 (13.9)</td>
<td>107.1 (17.5)</td>
<td></td>
</tr>
<tr>
<td>WHQ</td>
<td>Baseline</td>
<td>78.2 (18.0)</td>
<td>60.9 (14.0)</td>
<td><strong>p &lt;0.001</strong></td>
</tr>
<tr>
<td></td>
<td>5 – weeks</td>
<td>60.8 (16.9)</td>
<td>52.7 (14.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>61.3 (15.6)</td>
<td>52.6 (15.3)</td>
<td></td>
</tr>
<tr>
<td>STAI</td>
<td>Baseline</td>
<td>45.5 (9.0)</td>
<td>32.6 (8.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 – weeks</td>
<td>40.2 (10.1)</td>
<td>30.3 (8.7)</td>
<td><strong>p &lt;0.001</strong></td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>38.4 (8.4)</td>
<td>31.0 (9.4)</td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>Baseline</td>
<td>12.2 (6.7)</td>
<td>5.4 (5.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 – weeks</td>
<td>7.0 (8.4)</td>
<td>4.2 (5.3)</td>
<td><strong>p &lt;0.001</strong></td>
</tr>
<tr>
<td></td>
<td>6 - months</td>
<td>6.6 (6.3)</td>
<td>4.1 (5.9)</td>
<td></td>
</tr>
</tbody>
</table>

PGWB score 22 -132; high score indicates greater wellbeing. WHQ score 36 – 144; high score indicates greater distress/dysfunction. STAI score 20 -80; high score indicates greater psychological stress. BDI score 0 – 63; high score indicated more depressed state.
Psychometric measures

The level of psychological well-being preoperatively was strongly associated with the day-by-day recovery of general well-being (Table 11).

Table 11. Associations between day-by-day general well-being pre- and postoperatively and the four psychometric measurements. A) Trial 1: LH vs. AH. B) Trial 2: SH vs. TH.

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Comparison between</th>
<th>Timing</th>
<th>Main effect between groups</th>
<th>Main effect over time</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>General well-being</td>
<td>PGWB low vs. high</td>
<td>Preoperative day -7 to day -1</td>
<td>p &lt; 0.0001</td>
<td>p &lt; 0.0001</td>
<td>p = 0.1721</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postoperative day 1 to day 35</td>
<td>p = 0.0112</td>
<td>p &lt; 0.0001</td>
<td>p = 0.6114</td>
</tr>
<tr>
<td>General well-being</td>
<td>WHQ high vs. low</td>
<td>Preoperative day -7 to day -1</td>
<td>p &lt; 0.0001</td>
<td>p &lt; 0.0001</td>
<td>p = 0.0004</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postoperative day 1 to day 35</td>
<td>p = 0.0024</td>
<td>p &lt; 0.0001</td>
<td>p = 0.9717</td>
</tr>
<tr>
<td>General well-being</td>
<td>BDI high vs. low</td>
<td>Preoperative day -7 to day -1</td>
<td>p &lt; 0.0001</td>
<td>p &lt; 0.0001</td>
<td>p = 0.1515</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postoperative day 1 to day 35</td>
<td>p = 0.2655</td>
<td>p &lt; 0.0001</td>
<td>p = 0.8641</td>
</tr>
<tr>
<td>General well-being</td>
<td>STAI high vs. low</td>
<td>Preoperative day -7 to day -1</td>
<td>p = 0.067</td>
<td>p &lt; 0.0001</td>
<td>p = 0.0196</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Postoperative day 1 to day 35</td>
<td>p = 0.0183</td>
<td>p &lt; 0.0001</td>
<td>p = 0.9976</td>
</tr>
</tbody>
</table>

PGBW low vs. high: sum score of PGBW ≤ or > than 101; WHQ high vs. low: sum score of WHQ ≥ or < than 62; BDI high vs. low: sum score of BDI > or ≤ than 9; STAI high vs. low: sum score of STAI > or ≤ than 33.

Even in the week prior to surgery general well-being deteriorated significantly more in the women with low psychological well-being than in women with high psychological well-being.

This result is in accordance with previous studies [Carlson 1994, Ryan 1989, Kjerulff 2000a].
Complications/complaints
As previously noted, the women undergoing SH had significantly more complaints at the 12 month follow-up compared with women who had had TH. However, the occurrence of blood staining discharge or monthly bleeding was not associated with any outcome of the psychometric measures. Although bleeding does not seem to influence psychological well-being in women after hysterectomy as shown in the present study, information about the risk of persistent bleeding should always be given at the time of preoperative counselling. Presentation of the alternative of having SH must also include a discussion of the need for continuing regular cervical smear testing.

