National Institute for Public Health
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A literature review

RIVM Letter report 2018-0130
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Colophon

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Synopsis

Long-term complications of transvaginal mesh implants
A literature review

Since 2002 synthetic mesh implants are used to treat patients with pelvic organ prolapse.
Because of serious complaints, measures were taken in the Netherlands in 2011-2012. Since then mesh products are only implanted if alternative treatments such as physiotherapy, a vaginal ring and an operation using the body's own tissue were not effective to treat pelvic organ prolapse. In addition, mesh implantation may only take place in a limited number of specialized centers by well-trained recognized specialists. This is because mesh implantation requires experience and precision.

International scientific literature was examined by National Institute for Public Health and the Environment (RIVM) to determine complications that can occur one year or longer after mesh implantation. Complications that were observed in literature were: pain, mesh exposure and erosion, incontinence and pain during intercourse. In addition, a prolapse can recur, for example in another area then where the mesh was implanted. The complication rates varied widely in the literature. Additionally, data on the duration and severity of a complication was limited. This variation and the limited data can partially be attributed to the lack of an unambiguous, international inventory of complications. There is a lot of attention for mesh implants in the international media. Complaints reported to the Dutch Health and Youth Care Inspectorate between 2009 and 2012 demonstrated the occurrence of serious complications. For these reasons, RIVM is calling for a standardized guideline with universal definitions to facilitate the reporting of the complications of mesh implants for pelvic organ prolapse.

In the meantime, newly developed mesh implants entered the market, that are expected to have less complications. In this literature study, identified complications were primarily associated with products that are no longer available on the Dutch market.

Keywords: transvaginal mesh, pelvic organ prolapse, female, implant, health problems, long-term complications

Publiekssamenvatting

Lange-termijncomplicaties van vaginaal ingebrachte bekkenbodemmatjes

Een literatuuronderzoek

Bekkenbodemmatjes worden al sinds 2002 gebruikt en kunnen worden geplaatst bij verzakkingen in het bekkenbodemgebied. Naar aanleiding van klachten zijn in Nederland sinds 2011-2012 maatregelen getroffen. Sindsdien worden bekkenbodemmatjes alleen nog geplaatst wanneer alternatieve behandelingen zoals fysiotherapie, een pessarium, en een operatie met behulp van lichaamseigen materiaal onvoldoende effect hebben gehad. Bovendien mogen de behandelingen uitsluitend in een beperkt aantal, gespecialiseerde centra worden uitgevoerd door erkende specialisten. Dit omdat de plaatsing precisie en maatwerk vergt.

Het RIVM heeft in de internationale wetenschappelijke literatuur onderzocht welke complicaties een jaar of langer na de plaatsing van bekkenbodemmatjes zijn opgetreden. Dit zijn pijn, het zichtbaar worden van het bekkenbodemmatje in de vagina, incontinentie en pijn bij het vrijen. Ook kan opnieuw een verzakking optreden, bijvoorbeeld op een andere plaats dan waar het matje is geplaatst. Hoe vaak de onderzochte complicaties voorkomen varieert sterk in de literatuur. Daarnaast zijn in de literatuur weinig gegevens te vinden over de duur en de ernst van deze complicaties. Dit komt onder andere doordat de complicaties internationaal niet eenduidig worden geïnventariseerd. In de internationale media is veel aandacht voor complicaties bij bekkenbodemmatjes. Uit klachten die gemeld zijn bij Inspectie Gezondheidszorg en Jeugd (IGJ) tussen 2009 en 2012 blijkt dat er ernstige complicaties op kunnen treden. Het RIVM pleit daarom voor een gestandaardiseerde richtlijn om complicaties van bekkenbodemmatjes te rapporteren.

Inmiddels zijn er vernieuwde producten op de markt gekomen die naar verwachting minder complicaties veroorzaken. In deze literatuurstudie zijn voornamelijk complicaties gevonden bij producten die niet meer op de Nederlandse markt zijn.

Kernwoorden: transvaginaal synthetisch bekkenbodemmatje, verzakking in bekkenbodem, vrouw, implantaat, gezondheidsproblemen, lange-termijncomplicaties, gezondheidsproblemen

Contents

Summary

In 2011, the Dutch Health Care Inspectorate, currently the Dutch Health and Youth Care Inspectorate (IGJ) received and analysed incident reports with transvaginal mesh (TVM) implants for the treatment of pelvic organ prolapse (POP). The Inspectorate started an investigation and published a report warranting caution regarding the use of TVM implants [1]. Upon finalisation of the report, media attention in December 2012 led to an increase in reports to the Inspectorate regarding serious complications experienced by patients after receiving a TVM implant, which were included in the report. The Netherlands Society of Obstetrics and Gynaecology (NVOG) took several measures to improve TVM implantation. They implemented a multidisciplinary guideline, and added contra-indications for the treatment with the purpose of decreasing the number and severity of complications following TVM implantation. In addition, synthetic mesh implants evolved and became lighter, more elastic and have smaller pores [2], which is expected to contribute to further decreasing the number and severity of complications. Since 2013, the number of reports received by the Inspectorate on TVM implant complications has decreased in the Netherlands. However, in the USA, Australia, New Zealand, Ireland and the UK mesh implants for POP continue to cause complaints. This has led to new guidelines for the use of TVM implants that are more stringent. In the UK and Australia, several mesh products were withdrawn from the market.

As more than a decade has passed since the first implantation of TVM implants, it was expected that data on long-term complications are now available. To gain insight in the long-term complications (type, rate, duration and severity of complications) the National Institute for Public Health and the Environment (RIVM) conducted this literature study. Insights in the possible effects on complications caused by factors such as the implementation of the multidisciplinary guidelines or evolved mesh implants were beyond the scope of this study.

In the international literature published between 2012 and 2018, complications such as pain, mesh exposure and erosion, recurrent prolapse, dyspareunia and incontinence were the most reported long-term complications. Similar types of complications and complication rates were seen in the previous RIVM study focusing on literature published before 2012 [3]. Data on the duration and severity of complications were lacking and limited, respectively. Interventions performed to resolve complications were described. These interventions varied from simple treatment with oestrogen cream to major interventions such as an operation. Data on the success rate, if applicable, were collected to place the complications in some perspective. It was found that in the past (2014-2015) the success rate of the treatment was mainly linked to the anatomical success observed by physicians. In later studies (2016-2018) a shift was seen towards reports on patient satisfaction.

1 Introduction

1.1 Background

More than half of the women worldwide are affected by some degree of pelvic organ prolapse (POP) and urinary incontinence during their life [4]. For example, overstretching of soft connective tissue like fascia during pregnancy, can result in damage of the tissue which may lead to POP [5]. Complications following POP vary from overactive bladder to vaginal pain. Depending on the type of POP and the severity of the complications, POP is treated with or without an operation. A pessary may help in patients with strong pelvic floor muscles with posterior POP. Another treatment option is physiotherapy to strengthen the pelvic floor muscles. When POP complications are severe, an operation may be necessary. With traditional surgical techniques, damaged tissue is connected with sutures of absorbable material [6]. The last decades, POP is also treated by implanting synthetic mesh implants via the abdominal or transvaginal approach [3].

1.1.1 Complications of transvaginal mesh (TVM) implants

Between 2009 and 2012, the Dutch Health Care Inspectorate (currently the Dutch Health and Youth Care Inspectorate (IGJ)) received incident reports on serious complications with transvaginal mesh implants (TVM). The Inspectorate reported that the complaints came from patients who received polypropylene mesh implants through the transvaginal route for the repair of POP. The Inspectorate investigated the complaints thoroughly and found that despite the severe complications in some women, many women experienced benefit from the treatment. The treatment of POP through the transvaginal route with polypropylene mesh implants was at that time a relatively new treatment method. The Inspectorate called upon gynaecologists, urologists and surgeons to exercise caution regarding the application of TVM implants [1].

