VALORISATION ADDENDUM

Why is this thesis relevant?
The treatment of pelvic organ prolapse (POP) has been studied for many years and many different conservative and surgical treatments have been developed. The most optimal treatment will restore the anatomy, resulting in improvement of disease specific quality of life. Preferably, this treatment has a low risk of complications and recurrence of POP. The studies presented in this thesis focus on the effectiveness of different treatments for POP.

Relevance
Pelvic organ prolapse (POP) is a common gynaecological condition, and its aetiology is multifactorial. Risk factors include increased age, vaginal childbirth, obesity, constipation, connective tissue disorders, obstetric factors (forceps, prolonged second stage of labour, macrosomia), race, heavy lifting and a family history of prolapse. In a general Dutch female population aged 45-85 years, 75% of women had some degree of POP. POP can negatively affect women’s quality of life by local physical effects (pressure, bulging, heaviness or discomfort) or its effect on urinary, bowel or sexual function. Around 10% of women undergo surgery at some time in their lives for the management of prolapse or urinary incontinence. Consequently, about 13,000 surgeries are performed for this health problem in the Netherlands every year. About 30-50% of women who underwent POP surgery are confronted with recurrent POP. Women tend to get older and older and due to this improved life expectancy, there will be an enormous extra demand for future prolapse treatment.

Pessaries have been used as conservative treatment since the beginning of recorded history. Although pessaries have been reported to be effective in reducing prolapse symptoms, 20-50% of women will discontinue their pessary use within 1 year. Side effects are reported to occur in half of the women and are the main reason for discontinuation. Unfortunately, POP surgery could be accompanied by complications. Furthermore, there are significant cost implications for POP surgery, particularly when the index surgery has a quoted failure rate of up to 30%. In view of this dilemma, we decided to start a trial with a prospective cohort group treated with either pessary treatment or POP surgery, in order to individualize the counselling about treatment options and guide patients better to the decision process of the treatment of choice. We found that women treated with a pessary are bothered more by prolapse symptoms and undergo more often surgery in the first year of follow-up as compared to patients who undergo surgery. However, pessary treatment prevents
surgery in 72%, although prolapse symptoms are less in those who have been operated. These outcomes will help in order to individualize the counselling about treatment options and guide patients better to the decision process of the treatment of a symptomatic POP.

If chosen for a surgical treatment of a symptomatic POP, many techniques are described. Traditionally, vaginal hysterectomy was the standard treatment for uterine descent. However, the discussion is ongoing whether or not vaginal hysterectomy is the rational first choice in the treatment of uterine descent, and interest in uterus preservation seems to be increasing. Unfortunately, according to the evidence, the first-choice treatment for the surgical treatment of apical prolapse could not be determined. Our retrospective cohort study compared two of the most frequently used techniques: the uterine preserving Manchester Fothergill and vaginal hysterectomy. Vaginal hysterectomy (VH) and Manchester Fothergill (MF) have similar recurrence rates and re-interventions in this retrospective trial. Although small differences were found (less blood loss and operation time in the MF group and less urinary retention in the VH group), both procedures seemed to be equal effective.

Up to 10% of the women who had a hysterectomy because of prolapse symptoms, will subsequently need surgical repair for vaginal vault prolapse thereafter. Hysterectomy is a proven risk factor for POP, and also one of the top ten most common surgeries performed among Dutch women. The risk of prolapse following hysterectomy is 5.5 times higher in women whose initial indication for hysterectomy was genital prolapse as opposed to other indications. In case of post-hysterectomy vaginal vault prolapse (VVP), great variety of different surgical procedures to correct VVP has been reported. A standard approach or published guideline for the management of VVP is lacking. In this thesis, several treatments of VVP have been evaluated in a RCT and review. Although, abdominal sacrocolpopexy is considered as the first-choice treatment for VVP according to a Cochrane review on the topic, our trial provides evidence to support a laparoscopic approach over the abdominal approach. These results are in line with our review, although the reported differences in outcome between the techniques available for VVP are very minimal. All techniques have proved to be effective, and all trials reported good results for the anatomical and subjective outcome. Therefore, the first-choice treatment of VVP could not be given according to this review.
Although laparoscopic sacrocolpopexy (LSC) shows good results, sacrospinous fixation (SSF) is still the most performed surgical treatment for VVP, according to our survey of March 2017. These two techniques have never been compared in a RCT, therefore we started the SALTO 2 multicenter trial comparing SSF versus LSC in case of VVP.

**Target groups**

The results of this thesis are interesting for physicians, general practitioners, patients and the medical industry. Together we need to determine what the best treatment for POP is and continue innovations on existing and new techniques and materials. The survey we conducted in March 2017 concludes that there is no standardized method of treatment of VVP in the Netherlands and the practice pattern variation is high. These results of our survey are in line with a previous survey of the Urogynaecological Association (IUGA) in 2002. The procedure that the surgeon selects, is influenced by many factors, which include the nature, site and severity of the prolapse, the general health of the patient and of course the surgeon’s preference and capability. Unfortunately, this decision is not always based on evidence. The results presented in this thesis on the effectiveness of the different treatment options for POP, will contribute to further improvement of patient counselling and development of guidelines and would therefore hopefully lead to an increase in patient satisfaction and reduction of complications and recurrences.

**Activities and innovation**

All our results have been submitted to scientific research journals. We also had the opportunity to discuss our findings nationally and internationally to gain more attention for our work. Since no consensus on the best treatment has been reached yet, further research on promising therapies need to continue. Therefore, we conducted a multicentre randomized controlled trial comparing laparoscopic sacrocolpopexy to sacrospinous fixation; the SALTO-2 trial [chapter 7].

**Schedule and implementation**

In order to evaluate treatments for POP, and to determine the best treatment, with the lowest complication and recurrence rates, further research is necessary. The relevant ongoing trials and the relevant future research on the topic are described in the general discussion of this thesis [chapter 8]. Several existing treatment options should be evaluated in prospective RCT’s to determine the best treatment for the apical (vault) prolapse. Innovations, training and research on techniques and materials also needs to continue in order to optimize success rates and minimize complications.
However, the heterogeneity of outcome measures and standard treatments in the present literature is high. Therefore, a network meta-analysis was not possible, and the best treatment for VVP could not be determined. Initiators of future trials should be aware of this heterogeneity and need to choose carefully which treatments they want to compare and which measurement tools and outcomes they need to use. The measurement tools should be in line with the recommendations of ICS/IUGA.