Sick-leave
In trial 1, the mean duration of sick-leave was significantly shorter for LH than for AH (27.5 ±15.2 days, and 34.3 ±10.8 days respectively: p = 0.010). This result is in line with studies in the Cochrane review [Johnson 2006]. When looking at the figures it is striking that the mean duration of the sick-leave in the AH group in this trial was shorter than that of the LH group in the largest of the studies in the review, the 'eVALuate' study [Garry 2004a,b]. In the present trial the women themselves decided when to return to work, whereas in the 'eVALuate' study the surgeon's practice had standardized the advice to be given concerning resumption of normal activities including work. This indicates that the length of the sick-leave can be compared within a specific study but it seems to be a blunt and imprecise measure of recovery when efforts are made to compare studies. The point in time when the women had regained their self reported level of general well-being equivalent to the baseline assessment occurred on postoperative day 17 in the LH group and on day 20 in the AH group. This emphasizes that the importance of the entry procedure in surgery may have played out its role in a three-week period.

In trial 2 there was no significant difference in the length of sick-leave between the SH and the TH group, 32.5 ± 9.4 vs. 33.6 ± 11.3 days respectively. In this trial the initial duration of sick-leave was 21 days as compared with the 14 day period in trial 1. In both studies the research nurse had telephone contact with the woman at the end of the initial sick-leave period and the sick-leave was prolonged by 7 days at most on the basis of the woman’s request. Learman [2003] reported a similar length of the time to return to work with a mean of missed days at work in SH and TH of 29.2 ± 18.5 and 28.8 ± 18.8 days of work, respectively. In that study it is unclear if the stay in hospital was included in the time period.
It is notable that the length of the period needed to regain normal activities after open hysterectomy in both trials in the present study is comparable with that of the studies of laparoscopic hysterectomy in the Cochrane review [Johnson 2006].

In both trials, the occurrence of minor complication was strongly associated with length of sick-leave (trial 1, $p = 0.025$ and trial 2, $p < 0.001$, respectively). No associations were found between the occurrence of major complications and length of the sick-leave in any of the trials. These results may be explained by the fact that a major complication, often bleeding or a re-operation, arises in the operating room or in the immediate postoperative period. If adequately and properly managed major complications seldom have an impact on postoperative recovery after two to three weeks. Contrary, minor complications as for instance a wound infection arising in the postoperative period when the woman is back in her domestic environment trying to return to daily life, would interfere significantly with her recovery.
**General discussion**

*Comments on methodology.*

The randomised, controlled trial is considered the most reliable and impartial method of determining what medical interventions work best. Research participants are randomised in clinical trials so that bias does not weaken the study results. Bias consists of human choices, beliefs or any other factors in addition to those being studied that can affect the results of a clinical trial. However, it is important to realise that the individual’s decision to participate in a clinical trial constitutes a possible selection bias. This does not, however, influence the randomisation of allocated treatment/intervention but may influence the possibility of generalising the results.

*Randomisation*

In this study sealed opaque envelopes were used. The envelopes were serially numbered and opened consecutively. The envelopes contained the surgical method written on a label. This was done in order to avoid violations of the randomisation. No woman was randomised more than once and none of the women excluded from the studies withdrew consent in connection with the randomisation.

*Blinded or open*

Both trial 1 and 2 were not blinded. To my knowledge there is only one randomised blinded study comparing different modes of hysterectomy [Thakar 2002] and that study compared SH and TH. The authors wrote that they strongly encouraged the women not to do self-examination and the participating physicians not to break the blind. One can argue about the reliability of the blinding since most of the women were sexually active and had a partner. Besides, about 7% had periodical vaginal bleeding even one year after the operation. The follow-up time was one year and it seems likely that breaking of the blind was a fact for a great number of the women. Regarding studies comparing LH and AH, the difficulties with a blinded design are well reflected in the Cochrane review since none of the studies included in that review were blinded.

*Analysis of non-eligible patients*

A weakness of the present study is that there is no analysis of the women not included in the trials. Trial 1 and 2 were partly parallel in time and four clinics participated in both studies. Thus a woman could have been eligible for both studies. This together with the fact that not
all surgeons at each department recruited participants to the studies led to an incomplete reporting of non-eligibility. A retrospective analysis of all hysterectomies on benign indications over the study period in trial 1 in the participating centres showed that of the 1,235 women who were excluded, 711 (58%) had the primary diagnosis of uterine fibroids. This indicates that a substantial percentage of the women were not suitable candidates for laparoscopic hysterectomy.