In 2011, the National Institute for Public Health and the Environment (RIVM) performed a study commissioned by the Inspectorate on complications of pelvic floor repair systems in the international literature to gain information on the risks of gynaecological mesh implants in general [3]. The most frequently reported complications described in the literature until 2011 were: mesh exposure/vaginal erosion, urinary symptoms, recurrent prolapse, dyspareunia, infection, and constipation/voiding difficulty. Occurrence rate of complications varied considerably, e.g. between 2% and 69%, and a major variation was observed in the follow-up period (1 day to 3.5 years) [3].

1.1.2 Renewed world-wide attention for complications of TVM implants

The last few years TVM implants received political and media attention in the USA, Australia, New Zealand, Ireland and the UK. Reasons are the ongoing reports of serious complications in these countries and the number of filed lawsuits against manufacturers of mesh implants [7]. This led to new more stringent guidelines in these countries for the use of TVM implants. In Australia, some of these products were removed from the market [8].

In 2016, the US Food and Drug Administration (FDA) reclassified TVM implants from class II (moderate-risk) to class III (high-risk) devices. The FDA decided to reclassify, because new information showed that the control measures were not sufficient to assure safety and effectiveness of the implants. Moreover, manufacturers now need to submit a premarket approval (PMA) application to support the safety and effectiveness of their TVM implants for POP repair [9]. Safety and performance data and evaluation requirements will be more stringent in Europe under the recently published new medical device regulations [10].

In 2017, The Australian Therapeutics Goods Administration (TGA) decided to remove some TVM mesh implants from the Australian Register of Therapeutic Goods (ARTG). The TGA based their decision on their latest review of published international studies and an examination of the clinical evidence for these products. TGA stated that the benefits of using TVM products for POP repair did not outweigh the risks of these products posed to patients [8]. In 2018, the Australian Government responded to the 13 recommendations made by the Senate Committee and stated to take sweeping steps to deal with the adverse effects of TVM [11]. The recommendations of the Senate Committee included, for example, enhancing safety and transparency for patients and medical practitioners and strengthen post-market vigilance [12]. Furthermore, the Australian Government issued a national apology to women affected by a vaginal mesh [13].

Following the actions of TGA, the New Zealand Medicines and Medical Devices Safety Authority (Medsafe), requested safety information from all suppliers of TVM products in New Zealand. The companies commented that products removed from the Australian register were no longer supplied in New Zealand [14].

The Health Products Regulatory Authority (HPRA) in Ireland continues to encourage reporting of complications relating to TVM [15] and the National Institute for Health and Care Excellence (NICE) in the UK issued new guidelines in 2017 to limit the use of TVM implant interventions [16].

1.1.3 Development of TVM implantation in the Netherlands

Since 2013, the number of reported complications received by the Inspectorate in the Netherlands has decreased. In USA, Australia, New Zealand, Ireland and the UK, TVM implants received attention over the last few years. To gain insight in the developments regarding TVM implants in the Netherlands the RIVM has recently started a new study. This investigation consists of a market analysis, assessment of technical dossiers, and a biocompatibility study of mesh implants.

Preliminary findings of this ongoing Dutch investigation indicate that a part of the most frequently studied mesh implants described in the international literature are not used anymore in the Netherlands. Moreover, there have been developments in the type of TVM. Synthetic mesh implants have become lighter, more elastic, have smaller pores and the material is fixated with less tension [2]. The methodology for TVM implantation has been professionalised over the years and a

multidisciplinary guideline is implemented. Mesh implant surgery is centralized in a limited number of hospitals in the Netherlands. Additionally, TVM implant surgery is specialized and only performed by uro-gynaecologists, who are extensively trained (under supervision) to perform this type of surgery. Furthermore, there is a registry for registration of TVM implantation and detected complications. Finally, the indication for TVM implantation has changed over the years. Only women who have a recurrent prolapse, are eligible for treatment with TVM implants. Women with weak connective tissue or chronic lung disease are also more eligible for TVM implantation, because in these patients the traditional surgery technique is more likely to fail. Patients with severe pain complaints before surgery are at increased risk of more severe pain complications after TVM implantation [17, 18].

More details and results of the new study on TVM implants in the Netherlands will be published in the future.

1.2 Objective of the current literature study

Complications up to one year after TVM implantation are described in detail in numerous reports [1, 3, 8]. However, long-term complications (>1 year) are less frequently described. As more than a decade has passed since the first TVM was implanted, data on long-term complications should now be available in the international literature. The objective of this literature study is to gain insight in the long-term complications of synthetic TVM, focussing on types of complications, complication rates, follow-up periods, duration and severity of the complications and used classification systems. In addition, a comparison will be made with the data from the previous RIVM literature [3] in order to identify new complications.

2 Method

2.1 Literature search

2.1.1 Identification of long-term complications

For the identification of long-term complications, international literature published between 2012 and February 2018 was reviewed. The year 2012 was chosen, because the previous literature review was performed in 2011 [3]. The search strategy consisted of three steps:

- First, information from reports and literature on TVM implants was used to identify keywords (Table 1) [1, 3, 19-25].
- Second, an information specialist built a syntax with the keywords (Annex 3).
- Third, the syntax was used to scan for relevant articles in the following databases: Elsevier Embase® and NCBI PubMed.

Table 1. Keywords search strategy long-term complications

Keywords	Limited	Excluded
Transvaginal mesh	2012-2018	Conference abstract
Mesh	Dutch/English	Conference paper
Pelvic organ prolapse		Editorial
Stress incontinence		Letter
Urinary incontinence		Review
Medical device		Note
Complication		Short survey
Adverse event		
Humans		

2.1.2 Classification methods for severity and duration of long-term complications

NCBI PubMed and Elsevier Scopus® were used to identify articles describing methods for categorization or classification of severity and duration of long-term complications with TVM implants. Keywords in various combinations were used for this search (Table 2).

Table 2. Keywords search strategy classification methods

Keywords	Limited
medical devices, adverse events, effects, criteria, index, complications, severity, classifications, category, categories, long-term, surgery complications, and surgical complications, meddra, implants, transvaginal mesh, duration, seriousness, postoperative complications, etiology, prosthesis, humans, urogenital procedure, pelvic floor	Dutch/English

2.1.3 Traditional POP surgery and TVM implantation

NCBI PubMed and Elsevier Scopus® were used to identify articles comparing traditional POP surgery and TVM implantation. Keywords in various combinations were used for this search (Table 3).

Table 3. Keywords search strategy traditional POP surgery and TVM

Keywords	Limited
traditional, POP, surgery, colporrhaphy, mesh, transvaginal mesh, complications, long-term, surgical complications, surgery complications, pelvic organ prolapse	Dutch/English 2012-2018 trans obturator

2.2 Data collection, classification and analyses

A selection of relevant articles was made, based on the information in title and abstract. Only polypropylene mesh products implanted through the transvaginal route were included. Articles with clinical trial data, including long-term follow-up data and comprehensive meta-analyses were included.

Exclusion criteria are listed below:

- Articles with objectives such as: compare safety and effectiveness of medical procedure/incidence of organ prolapse with no reference to mesh/cost analysis/surgical procedures/decision modelling/complications after mesh excision
- Case reports
- Articles with study population of males
- Articles only describing postoperative or short-term complications
- Articles studying sling/artificial urinary sphincter implantation/ intrinsic sphincter deficiency/urethral wrap/combination of mesh and sling together
- Articles on a Laparoscopic sacro-colpopexy procedure (Definitions)
- Guidelines

For the identification of long-term complications, we initially identified 206 articles of interest. After reviewing the titles and abstracts, 98 articles remained. A further analysis of the content of the articles, using the exclusion criteria, reduced the number of articles to 89.
The following information from these articles was collected:

- Study population, i.e. number of patients
- Mesh product(s),
- Type of complications,
- Complication rate,
- Follow-up period (≥ 12 months),
- Duration of complications,
- Severity of complications,
- Classification methods, i.e. Clavien-Dindo or International Urogynecological Association (IUGA)/International Continence Society (ICS) or Pelvic Organ Prolapse Quantification (POP-Q) [26-28].

All the information was summarized in an Excel table for further analysis.

Only long-term complications diagnosed or reported at 12 months or more were used in the analyses. Complications were excluded from analysis, if a certain complication occurred before 12 months, despite the fact that the article described a longer follow-up period.