*Time for inclusion.*

The inclusion times in the trials were 6.5 years and six years, respectively. This may seem to be a rather long time, but one must bear in mind that the majority of the studies comparing LH and AH were done before the decline in the rate of LH that began to occur around 1999 in Sweden as shown in Table 1. In trial 1, 63 women who were allocated to LH are included. That figure corresponds to the total number of LH performed in Sweden 1999 according to the national database [www.socialstyrelsen.se/en/Statistics]. This illustrates the difficulty in performing a study in a short time in a country with a low hysterectomy rate even though a multicenter design was used. Women scheduled for concomitant bilateral oophorectomy were not eligible for the study, which further reduced the number of participants.

Trial 2 started approximately 1.5 years after trial 1. Four of the centres participated in both trials. This may have reduced the number of candidates for each study and led to a slower inclusion rate. When comparing inclusion time in randomised studies of SH vs. TH the inclusion period in the studies by Thakar [2002] and Gimbel [2003] was four years and approximately 300 women were included; Learman [2003] used 2.5 years and included 135 women; Gorlero [2008] had three years to perform his study with 105 women compared with six years and 200 women in our study. The fact that the hysterectomy rate in Sweden is relatively low and the fact that the inclusion and exclusion criteria were created with the intent of making the patient material homogeneous both led to restricting the number of women who could participate in the study.

During the study period of both trials the hysterectomy rate in Sweden has declined in general and the relative number of vaginal hysterectomies has increased, which may have further influenced the time of inclusion in the present studies. Given these circumstances the time of inclusion in the trials are acceptable.
Multicenter/multi-surgeon

In surgical studies aimed at detecting differences between highly specific surgical methods, there is always a risk of inaccuracy arising from the use of several surgeons and multiple centres. On the other hand, the results from a multicenter/multi-surgeon study give a broader view and in that way more likely reflect common practice in general. The purpose of the present trials was to evaluate the different methods of hysterectomy in a general perspective and, in that way, to also complement to previously published single-surgeon and single-centre studies comparing LH/AH and SH/TH, respectively. When a new surgical method is introduced, the first reports are usually case reports followed by feasibility studies. This is often followed by (hopefully) randomised single surgeon and single centre studies. The last step in the pathway of scientific evaluation is the conduction of meta-analyses, but as these results are pooled results of the included RCTs, there is always a risk of enhancement of a bias included in the separate RCTs. This holds especially true regarding short-term outcome in non-blinded randomised studies because of the risk that a “biased” surgeon, who favours a new method, informs the patient differently about, for instance, the time in hospital and the length of sick-leave.

Surgical technique

When assessing a relatively new surgical technique, the surgeons' experience might affect the results. A Finnish study showed that the risk of major complications was higher during the first 30 cases of LH than in subsequent procedure [Mäkinen 2001]. In trial 1 all surgeons were skilled laparoscopists and had experience in LH but most of them had not performed 30 laparoscopic hysterectomies when the trial started. However, since the frequency of major complications in trial 1 was comparable with that of other RCTs, it seems less likely that this surgeon related effect influenced the results of this study adversely.

Because cervix is left in SH, in contrary to TH, there is risk of a persistent monthly bleeding from the endocervical epithelium. There were no precise recommendations in the study protocol of how to treat the endocervix in trial 2. With personal knowledge of the local traditions in the participating centres, the majority of the surgeons seemed to use electro coagulation. Twenty per cent of the women in trial 2 reported monthly bleeding/discharge one year after surgery. This figure is corresponds to the results from Gimbel [2003] where electro coagulation of the cervical canal was instructed in the study protocol. Thakar [2002] reported 7% with bleedings one year after surgery and electro coagulation was compulsory
in their study. Thus, monthly bleeding after SH regardless of electro coagulation of the endocervical epithelium seems to be a complication or side-effect that should not be neglected in the preoperative counselling.

Psychometric measures
The psychometric measures used in this study i.e. PGWB, WHQ, BDI and STAI were chosen in order to detect changes in psychological well-being overall and more specifically in the domains of anxiety and depression. They are all widely used in several geographical populations including Sweden and they are also used in perimenopausal women. PGWB, WHQ and STAI are validated for Swedish circumstances but to my knowledge BDI has not been validated for this age-group in Sweden. The Stress Coping Inventory (SCI) has previously been used in the age group 18-43 years in Sweden but it has not previously been validated and the form has not been published previously (Appendix ). In trial 1, there was strong correlations between SCI and all psychometric measures with Pearson correlation coefficients of > |0.5|. The SCI also demonstrated an excellent internal consistency reliability with a Cronbach’s \( \alpha = 0.948 \). There was no statistical difference in SCI sum score at baseline between the groups of laparoscopic and abdominal hysterectomy (mean 183.5±27.3 vs. 185.2±25.2; \( p = 0.728 \)). In such way the SCI was partly validated in the present study.