Different descriptions for the same sort of complications were used. Therefore, data on the same sort of complications were aggregated (Annex 4). For the aggregation step, complications described in the previous RIVM literature review [3] and IGJ report [1] were used. In addition, a distinction was made for pain and dyspareunia complications. For the complication rate, we determined the range per complication type. A comparison of the results found in this literature search was made with the previous RIVM literature review [3]. When duration or severity of a complication, or classification method was mentioned in an article, this was included in the Excel table for further analysis. Also, available data on interventions, patient's satisfaction or anatomic success were included to place the complication rates in perspective.

3 Results

3.1 Long-term complications of TVM implants

Review of the scientific literature showed that various complications occurred after TVM implantation. Unfortunately, large variations were observed in complication rates, study setups, number of patients and follow-up periods. Information on severity and duration of complications was limited.
Details of type of complications and complication rates are provided in Annex 5. The most important findings are summarized below and compared with findings from the previous RIVM literature review [3].

Complication types
Complications were differently described in the international literature. For example, there were 33 different descriptions for pain-related complications (Annex 4). With the aggregation step, 8 complication types were identified: pain, mesh exposure and erosion, recurrent prolapse (POP-Q prolapse ≥2), dyspareunia, de novo dyspareunia, incontinence, de novo incontinence and 'other complications' (e.g. infection, bowel-, vaginal- and urinary tract complications).

Textbox 1.
Review of the scientific literature showed that patients with dyspareunia and/or incontinence complications consisted of 2 groups:
1. Women who experienced dyspareunia and/or incontinence before and after TVM implantation,
2. And women who only experienced the complication after TVM implantation. Several, however not all articles described this as de novo dyspareunia or de novo incontinence.

Most articles did not describe if pre-operative dyspareunia or incontinence symptoms were worse, better or equal compared to the situation after TVM implantation.
In the literature, the complications dyspareunia and incontinence were more frequently described compared to de novo dyspareunia and de novo incontinence. Less than half of the articles made a distinction between de novo dyspareunia and dyspareunia or de novo incontinence and incontinence. Standardized description of study setups and outcomes regarding pre-operative symptoms and de novo complications observed after TVM implantation are necessary to enable systematic analysis of TVM implantation.

Many articles did not universally describe the complications dyspareunia and incontinence (Textbox 1). Farthmann *et al*. made a distinction between patients who reported dyspareunia before and after TVM implantation and patients who only reported dyspareunia after TVM implantation (de novo dyspareunia) [29]. Ow *et al*. reported dyspareunia at a follow-up of 1 year and long-term [30]. In articles similar to Ow *et al*. it was unfortunately not possible to determine if dyspareunia was de novo dyspareunia or if patients experienced dyspareunia before TVM implantation. This was also observed for the complications incontinence and de novo incontinence. De Landsheere *et*

al. made a distinction between these complications and reported 4.4% of patients with de novo incontinence, 6.9% urinary incontinence and 0.4% recurrent incontinence [31]. This distinction was not made by Bjelic-radisic *et al*. that included 15 patients with incontinence symptoms before TVM implantation. At 3 months follow-up after TVM implantation 4 patients had incontinence complications and at 1 year follow-up 8 patients had incontinence complications [32]. In this article and comparable articles, it was unfortunately not possible to determine if incontinence was de novo incontinence or if patients experienced incontinence symptoms before TVM implantation.
Therefore, in the current overview complications dyspareunia and incontinence include two groups: women who only experienced the complication after TVM implantation and women who experienced dyspareunia and/or incontinence symptoms before TVM implantation. For a complete overview of all reported complications in the literature, see Annex 5.

The types of complications were compared with the data from the previous RIVM literature review [3]. No new complications were identified in the current study compared to the previous RIVM literature review. In the current study, the complications infection and constipation/voiding difficulty were aggregated into the group 'other complications'. In addition, a distinction was made between the complications pain and dyspareunia.

Complication rates
The complication rates at 1 year or more follow-up varied considerably per complication (Table 4, Figure 1 and 2). Table 4 represents the range of complication rates identified in all articles taken together. Figure 1 and 2 represent the complication rates identified in the international literature. Especially, for dyspareunia, the range of complication rates was wider than for other complications. Dyspareunia is only applicable to people who are sexually active.

All 8 different complication types were typically not simultaneously described within 1 article. For example, 1 article may describe dyspareunia and/or recurrent prolapse complications, while another may describe mesh exposure and erosion.

The complication rates were compared with the data from the previous RIVM literature review in which a top 5 of most reported/observed complications was described [3]. No large changes in complication rates were identified in the current study compared to the previous RIVM literature review (Table 4).

Table 4. Range of complication rates after TVM implantation

Complications	**Current RIVM literature study:**	**Previous RIVM literature study [3]:**	
	Range of complication rates (follow-up period ≥1 year)	Range of complication rates 2011[3] [a]	
	All studies	Prospective studies [b]	Review articles [c]
Pain	0-33.8%	-	-
Mesh exposure & erosion	0-22.9%	0.7-19.0%	0.0-25.0%
Recurrent prolapse ≥2	0-35.0%	3.5-41.0%	
De novo dyspareunia	0-17.6%	-	-
De novo incontinence	1.3-36.0%	-	-
Other complications	0-38.5% [d]	2.1-18.1% [e]	2.3-31.5% [f]
Total dyspareunia [g]	0-48.0%	1.0-22.2%	2.0-69.0%
Total incontinence [h]	0-44%	-	-

Table shows the range of complication rates identified in the current literature study and identified in the previous literature study of 2011.

a. Range of complication rates in 2011 was provided for the top 5 most reported/observed complications.
b. Complications during follow-up visits between 1 day to 3.5 years after surgery
c. Complications were observed between 8 weeks to 3.2 years after surgery.
d. See Annex 4
e. Urinary symptoms, urinary tract infection, constipation/difficult voiding
f. Urinary symptoms, infection, constipation/difficult voiding
g. Total dyspareunia includes de novo dyspareunia and dyspareunia (Textbox 1).
h. Total incontinence includes de novo incontinence and incontinence (Textbox 1).

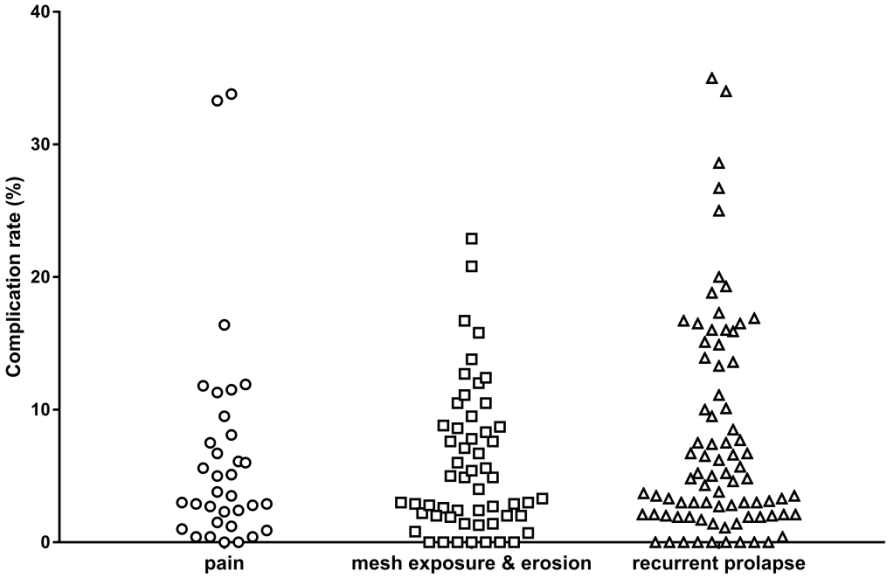

Figure 1. Scatter plot of pain, mesh exposure & erosion, and recurrent prolapse complications.
This scatter plot visualizes the variation in complication rates between the different articles. Multiple factors [2], such as surgeon's experience, patient indications and study design can cause differences in complication rates (more details are described in paragraph 3.2).

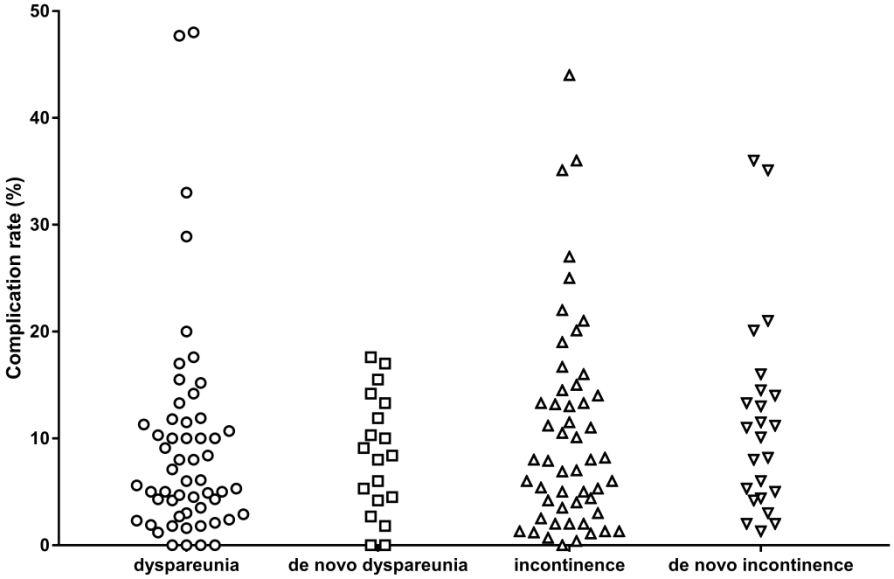

Figure 2. Scatter plot of (de novo) dyspareunia and (de novo) incontinence complications.
This scatter plot visualizes the variation in complication rates between the different articles. Multiple factors [2], such as surgeon's experience, patient indications and study design can cause differences in complication rates (more details are described in paragraph 3.2). Complication rates of de novo dyspareunia and de novo incontinence also appear in the scatters of dyspareunia and incontinence, respectively.

Duration and severity of complications
Only 3% of the identified articles reported duration of a complication. Vaiyapuri *et al*. reported that the complication healed spontaneously within 2 months [33]. Information on severity of complications was very limited and not standardized. Subjective terms like 'severe', 'mild' and 'bothersome' were used [34, 35]. In addition, some articles reported whether a complication was symptomatic or asymptomatic [36], resolved or scored as a serious event [37]. The classifications of Clavien-Dindo [26], IUGA/ICS [27], or POP-Q [28] were used to describe the severity grade of the complication in 7%, 16% and 24% of the articles, respectively (Textbox 2). POP-Q was generally used to stage POP or overall success rate [6, 38]. Some articles described all classification methods [39]. Next to POP-Q, Nicita *et al*. used Clavien-Dindo grade for 30-day surgical complications and IUGA/ICS for mesh-related complications [38]. Due to the observed variation in the literature, it was not possible to draw any conclusions on duration or severity of a complication.

Textbox 2.
The search for literature on classification methods initially resulted in 102 articles of interest. After reviewing titles and abstracts the following classification methods were identified: the Clavien-Dindo classification [26], the IUGA/ICS classification method [27], and the POP-Q method [28].

The Clavien-Dindo classification is based on the type of therapy needed to correct the complication after surgical procedures in general [26]. The method is not specific for transvaginal mesh implant complications, but for surgical complications. For the classification, seven grades of complications are described, including two subgroups for grade three and four. Grade I complications do not require therapy and are less severe than grade V complications, i.e. death of a patient. Dindo *et al*. studied the length of hospital stay related to the types of complications that were reported. As could be expected, the length of hospital stay increased when the complication was more severe, i.e. median hospital stay grade I complications was 14 days versus grade IVb 53 days [40]. Unfortunately, no specific classification rules for the duration of a complication are described in the Clavien-Dindo method.

The IUGA and ICS published a joint classification method specifically for complications directly related to the insertion of prostheses, such as mesh implants, tapes, etc. in female pelvic floor surgery [27]. The classification summarizes possible clinical scenarios into a code using three letters; category (C), time (T) and site (S).
The category (C) code stands for the general description and severity of the complication, the higher the number the more severe the complication. The time (T) stands for when a complication is clinically diagnosed and the site (S) stands for where the complication have been noted.

Bump *et al*. presented a standard system of terminology for female pelvic organ prolapse and dysfunction, POP-Q. This methodology was also used to classify the anatomical success rate after surgery, e.g. mesh implantation [28].

All three methods were used in some of the studies on long-term complications of TVM implants.

Interventions performed to resolve complications
Several complications can be resolved by an intervention, for example mesh removal. In 57% of the articles, an intervention in 1 or more patients was described. Most interventions were performed for the treatment of complications such as mesh exposure and erosion, recurrent prolapse or incontinence. Interventions performed for resolving complications varied from simple to drastic, for example applying vaginal oestrogen cream, release of mesh arm, removal of (part of) the mesh or vaginal hysterectomy [41-43].

Anatomical success rate and patient satisfaction rate
In several articles, the anatomical success rate or patient satisfaction rate were described. In most articles from 2012-2014 anatomical success rate represented the success of treatment, while in more recent years (i.e., after 2014) patient satisfaction rate was used. Overall, the anatomical success rate ranged from 34.2% to 100% and patient satisfaction rate ranged from 68% to 99.3%.

Comparison of study outcomes of traditional POP surgery and TVM implantation
A comparison was made between traditional POP surgery and TVM implantation, focussing on complication types, rates and success rates. The initial search resulted in 26 articles; after reviewing titles and abstracts 6 articles remained. A few articles made this comparison, indicating a higher success rate for TVM implantation surgery compared to traditional surgery (Table 5). Mesh exposure was observed in patients who underwent mesh implantation surgery. The number of articles comparing long-term complications between these types of surgeries was limited. Unfortunately, the number or articles that included incidence of complications were very limited.

Table 5. Mesh and traditional surgery outcomes

Author	**Study result**	**Mesh implantation surgery** [a]	**Traditional surgery**
Cao [b] [44]	anatomic success rate	88.1%	64.9%
	mesh erosion	3.6%	-
Delroy [c] [45]	anatomic success rate	82.5%	56.4%
	mesh exposure	5%	-
Dias [46]	patient satisfaction	97.3%	81.8%
	new onset incontinence	0 patients	2/14 patients
	pain	10.8%	12.1%
	vaginal bulge	5.4%	9%
	mesh exposure	13.5%	-
Gomelsky [d] [47]	anatomical (POP-Q) success rate	38-91%	24-72%

Author	Study result	Mesh implantation surgery [a]	Traditional surgery
Lo [35]	3 year objective cure rate	90.3%	73.6%
	3 year subjective cure rate	88.6%	70.8%
Turgal [48]	anatomic cure rates	95%	75%
	de novo SUI	-	5%
	mesh erosion	15%	

a. Delroy [45], Dias [46] and Lo [35] described transvaginal mesh surgery. Gomelsky [47] did not specify the route of mesh surgery.
b. Complication rates did not differ significantly between mesh implantation and traditional surgery [44].
c. Similar total complication rates were seen comparing mesh surgery versus traditional POP surgery.
d. Mesh was compared to traditional POP surgery using 12 randomized controlled trials.

3.2 Study variations in the international literature

In order to compare TVM implantation studies, it is important that articles report outcomes in a comparable manner, include an appropriate number of patients and have a proper follow-up period. With regard to study setup, prospective studies as well as retrospective studies, were observed. In some articles abdominal and transvaginal surgical techniques were compared. Sometimes the implantation of TVM in combination with slings was described, without making a clear distinction between the observed complications, i.e. mesh-related or sling-related. The indication for mesh treatment varied considerably. In some articles, patients with first prolapse were included, while in others women with recurrent prolapse were included. Other variations like concomitant surgeries, made it difficult to analyse the complications. Next to TVM implantation, these patients simultaneously underwent another surgery such as hysterectomy. Methods to register complications and success of the treatment were very diverse. For example, complications and successes were self-reported by patients in some studies, whereas in other studies anatomical observation by the physician during a follow-up visit was used. In some cases standardized methods to classify complications or success were used, such as the POP-Q method [28].