Missing data in questionnaires
In studies using psychometric measures on several occasions missing answers in questionnaires or missing questionnaires has to be considered. In the eVALuate study [Garry 2004b] 15.7% of the questionnaires were missing at 4-months follow-up and 18.2 % at one year follow-up. The corresponding figure in trial 1 was 1.1 % at six-month follow-up. Regarding studies of QoL after SH and TH, Thakar [2004] reported 18% missing questionnaires at one year follow-up, Kupperman [2005] reported data from 93% of the included patient after two years but it is unclear whether this figure included missing questionnaires. Information about missing questionnaires is lacking in the Gimbel study [2003] and Golero [2008] reported no missing questionnaires. In the present trial of SH and TH, 2.2% of questionnaires were missing at one year follow-up. In order to obtain the statistical analyses of variance a missing questionnaire was replaced with the mean value of that specific questionnaire for the group at the same occasion. In summary, compared with the literature, both trials in the present study report a low rate of missing questionnaires which strengthen the conclusions regarding psychological well-being.
Preoperative psychological status

Severe psychiatric disease was an exclusion criterion in both trials. It was left to the investigator to decide whether the woman suffered severe psychiatric disease at the time of enrolment in the study. Use of anti depressive medication was allowed in the study. Anti depressants per se could affect the psychological well-being and the potential effect of the surgical procedure on the psychological well-being and in that way bias the results. In the present trials only a few women were using antidepressants (eight in trial 1 and six in trial 2) and they were evenly distributed between the study groups making the risk of confounding low for this reason. The preoperative mean sum scores of trait anxiety (STAI) in the present studies correspond with that of a normal population of women in a similar age group (sum score 35 ± 9.2) previously described [Spielberger 1983]. This indicates that the women in this study were comparable with those of a normal population.

Psychological well-being is a subjective term that covers a wide span of personal affective states. It is highly individual and therefore difficult to categorise. In scientific settings psychological measures often study variations or changes over time in relation to an intervention. In order to evaluate psychological well-being we used a broad range of psychometric tests with four measures. Two of these (the PGWB and WHQ) give a generic measure of psychological well-being whereas the BDI and the STAI are associated with specific psychic conditions – depression and anxiety. In comparison, the other four randomised trials comparing SH and TH (subdivided in different publications) [Thakar 2002/2004; Gimbel 2003/Zobbe 2004; Learman 2003/Kupperman 2005; Gorlero 2008] all used generic tests: the SF-36 or EQ 5-D. Only the British study by Thakar et al. combined it with a specific test, the General Health Questionnaire (GHQ-28) that is an instrument used to detect current psychiatric disorders [Thakar 2002; Thakar 2004] and the Italian study [Gorlero 2008] that combined it with a specific test, the Body Imaging scale (BIS), that measures the persons’ own perceptions of body image. The results of the four psychometric tests in the present study were unanimous in demonstrating no difference between modes of hysterectomy. The combination of various generic and specific tests, showing unanimous results, strengthened the conclusion of the present study.

The time of completing the baseline questionnaires was specified to a fixed time two weeks prior to surgery in the Italian study [Gorlero 2008] whereas the other three studies either did not describe the time [Thakar 2004] or stated a poorly specified interval [Gimbel 2003;
Kupperman 2005]. In the present study the questionnaires at baseline were completed one week prior to surgery. The woman’s perception of her psychological well being may be influenced by the time interval between completing the questionnaire and surgery. The anxiety level increases the closer the time to surgery even before admission to hospital [Carr 2006]. It therefore seems important to use a fixed time for the measurements in order to correctly evaluate the development in well-being after surgery.

Several life events unrelated to the hysterectomy can occur in a woman’s life during a follow-up time of 6-12 months that could influence her psychological health. The lack of information of major life events during the study period might influence the interpretation of the results of the studies. None of the previously mentioned studies of hysterectomy was controlled for major life events. In the present study at the time of the follow-up visits at six months (trial 1) and at one year (trial 2), respectively, the women were asked if new problems had occurred during the follow-up period or if new medications or other medical treatments had been prescribed. Although they were not specifically asked for specific life events in the study it is plausible that these would have appeared in the follow-up visit interviews. Thus other possible major life events should most likely not play a role in the results of the study.