Mesh implants
From 2012 to 2018, a variety of mesh implants were described in the articles on long-term complications. The most studied mesh implants in the literature were: Apogee, Avaulta, Elevate, Gynemesh, Perigee and Prolift. Several mesh implants were used in only 1 or a limited number of studies. In a few cases, the product name was not specified (Textbox 3).

Textbox 3. List of mesh implants in one or a limited number of studies

Specified TVM product name:
Anterior pinnacle, Elevate Anterior/Apical (EAA), Prosima, Gynecare, Restorelle Flat mesh, Intepro, Intepro Lite, Nazca TC, Novasilk, PelviSoft Acellular Collagen Biomesh, Polyform, Seratom, surgeon-tailored polypropylene mesh monofilament knitted macroporous polypropylene mesh (Gal-Mesh), Surgimesh, Surgimesh prolapse kit, Surgimesh Prolaps Xlight, Titanized polypropylene mesh (TiLOOP Total 6)

Not specified TVM product name:
anterior polypropylene mesh, anterior self-tailored mesh, polypropylene mesh, non-absorbable mesh, non-absorbable type 1 monofilaments macroporous polypropylene mesh, retropubic mesh, synthetic mesh, transobturator mesh

Number of patients
The lowest number of patients included in a study was 23 [49], the highest was 20,760 [50]. The median number of patients was 113. In 36 articles, the study population included less than 100 patients, in 53 articles 100 or more patients were included.

Follow-up
The follow-up period varied from 12 months to 85 months. The median follow-up period was 26 months. In several articles, a mean follow-up period was used. Most of the studies had to cope with patients lost to follow-up. Reasons for potential loss to follow-up are: loss of contact, withdrew consent, non-adherent, deceased [51]. Overall, the percentage of patients lost to follow-up after 12 months varied between 1% and 28%. In addition, 2 articles reported 51% and 68% patients lost to follow-up [32, 52].

4 Discussion

4.1 Overall conclusion

This report describes the results of a scientific literature review of complications that were observed 1 year or longer after implantation of TVM. The primary goal was to obtain insight in the type, rate, severity and duration of these complications.

Most important findings:

- Pain, mesh exposure & erosion, recurrent prolapse, (de novo) dyspareunia, and (de novo) incontinence were the most frequently reported long-term complications.
- Overall, complication rates ranged from 0% to 48%.
- Articles with a follow-up of 12 months and longer were included in this study. The median follow-up period was 26 months and the maximum observed follow-up period was 85 months [53].
- Complication types and rates described in the recent published international literature (2012-2018) were comparable with those found in the previous RIVM literature review [3].
- Information on duration and severity of complications was limited.
- The classification systems of Clavien-Dindo [26], IUGA/ICS [27], or POP-Q were used in a limited number of articles.
- Comparing the international literature, abundant variations were found, for example the used methods to report results.
- Besides the complication rate and description of interventions, patient satisfaction is an important factor to gain more information on the success or failure of a TVM implantation.

Taking this together, numerous types of complications were reported after TVM implantation. Unfortunately, large variations between studies were observed and limited information on severity and duration of complications was observed. Standardized description of study setups and outcomes are necessary to enable systematic analysis. Therefore, we recommend that articles report outcomes in a standardized method with universal definitions in order to compare studies of TVM implants. The findings described in this report can initiate new scientific research. In the paragraphs below, the findings of this literature review are discussed in more detail.

4.2 Long-term complications

An in-depth analysis of long-term complications was not possible, due to the nature and characteristics of the articles. Therefore, we used a pragmatic approach to achieve the objective of this study, i.e. to gain insight in long-term complications and the severity of these complications. In the next paragraphs, the encountered issues are discussed.

Type and rates of complications
Many descriptions of long-term complications were used in literature. The use of standardized methods for classifications of these complication

types were however missing. An aggregation step resulted in 8 types of complications, i.e. pain, mesh exposure and erosion, recurrent prolapse, dyspareunia, de novo dyspareunia, incontinence, de novo incontinence and other complications. The terms mesh exposure and mesh erosion were used interchangeably in studies, therefore these were combined.

In some articles, complications like de novo dyspareunia and de novo incontinence were described. In other articles, these complications were grouped with pre-operative complaints, i.e. dyspareunia and incontinence in general. De novo dyspareunia and de novo incontinence complications could be related to the TVM implantation. For dyspareunia and incontinence, this was uncertain, because women could experience the same complaint before and after TVM implantation. Therefore, for these patients it is debatable whether the complication was related to the TVM implantation. Caution should be taken when interpreting dyspareunia and incontinence rates.

As with every surgery and prosthetic implantation, TVM implantation has certain risks for complications. In order to put long-term TVM complications in perspective, it is important to compare the complication types, rates and success rates of TVM implantation with traditional surgical techniques used for POP. Results observed in the international literature indicated a higher success rate for TVM surgery. However, the number of articles was limited, especially the number of articles that compared the two surgeries and focussed on long-term complications.

Not only is it essential to report the type of complication, but also the reason for the occurrence of a complication is important. For example, a complication can be caused by material properties, such as composition, biocompatibility, mechanical properties shape and structure. Also, the surgical technique, the surgeon's experience, the route of implantation and patient-related factors can be of influence [2]. In none of the analysed articles, a clear distinction was made with respect to causes of complications.

TVM implants and the Netherlands

As described above, similar results were observed in recent published international literature (2012-2018) compared to the previous RIVM literature review [3]. However in the Netherlands the number of to the authorities reported complaints after TVM implantation has decreased in the past 5 years. Factors that may have contributed to this decrease are:

1. The implementation of the Dutch multidisciplinary guideline on surgical treatment of vaginal prolapse [17, 18].
2. Further specialization / centralization, i.e. the Netherlands is one of the very few countries with urogynaecology as a recognized sub-specialism [18]. In addition, TVM implantation and interventions performed to resolve complications are centralized in a limited number of hospitals.
3. Change in the indication for TVM implantation, i.e. only women with a recurrent prolapse have an indication for use of TVM implants [18].
4. Development of new mesh implants. Synthetic mesh implants have become lighter, more elastic, have smaller pores and the material is fixated with less tension [2].

Mesh implants
The most frequently studied TVM implants identified in this study were the same as the mesh implants found in literature until 2011 [3]. It was not possible to associate complications to a specific TVM implant. In addition, international literature did not allow for determining which of the TVM implants are currently used in the Netherlands.
Some articles reported complications of surgeries where TVM implants were implanted in combination with sling devices or other concomitant surgeries. Complications could be the result of the implant (i.e. TVM or sling), other concomitant surgeries or the combination. Studies were excluded when this was not clearly described. Studies which did not specify the names of mesh implants were included. As the objective of this study was to gain insight in long-term complications of synthetic mesh implants in general, the name or type of TVM implant was less important.

Measuring success of mesh implantations
The success rate of treatments was reported in some of the studies. Two methods were used, i.e. through physical examination by the physician and/or through the perspective of patients by using questionnaires (e.g. the Pelvic Floor Distress Inventory (PFDI) [54], POP-Q survey [28]). When combined with the overall complication rate, information on success rate could help to place the success or failure of the treatment in perspective. However, a comparison between success or failure outcomes of these studies was not possible, because of the large variations in the studies. Moreover, the patient's perspective might be very different from the physician's perspective. For example, a physician may find a surgical intervention successful based on the anatomical success, while the patient may still experience complications and is less satisfied. On the other hand, a patient might be satisfied despite the fact that the anatomical success is not optimal [55]. In older articles, most reports on success focussed on the anatomical success observed by the physicians, in newer studies a shift is seen towards reports on patient satisfaction. This indicates that the patient perspective is seen as a valuable asset to the success of the treatment.

4.3 Study limitations

This study focussed on long-term complications of TVM implants described in the international literature. Variations described in the articles may have a big impact on complication rates. In addition, there may be a possible effect on complication rate caused by factors like new stringent guidelines or new types of TVM implants. This study did not investigate the effect of these factors in the international literature. However, the results provide a general view on what type of complications occur and how often complications may occur in the long term.
The Inspectorate received numerous complaints on serious complications with TVM between 2009 and 2012. Media attention in USA, Australia, New Zealand, Ireland and the UK indicated that these serious complications are still occurring in these countries. In this study, we observed very limited data on severity of complications published in the scientific literature. It is important that articles report the severity of the complications.

Abundant variations were observed in the international literature. For example, variation was found in type of complications, complication rates, severity of complications, study setups, number of patients, follow-up periods, used classification methods, used method to report results. In addition, due to the observed dissimilarities it was not possible to draw any conclusions on duration or severity of a complication. It is important that articles report outcomes in a standardized method with universal definitions to provide a clear overview of observed complications and to make comparisons between studies of TVM implants possible [56].

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Annex 1 Abbreviations

ARTG	Australian Register of Therapeutic Goods
FDA	U.S. Food and Drug Administration
ICS	International Continence Society
IGJ	Health and Youth Care Inspectorate
IUGA	International Urogynecological Association
NVOG	Netherlands Society of Obstetrics and Gynaecology
NICE	National Institute for Health and Care Excellence
POP	Pelvic Organ Prolapse
POP-Q	Pelvic Organ Prolapse Quantification
RIVM	National Institute for Public Health and the Environment
SUI	Stress Urinary Incontinence
USI	Urodynamic Stress Incontinence
TGA	Australian Therapeutics Goods Administration
TVM	Transvaginal Mesh

Annex 2 Definitions

Pelvic organ prolapse (POP) occurs when tissue and muscles of the pelvic floor no longer support the pelvic organs resulting in the drop (prolapse) of the pelvic organs from their normal position. Pelvic organs include the vagina, cervix, uterus, bladder, urethra, and rectum [57].

Three levels of pelvic visceral prolapse [58]:
1-Upper –anterior vaginal wall prolapse, called cystocele
2-Posterior vaginal wall prolapse, called rectocele
3-Entrocele and cervical prolapsed.

Colporrhaphy is the surgical repair of a defect in the vaginal wall, including a cystocele (when the bladder protrudes into the vagina) and a rectocele (when the rectum protrudes into the vagina) [59].

Laparoscopic sacro-colpopexy is a surgical procedure in which a mesh is used to suspend the uterus / the vaginal vault to the sacrum. The procedure is performed through an abdominal incision or via keyhole with minimally invasive surgery [60]

Transvaginal mesh (TVM) repair of anterior or posterior vaginal wall prolapse involves removing some of the stretched tissue if needed, and tightening the underlying tissue (colporrhaphy). Mesh is used to support the repair [61].

Annex 3 Syntax literature search long-term complications

#24 #20 NOT (#21 OR #23)

#23 #22 AND ('review'/it OR 'review'/exp OR review*:ti)

#22 #20 NOT #21

#21 #20 AND ('article in press'/it OR 'conference abstract'/it OR 'conference paper'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it)

#20 (#8 OR #11 OR #12 OR #13 OR #16) AND [humans]/lim AND [2012-2018]/py AND ([dutch]/lim OR [english]/lim)
#19 (#8 OR #11 OR #12 OR #13 OR #16) AND [humans]/lim AND [2012-2018]/py
#18 (#8 OR #11 OR #12 OR #13 OR #16) AND [humans]/lim

#17 #8 OR #11 OR #12 OR #13 OR #16
#16 #14 AND #15
#15 mesh*:ti,ab
#14 (#1 OR #2 OR #4) AND (#5 OR #6)
#13 #4 AND #10 AND (#5 OR #6 OR #7)
#12 (#1 OR #2 OR #4) AND #7
#11 (#4 OR #5 OR #6 OR #7) AND #9
#10 #1 OR #2 OR #3
#9 #1 OR #2
#8 'transvaginal mesh*':ti AND ('pelvic organ prolaps*':ti OR 'stress incontinen*':ti OR 'urinary incontinen*':ti)
#7 'adverse event'/exp
#6 complication*:ti OR 'complication'/exp/mj
#5 'medical device complication'/exp
#4 'pelvic organ prolapse'/exp/mj OR 'stress incontinence'/exp/mj
#3 mesh*:ti
#2 'transvaginal mesh*':ti
#1 'transvaginal mesh'/exp

Annex 4 Complication types described in literature

pain	Any type of pain symptom, Back pain, Buttock pain, Buttock, groin, vaginal pain/tenderness, Chronic pain, Chronic pain at the inner side of the thigh, Chronic pelvic pain, De novo pelvic pain, Groin pain, Leg pain, Pain, Pain during pelvic examination, Pelvic floor myalgia, Pelvic or vaginal pain, Pelvic pain, local pain, medically refractory neuropathic pain, painful during examination, pelvic floor pain, vaginal pain - spontaneous, De novo pain (lower abdomen or genital area), De novo pain in groin/gluteal region, Pain other than dyspareunia in the vagina, Urethral pain/discomfort, Urogenital pain/discomfort, vaginal pain - on vaginal examination, pelvic or perineal pain, pudendal neuralgia, skin and/or musculoskeletal pain, vaginal or buttock pain, vaginal pain, bladder pain, buttock/thigh pain, dynia, perineal pain, persistent pain, spontaneous pain, thigh pain, vaginal pain - on vaginal examination, vaginal pain/tenderness.
dyspareunia	Dyspareunia, Dyspareunia - worsened, Pain to male partner during vaginal intercourse, Partner dyspareunia, improved dyspareunia, pain during sexual intercourse, sexual activity not modified, Persistent dyspareunia, Resolved dyspareunia
de novo dyspareunia	De novo dyspareunia
mesh exposure	Mesh erosion, Mesh exposure, Mesh extrusion, Vaginal exposure rate, apical recurrence, erosion, vaginal erosion, vaginal exposure, vaginal mesh exposure, mesh exposure/ contraction, vaginal erosion / mesh removal, Asymptomatic mesh extrusion, Suture exposure
recurrent prolapse	POP sensation, Recurrence, Recurrent or de novo prolapse, Recurrent POP stage II, Recurrent prolapse, Recurrent prolapse symptoms, prolaps, anterior vaginal wall prolaps, de novo prolaps in opposite compartment to that of the original surgery, enterocele, pelvic organ prolaps, prolaps recurrence, recurrent cystourethrocoeles, recurrent uterine descent, recurrent vault prolaps, something coming down, uterine prolaps, POP stage, POP-Q anterior, symptomatic prolapse, symptomatic recurrence POP, symptomatic relapse or novel prolapse with necessity of reoperation, Prolapse beyond the hymen, Recurrent POP symptoms, Symptomatic pelvic organ prolapse
incontinence	Anal incontinence, Clinical SUI, Faecal incontinence, Incontinence (bowel symptoms), Latent SUI, Mixed incontinence, Mixed urinary incontinence, Occult urodynamic stress incontinence, Overt USI, Postoperative SUI, Recurrent or de novo incontinence, Stress incontinence, SUI, Urge incontinence, total urinary incontinence, urgency-frequency syndrome with or without urge incontinence, urinary incontinence, de novo or worsening incontinence, urge incontinence / overactive bladder, urgency urinary incontinence, Urinary incontinence - worsened, apparition SUI, incontinence, persistent SUI, stress urinary incontinence
de novo incontinence	De novo stress incontinence, De novo SUI, De novo urge urinary incontinence, De novo urinary incontinence, New onset