The preoperative measurement of the psychological well-being was done one week before surgery. It might be assumed that the women at that time were more distressed by the imminent operation than in general. However, the result of the randomisation, i.e. the allocated method of hysterectomy, did not seem to influence the psychological function differently in the two groups. In both trials significant improvements in psychological measures were found at follow-up compared with the baseline assessment. This is consistent with other studies concerning abdominal hysterectomy [Carlson 1994; Clarke 1995; Kjerulff 2000a,b]. The improvements found at the first follow-up were either preserved or increased in the final assessment which occurred after six months (trial 1) or after one year (trial 2).

VAS

In the present trials (paper II and paper IV) a VAS was used to measure the day-by-day recovery of the general well-being. The use of a visual analogue scale (VAS) to measure the general well-being may seem to be a blunt method. However, the method has been used in several studies of hysterectomy concerning quality of life assessments and general well-
being [Lumsden 2000; Davies 2002] and found to be useful. A similar VAS is used in the EQ5-D, which is a well accepted standardised instrument for use as a measure of health outcome [EuroQol group 1990].

In the present trials there were strong associations between preoperative general well-being measured by the VAS and the four psychometric tests. There was also a strong association between the recovery of the postoperative day-by-day general well-being and the dichotomised (low – high) outcome of the psychometric measures (paper IV). These results support the use and reliability of the VAS as being a sensitive and adequate measurement under these circumstances.

Routine for length of sick-leave

Though there is a lack of scientific evidence for recommendations regarding length of sick-leave after hysterectomy, the recommendations are legio based among other things on local traditions, social welfare, physician’s discretion and social entities [Møller 2001]. In many studies concerning hysterectomy, information about the recommendations is lacking. In the present trials the women themselves decided when they were fit to return to work. After the initial sick-leave period of 14 and 21 days respectively in trial 1 and 2, the length of sick-leave was prolonged with a maximum of seven days at a time. Thus, the local tradition and surgeons’ discretion was intended to be kept at a minimum in the present trials.

Complications/complaints

In order to detect a significant difference in complication rate between modes of hysterectomy, a large study is needed. Only one study in this field, the parallel two-armed ‘eVALuate’ study (AH/LH and VH/LH) with 1,380 women included was powered for the purpose of detecting a 50% reduction rate in major complication, but only in the arm comparing LH/AH. Eventually even this study was under powered (1,141 patients per treatment arm were needed to gain power) [Garry 2004a,b]. The present trials were not primarily powered to detect differences in complication rates. Complications were recorded prospectively during the time in hospital and at the time of follow-up visits. The women were asked if they had been in contact with medical services due to a complication but no systematic information from the health care system was collected.

The influence of concomitant oophorectomy

The majority of studies focusing on well-being after hysterectomy include both hysterectomy alone and hysterectomy with concomitant bilateral oophorectomy. Since loss
of sex hormones may influence the outcome in psychological wellbeing, this might be a bias [Kastgir 1998; Taylor 2001]. In studies focusing on the effect of hysterectomy with or without concomitant bilateral oophorectomy Nathorst-Böös et al. in a retrospective study found significantly more depression and anxiety measured by the PGWB in the oophorectomy group compared with women with preserved ovaries [Nathorst-Böös 1993]. In contrast with this, in a prospectively but not randomised study Aziz et al. found that one year after hysterectomy there were no difference in the PGWB scores between the oophorectomy and non-oophorectomy groups [Aziz 2005]. However, in that study all women in the oophorectomy group were advised to take oestrogen after surgery. Recently a review investigating the issue of hysterectomy versus hysterectomy plus oophorectomy for premenopausal women and primarily focusing on mortality rate and the need for future surgical interventions concluded that of the 119 identified studies, only one was controlled but not completely randomised and the authors proposed that more research should be done with a higher methodological quality [Orozco 2008].
Conclusions

- No difference was found in postoperative psychological well-being between women undergoing laparoscopic and abdominal hysterectomy (trial 1) and subtotal abdominal and total abdominal hysterectomy (trial 2).

- Long-term psychological well-being had improved in both groups as shown by results from the six-month follow-up for the group who had laparoscopic/abdominal hysterectomy and the 12-month follow-up for the group that had subtotal/total hysterectomy.

- Compared with abdominal hysterectomy, operating time is significantly longer for laparoscopic hysterectomy but stay in hospital and the length of sick-leave are both shorter.