	incontinence, de novo stress urinary incontinence, de novo urge incontinence, de novo USI, de novo UUI, new-onset incontinence
other	Abnormal sensation, Any lower urinary tract symptom, Any type of vaginal symptom, Bulge sensation, De novo bladder symptoms, De novo bowel symptoms, De novo detrusor overactivity, De novo overactive bladder, De novo urge, Defecatory dysfunction, Detrusor overactivity, Detrusor underactivity, Difficulty of defecation, Fistula lower urinary tract, Fixation stiches exposure, Imperative defecation (bowel symptoms), Localized infection/abcess, Lower extremity neuralgia and numbness, Mesh related infection, renal failure, reoperation for incurrence, skin tenderness, suburethral tape, temporary urinary retention, temporary urinary retention, Mesh retraction, Obstructive defecation/tenesmus, Other lower urinary tract complaint, Overactive bladder (bladder symptoms), Painful defecation/dyschezia, Painful voiding, Persisting bladder symptoms, Persisting bowel symptoms, Rectovaginal fistula, Recurrent infection, Recurrent urinary tract infection, Residual volume (bladder symptoms), Systemic infection, Urge problems - worsened, Urinary obstruction, Urinary retention, Urinary tract infection, Vaginal constriction, Vaginal discharge, loss of Prosima pessary, voiding difficulty, neurological complications, rectal erosion, reduntant vaginal tissue, release of mesh trap, Vaginal spotting, Vesicovaginal fistula, Voiding dysfunction, any type of inflammatory reaction to the mesh, bladder erosion, bladder extrusion, bladder injuries, cervix elongation, complaint related to bowel function, constipation, dyschesia, fistula formation, forgotten gauze, hematoma, infection, lower urinary tract infections, mesh contraction, mesh wrinkling or shrinkage, necrosis, granulation, granuloma cuff., infective vaginal discharge, limp sensation, cervical cuff haemorrhage, wound dehiscence, palpable, pelvic abscess, perineal hematoma, persistent dysuria, postoperative complication admissions, rectal extrusion, rectovesical fistula, obstructive symptoms, secondary mesh infections, systemic infectious symptoms, ureteral kinking, urinary tract infection, vaginal adhesion, vaginal erosion, vaginal spotting and discharge, vesico vaginal fistula wound cellulitis

Annex 5 Overview of identified articles that described long-term complications after TVM implantation

The following tables are included in Annex 5
Table 5.1 Pain
Table 5.2 Dyspareunia, including de novo dyspareunia
Table 5.3 Mesh exposure & erosion
Table 5.4 Recurrent prolapse
Table 5.5 Incontinence, including de novo incontinence

Table 5.1 Overview of publications reporting pain as complication

Reference	Study population (n)	Complication	Complication rate (%)	Follow-up period[a]	Remark
Alperin [62]	126	Pain other than dyspareunia	2.3	2 years	
Barros-Pereira [63]	100	Pelvic floor pain Pelvic floor pain	3.0 5.0	1 year 1 year	TVM1 implanted TVM2 implanted
Bontje [42]	107	Vaginal pain Skin and/or musculoskeletal Local pain	2.9 1.0 2.9	32 months [10-46][1] After 1 year After 1 year	
Damiani [6]	58	Dynia	6.7	3 months and 1 year	
Dandolu [50]	20760	Pelvic pain	16.4	During 2-year FU	
Farthmann [29]	289	Pull pain	5.6	1 year	
Fünfgeld [64]	289	Pain in the area of the mesh Pain	0.4 1.5	Between 1 and 3 years Between 1 and 3 years	
Halaska [65]	85	Pelvic pain	8.1	1 year	
Hugele [43]	270	Painful during examination Painful during examination Buttock pain Pudendal neuralgia	7.5 5.1 0.4 0.4	1 year 2 years After 2 years After 2 years	
Hüsch [52]	148	Perineal pain Vaginal pain	33.8 33.3	37.4±10.9 months[2] 37.4±10.9 months[2]	
Jacquetin [66]	90	De novo pelvic pain Pain during pelvic examination	1.2 6.1	5 years 5 years	
Lamblin [67]	126	Vaginal pain – on vaginal Vaginal pain – on vaginal Vaginal pain – on vaginal Vaginal pain – on vaginal	9.5 6.0 2.4 11.9	1 year 2 years 1 year 2 years	TVM3 implanted TVM3 implanted TVM4 implanted TVM4 implanted
Laso-Garcia [68]	75	Pelvic pain	2.7	After 1 year	RIVM calculated rate
Ow [30]	161	Mesh pain Mesh pain Mesh pain Mesh pain	0.9 2.8 0 3.8	1 year >1 year 1 year >1 year	TVM5 implanted[3] TVM5 implanted[3] TVM6 implanted[4] TVM6 implanted[4]

Reference	Study population (n)	Complication	Complication rate (%)	Follow-up period[a]	Remark
Rogowski [69]	114	Pelvic floor pain Pelvic floor pain	11.5 11.3	18±2 months[2] 18±2 months[2]	TVM1 implanted TVM2 implanted
Stanford [70]	142	Buttock pain	3.5	2 years	
Vaiyapuri [33]	169	Pelvic pain	0	2 years	
Warembourg [71]	598	Residual pain or dyspareunia	11.8	33.4 months[5]	

Abbreviations: FU – follow-up, TVM – transvaginal mesh
[a] Period after surgery when complications are reported/follow-up period
[1] Median period [range]
[2] Mean period ± standard deviation
[3] A group of different TVMs used
[4] A group of different TVMs used
[5] Average period between initial mesh surgery and reoperation for treatment of the complication

Table 5.2 Overview of publications reporting dyspareunia as complication

Reference	Study population (n)	Complication	Complication rate (%)	Follow-up period[a]	Remark
Alperin [62]	126	Dyspareunia Dyspareunia De novo dyspareunia	33.0 28.9 15.5	1 year 2 years 2 years	
Barros-Pereira [63]	100	Dyspareunia Dyspareunia	0 5.0	1 year 1 year	TVM1 implanted TVM2 implanted
Bjelic-Radisic [32]	726	Dyspareunia	10.0	1 year	
Bontje [42]	107	Dyspareunia	2.9	After 1 year	RIVM calculated rate
Damiani [6]	58	Dyspareunia De novo dyspareunia	20.0 13.3	2 years 2 years	
Dandolu [50]	20760	Dyspareunia	6.1	During 2-year FU	
Delroy [45]	40	Dyspareunia	10.0	1 year	
de Tayrac [72]	111	Dyspareunia Dyspareunia	3.5 1.2	1 year 3 years	
Farthmann [29]	289	Dyspareunia De novo dyspareunia	2.4 4.2	1 year 1 year	
Fünfgeld [64]	289	Dyspareunia De novo dyspareunia	1.9 4.5	3 years 3 years	
Glazener [73]	435	Dyspareunia Dyspareunia	5.0 3.0	1 year 2 years	
Gutman [74]	33	Persistent dyspareunia De novo dyspareunia	15.2 8.0	3 years 3 years	
Halaska [65]	85	Dyspareunia	8.0	1 year	
Hugele [43]	270	De novo dyspareunia De novo dyspareunia	8.4 5.3	1 year 1 year	 Mesh-related

Reference	Study population (n)	Complication	Complication rate (%)	Follow-up period[a]	Remark
		Pain during sexual intercourse	1.6	1 year	
		Pain during sexual intercourse	2.1	2 years	
Jacquetin [66]	90	De novo dyspareunia	10.0	5 years	
Khandwala [75]	157	De novo dyspareunia	6.0	1 year	Partially absorbable TVM
Lukban [76]	141	De novo dyspareunia	11.9	1 year	
Nicita [38]	66	De novo dyspareunia De novo dyspareunia	17.6 10.3	1 year 5.6 years[1]	
Nüssler [77]	356	Dyspareunia – worsened De novo dyspareunia	48.0 17.0	1 year 1 year	
Önol [78]	74	Persisted dyspareunia De novo dyspareunia	47.7 14.2	41.2±19.3 months[2] 41.2±19.3 months[2]	
Ow [30]	161	Dyspareunia Dyspareunia Dyspareunia Dyspareunia	7.1 10.0 4.3 4.3	1 year >1 year 1 year >1 year	TVM5 implanted[3] TVM5 implanted[3] TVM6 implanted[4] TVM6 implanted[4]
Rapp [79]	42	Dyspareunia – not de novo De novo dyspareunia	5.0 0	2 years 2 years	
Rogowski [69]	114	Dyspareunia Dyspareunia	11.5 11.3	18±2 months[2] 18±2 months[2]	TVM1 implanted TVM2 implanted
Rudnicki [80]	79	De novo dyspareunia	2.7	1 year	
Sayer [81]	110	Ongoing dyspareunia De novo dyspareunia Dyspareunia – not de novo	0 1.8 1.8	2 years 2 years 2 years	
Sokol [82]		New-onset dyspareunia	9.1	1 year	