- The day-by-day recovery of general well-being after laparoscopic hysterectomy does not proceed more rapidly than after abdominal hysterectomy. General wellbeing after surgery improves up to 5 weeks postoperatively independent of the mode of hysterectomy.

- Personality factors have an impact on postoperative recovery. Women with high stress-coping abilities have a faster recovery in general wellbeing than women with low stress-coping abilities.

- The length of the sick-leave after hysterectomy is influenced by the occurrence of complications, but not by the woman’s stress-coping ability.

- The day-by-day recovery of general well-being after SH is equal to recovery after TH.

- The occurrence of postoperative complications and low preoperative level of psychological well-being impair postoperative recovery significantly and prolong the duration of sick-leave.
Future perspectives

The results of the studies in this thesis address the question of the motivating force that leads a gynaecological surgeon to choose the method of hysterectomy. The introduction of laparoscopic hysterectomy made way for the rebirth of vaginal hysterectomy and in fact even for subtotal hysterectomy. This rebirth showed that the trend toward choosing laparoscopic hysterectomy and subtotal hysterectomy was established before there was adequate scientific evidence for the potential advantages of these methods. Once results from randomised trials had been published both the LH and the SH decreased in popularity. It seems that fashion can be stronger than science in the field of hysterectomy. This view is supported by widespread acceptance of robotically assisted laparoscopic surgery [Diaz-Arrastia 2002], which has become a popular method in the last few years even though no long-term follow up has yet shown if there are advantages in the long term. Since the robot assisted technique is a laparoscopic technique regarding entry of the abdominal wall, nothing in the present literature yet speaks for advantages measured in terms of long-term outcomes for this method compared with vaginal or even abdominal hysterectomy. On the other hand, since the safety and physical and psychological well-being outcomes seem equal for the different methods of hysterectomy, the surgeon together with the patient is free to choose the best method based on surgical experience and the patient’s wishes. This is true, at least, if the costs for the different methods are not put into the equation. In my opinion future efforts in the research field of hysterectomy should be focused on long-term outcome measures and interventional studies with the goals of reducing minor and major complications and improving the well-being in risk groups of women. Studies regarding recovery with well defined and specific outcome measures comparing length of sick-leave should also be encouraged. These efforts should be combined with interventional studies in an effort to identify vulnerable individuals and to optimise the outcome for this group in particular.

Finally

The debate concerning the best way of determining the best way to undertake a hysterectomy is ongoing [Donnez 2009; Garry 2009] and it is a challenge for every gynaecologist to keep pace with the emerging literature in this field and to carefully and critically analyse the contents of it.
‘Most gynaecologists and their patients would agree that the optimum procedure is the one that can be performed with the greatest safety and produce the greatest relief of symptoms and improvement in quality of life in the most cost-effective manner.’

Sammanfattning på svenska.


De flesta vetenskapliga studierna rörande hysterektomimetoder har varit inriktade på hur metoderna skiljer sig åt avseende operationstid, vårdtid, sjukskrivningstid, komplikationer och kostnader, men mycket få studier har fokuserat på om metoderna ger någon skillnad vad gäller påverkan på det psykologiska välbefinnandet på lång sikt och återhämtningen av det generella välbefinnandet i anslutning till kirurgen. Förespråkare för titthålskirurgin har hävdat att denna är ett lindrigare ingrepp för kvinnan och därmed också förenad med en snabbare återhämtning och ett bättre välbefinnande efter operation. Mycket få studier har fokuserat på om personliga egenskaper hos kvinnan som skall genomgå hysterektomi har betydelse för välbefinnandet efter det kirurgiska ingreppet.

I den första delstudien i denna avhandling (artikel I och II) jämfördes 125 kvinnor som genomgått laparoskopisk hysterektomi och abdominell hysterektomi avseende psykologiskt välbefinnande och återhämtningen av det generella välbefinnandet. Operationstid, vårdtid, komplikationer och sjukskrivningstid jämfördes också. Operationsmetoden som användes i det enskilda fallet blev fastställd genom lottning, så det var inte kvinnan eller gynekologen som avgjorde vilken operationsmetod som skulle användas. En vecka innan operationen, 5 veckor respektive 6 månader efter operationen mättes det psykologiska välbefinnandet med hjälp av olika frågeformulär. I anslutning till operationen fick kvinnorna också dagligen skatta återhämtningen av sitt generella välbefinnande.

Studien visade att det inte förelåg någon skillnad i det psykologiska välbefinnandet efter operationen om man opererats med laparoskopisk hysterektomi eller med abdominell

Kvinnor med en hög förmåga att hantera en stressfull situation hade en snabbare återhämtning av det generella välbefinnandet jämfört med kvinnor med låg stresshanteringsförmåga. Stresshanteringsförmågan hade också ett starkt samband med kvinnans psykologiska välbefinnande innan operationen.

statistisk justering gjordes för effekten av smärtlindring, komplikationer och könshormonnivåer. Inte heller återhämtningen av det generella välbefinnandet skiljde sig mellan kvinnorna som genomgått subtotal respektive total hysterektomi.

Rörande förekomst av komplikationer till hysterektomi fanns i såväl delstudie 1 som delstudie 2 ett samband mellan förekomst av en komplikation efter hysterektomi och sjukskrivningstidens längd. Detta samband gällde dock bara förekomst av lindringare komplikationer av typen urinvägsinfektion eller sårinfektion men inte för allvarliga komplikationer av typen stor blödning vid eller efter operationen. Detta förklaras sannolikt av att en stor komplikation åtgärdas direkt under operationen eller vårdtiden till skillnad från den mindre komplikationen som inträffar när kvinnan lämnat sjukhuset och håller på att återhämta sig hemma. I delstudie 2 rapporterade kvinnorna som genomgått subtotal hysterektomi mer besvär ett år efter operationen än de kvinnor som genomgått total hysterektomi. Denna skillnad betingades i huvudsak av besvär med blödningar från den kvarlämnade livmodertappen. Det är därför mycket viktigt att kvinnor som önskar att livmodertappen kvarlämnas informeras om risken för detta (20 % i delstudie 2) innan operationen.

Sammanfattningsvis förbättras det psykologiska välbefinnandet generellt efter hysterektomi hos kvinnor som genomgår hysterektomi pga. blödningsrubningar och/eller muskelknutor. Någon säker skillnad i psykologisk välbefinnande hos kvinnor mellan de studerade operationsmetoderna kunde inte påvisas. Återhämtningen av det generella välbefinnandet skiljde sig inte heller mellan de jämförda operationsmetoderna. Den förmodade fördelen av de mindre invasiva metoderna laparoskopisk hysterektomi och subtotal hysterektomi kunde därmed inte påvisas. Återhämtningen av välbefinnandet var starkt kopplad till kvinnans stresshanteringsförmåga och psykologiska välbefinnande innan operationen. Operationsmetoderna tycktes ha mindre betydelse för återhämtningen. Detta bör beaktas vid rådgivningen och informationen inför hysterektomi och ger såväl kvinnan som gynekologen möjligheten att välja operationsmetod.

Att identifera kvinnor med låg stresshanteringsförmåga innan operationen och ge dessa kvinnor extra information och stöd i anslutning till operationen, samt att ytterligare minskas förekomsten av komplikationer efter operationen skulle kunna förbättra utfallet efter hysterektomi ytterligare och troligen även minska sjukskrivningstiden. Fortsatta studier behövs för detta.
Acknowledgments

Dear reader, I’m not surprised you are reading this section of the thesis, most people do. Regarding the rest of this book I hope it isn’t as Groucho Marx once said: “From the moment I picked your book up until I laid it down, I was convulsed with laughter. Someday I intend reading it”.

Many people have contributed generously to this thesis. I particularly wish to express my sincere gratitude to:

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My parents Berith and Börje for always believing in me and for all practical support. My sisters Helena and Ulla-Carin for being better piano players than me. Otherwise this would probably not have happened.

Helena, my playmate and companion in life for encouragement, support, comfort and love. Your lawyer –eyes made the Swedish summary.

Joar, my golden, curly, dream boy. You are the meaning of my life. Let’s go and explore the rest of it! Empire State Building, Petronas Towers, Taipei 101 or Sears Tower? You decide!

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**Web links**


[www.nice.org](http://www.nice.org)

Appendix

Frågeformulär angående ”stresshantering”

Stress Coping Inventory (SCI)

Instruktion:

I det här frågeformuläret finner Du ett antal påståenden. Läs varje påstående och sätt en ring runt den siffra som bäst motsvarar vad som gäller för Dig.

Om Du vill ändra Ditt svar gör Du en sol: 1 2 3 4 5 6

Och fyller sedan i rätta svaret: 1 2 3 4 5 6

Fundera inte för länge på Ditt svar!

© 1992 Klaas Wijma
<table>
<thead>
<tr>
<th></th>
<th>1. Min förmåga att hitta en lösning till ett problem tar snabbt slut</th>
<th>Nästan alltid</th>
<th>Mycket ofta</th>
<th>Ganska ofta</th>
<th>Ibland</th>
<th>Sällan</th>
<th>Nästan aldrig</th>
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<td>1</td>
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<td>4</td>
<td>5</td>
<td>6</td>
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<tr>
<td>2</td>
<td>När jag utsätts för påfrestningar kan jag trots allt tänka klart</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
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<tr>
<td>3</td>
<td>Jag blir nervös när det inte går som jag tänkt mig</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
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<td>När jag utsätts för påfrestningar kan jag trots allt hålla huvudet kallt</td>
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<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
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<td>5</td>
<td>Jag är bra på att hitta lösningar vid oväntade situationer</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>När jag utsätts för påfrestningar har jag svårt att hålla mig till det som skall göras</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>När det blir svårt &quot;ger jag jänet&quot;</td>
<td>1</td>
<td>2</td>
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<td>4</td>
<td>5</td>
<td>6</td>
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<tr>
<td>8</td>
<td>Jag får panik när det inte går som jag har förväntat mig</td>
<td>1</td>
<td>2</td>
<td>3</td>
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<td>6</td>
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<tr>
<td>9</td>
<td>Jag känner att jag klarar av det mesta i mitt liv</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>10</td>
<td>Jag upplever plötsliga förändringar som farliga</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>11</td>
<td>Jag presterar en extra insats om det plötsligt behövs</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
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<tr>
<td>12</td>
<td>Vid påfrestningar kan jag skilja mellan det som ska göras direkt och det som kan vänta</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
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<td>6</td>
</tr>
<tr>
<td>13</td>
<td>Jag blir rädd för att göra fel när jag måste göra något under stress</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
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<td>14</td>
<td>Jag får stöd av andra när jag hamnar i problem</td>
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<td>2</td>
<td>3</td>
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<td>Uttryck</td>
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<td>15</td>
<td>Jag känner mig handfallen vid plötsliga och oväntade händelser</td>
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<td></td>
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<td>Vid påfrestningar känner jag mig hotad</td>
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<td></td>
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<td>När jag hamnar i ett svårt läge klarar jag av situationen</td>
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<td>18</td>
<td>Vid påfrestningar kan jag tänka klart</td>
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<td></td>
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<td>19</td>
<td>Jag vill helst ha lugn och ro omkring mig</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>20</td>
<td>Jag vill helst gömma mig när jag utsätts för påfrestningar</td>
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<td>21</td>
<td>Jag känner mig stimulerad när något oväntat händer</td>
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<td>22</td>
<td>Jag blir apatisk när det inte går som jag tänkt mig</td>
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<td></td>
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<tr>
<td>23</td>
<td>Jag har en bra tolerans mot stress</td>
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<td>Jag litar på min förmåga att klara av svåra saker</td>
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<td>25</td>
<td>Plötsliga och oväntade händelser gör mig osäker</td>
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<td>26</td>
<td>När det inte går som jag har tänkt mig, tar jag mig tid att fundera igenom saken</td>
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<td>27</td>
<td>Jag vill att det händer något i livet</td>
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<td>28</td>
<td>Jag blir rädd när jag måste utföra ett uppdrag som jag har svårt att klara av</td>
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<td>29</td>
<td>Jag kan ta mig tid och överväga förändringar när jag har kört fast</td>
<td>Nästan alltid</td>
<td>Mycket ofta</td>
<td>Ganska ofta</td>
<td>Ibland</td>
<td>Sällan</td>
<td>Nästan aldrig</td>
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<td>Vid oklarheter försöker jag ta reda på hur jag kan göra något åt situationen</td>
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<td>Jag blir irriterad när det inte går som jag har tänkt mig</td>
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<td>Jag blir orolig när jag märker att jag kommer att misslyckas med en viktig uppgift</td>
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<td>Jag känner mig splittrad när jag har mycket att göra</td>
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<td>När det inte går som jag har tänkt mig försöker jag ändra det så att det blir mer som jag vill</td>
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<td>Jag kan samarbeta bra med andra när det kör ihop sig</td>
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<td>När jag får en kroppsskada tänker jag att det kommer att &quot;ordna sig&quot;</td>
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<td>Jag blir som förlamad när jag känner mig hotad</td>
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<td>Vid påfrestningar känner jag att jag inte kan tänka klart</td>
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<td>Jag lyckas med att klara av många uppgifter samtidigt</td>
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<td>Jag har svårt att reagera när jag utsätts för hot</td>
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