Reference	Study population (n)	Complication	Complication rate (%)	Follow-up period[a]	Remark
Stanford [70]	142	Dyspareunia	4.9	2 years	
Sun [83]	83	Dyspareunia	10.7	1 year	
Svabik [84]	36	Dyspareunia	5.6	1 year	
Tamanini [85]	45	Dyspareunia	2.3	1 year	RIVM calculated rate
Vaiyapuri [33]	169	De novo dyspareunia	0	2 years	
Warembourg [71]	598	Residual pain or dyspareunia	11.8	33.4 months[5]	
Weintraub [53]	79	Dyspareunia	4.7	85 months [79-104][6]	

Abbreviations: FU – follow-up, TVM – transvaginal mesh
[a] Period after surgery when complications are reported/follow-up period
[1] Mean FU
[2] Mean period ± standard deviation
[3] A group of different TVMs used
[4] A group of different TVMs used
[5] Average period between initial mesh surgery and reoperation for treatment of the complication
[6] Median period [range]

Table 5.3 Overview of publications reporting mesh exposure & erosion as complication

Reference	Study population (n)	Complication	Complication rate (%)	Follow-up period[a]	Remark
Alperin [62]	126	Mesh exposure Mesh exposure	8.7 0.8	2 years Between 1 and 2 years	
Barros-Pereira [63]	100	Vaginal mesh exposure Vaginal mesh exposure	3.0 0	1 year 1 year	TVM1 implanted TVM2 implanted
Benbouzid [86]	75	Mesh erosion	4.0	1 year	
Bjelic-Radisic [32]	726	Mesh erosion/vaginal tape exposure	12.0	1 year	
Bontje [42]	107	Mesh exposure Erosion	7.1 2.9	After 1 year 24 months [4-40][1]	
Damiani [6]	58	Mesh exposure	3.3	3 and 12 months	
de Landsheere [87]	524	Mesh exposure	2.7	13 months[2]	
Delroy [45]	40	Mesh extrusion	5.0	1 year	
de Tayrac [72]	111	Mesh extrusion	1.3	3 years	
Elmér [88]	353	Extrusion Number of exposure	2.0 8.6	1 year 1 year	
Farthmann [29]	289	Mesh exposure	10.5	1 year	
Fünfgeld [64]	289	Mesh erosion Mesh erosion	10.5 2.6	1 year Between 1 and 3 years	
Gutpa [89]	52	Mesh erosion	7.6	1 year	
Halaska [65]	85	Mesh exposure	20.8	1 year	
Heinonen [90]	161	Mesh exposure	22.9	7 years	FU unclear
Hong [91]	34	Mesh exposure	2.9	1 year	
Jacquetin [66]	90	Mesh exposure Mesh exposure	6.7 7.8	Between 1 and 3 years Between 3 and 5 years	
Karmakar [92]	158	Mesh extrusion/exposure	15.8	78 weeks[3]	
Khandwala [75]	157	Mesh exposure	2.2	1 year	Partially absorbable TVM
Lamblin [93]	33	Exposure	3.0	1 year	
Lamblin [67]	126	Vaginal exposure Vaginal exposure Vaginal exposure Vaginal exposure	0 0 2.4 2.4	1 year 2 years 1 year 2 years	TVM3 implanted TVM3 implanted TVM4 implanted TVM4 implanted

Reference	Study population (n)	Complication	Complication rate (%)	Follow-up period[a]	Remark
Laso-Garcia [68]	75	Mesh extrusion	8.8	After 1 year	
Lo [94]	124	Mesh erosion Mesh erosion	0 4.9	1 year 1 year	TVM3 implanted; FU TVM4 implanted; FU
Lo [95]	65	Mesh erosion	0	1 year	
Long [39]	124	Vaginal erosion	12.4	Up to 30 months	
Moore [96]	349	Mesh extrusion Mesh extrusion	11.1 6.0	Up to 2 years Up to 2 years	TVM7 implanted TVM8 implanted
Önol [78]	74	Mesh exposure, anterior repairs	1.4	2 years	
Ow [30]	161	Mesh exposure Mesh exposure	2.8 1.9	After 1 year After 1 year	TVM5 implanted[4]; RIVM TVM6 implanted[5]; RIVM calculated rate
Rogowski [69]	114	Vaginal exposure Vaginal exposure	7.6 0	18±2 months[6] 18±2 months[6]	TVM1 implanted TVM2 implanted
Rudnicki [80]	79	Mesh exposure	12.7	1 year	
Sayer [81]	110	Mesh exposure	2.0	1 year	
Stanford [70]	142	Mesh extrusion Mesh extrusion Mesh extrusion Mesh extrusion	5.6 4.9 13.8 2.0	2 years 2 years 2 years 2 years	Total group Baseline hysterectomy Concomitant hysterectomy No hysterectomy
Svabik [84]	36	Protrusion	0	1 year	
Tamanini [85]	45	Mesh exposure Mesh exposure	9.5 16.7	1 year 2 years	RIVM calculated rate RIVM calculated rate

Reference	Study population (n)	Complication	Complication rate (%)	Follow-up period[a]	Remark
To [97]	146	Mesh exposure	0.7	1 year	
Vaiyapuri [33]	169	Mesh extrusion	1.4	Up to 2 years	
Wu [98]	92	Mesh exposure	5.4	≥1 year	
Zhang [99]	206	Mesh exposure/contraction	8.3	>1 year	RIVM calculated rate

Abbreviations: FU – follow-up, TVM – transvaginal mesh
[a] Period after surgery when complications are reported/follow-up period
[1] Median period [range]
[2] Median period to intervention
[3] Mean period to diagnosis
[4] A group of different TVMs used
[5] A group of different TVMs used
[6] Mean period ± standard deviation

Table 5.4 Overview of publications reporting recurrent prolapse as complication

Reference	Study population (n)	Complication	Compli-cation rate	Follow-up period[a]	Remark
Alperin [62]	126	Symptomatic POP	8.5	2 years	
Barber [100]	188	Prolapse beyond the hymen	16.0	1 year	Transvaginal surgery: SSLF
		Prolapse beyond the hymen	16.5	1 year	Transvaginal surgery: ULS
		Prolapse beyond the hymen	19.3	2 years	Transvaginal surgery: SSLF
		Prolapse beyond the hymen	17.3	2 years	Transvaginal surgery: ULS
Damiani [6]	58	POP stage II	6.7	1 year	
		POP stage III	0	1 year	
		POP stage IV	0	1 year	
		POP stage II	13.3	2 years	
		POP stage III	6.7	2 years	
		POP stage IV	0	2 years	
Dandalu [50]	20760	Prolapse	6.2	During 2-year FU	
de Landsheere [87]	524	Total prolapse recurrence	3.0	23 months [3.2-61][1]	
Delroy [45]	40	Recurrent POP symptoms	5.0	1 year	
Dong [101]	158	Symptomatic prolapse	1.9	2nd year post-surgery	
Fan [34]	47	Recurrent POP stage II any compartment	11.1	23±12 months[2]	Vault prolapse group
		Recurrent POP stage II any compartment	28.6	32±15 months[2]	Uterus and pelvic floor
		Recurrent POP stage II any compartment	20.0	21±12 months[2]	Uterus and pelvic floor and hysterectomy group
Farthmann [29]	289	Recurrent cystocele	2.1	1 year	
		Recurrent prolapse posterior compartment	13.6	1 year	
Fünfgeld [64]	289	Prolapse grade II	15.1	3 years	
		Prolapse grade IV	0.4	3 years	

Reference	Study population (n)	Complication	Compli-cation rate	Follow-up period[a]	Remark
		Recurrent prolapse posterior compartment	10.1	1 year	
		Recurrent prolapse posterior	3.7	3 years	
		Recurrent prolapse apical compartment	2.8	1 year	
		Recurrent prolapse apical compartment	1.9	3 years	
		Recurrent prolapse operated	1.9	Between 1 and 3 years	
Fünfgeld [64]	289	Repeat prolapse	5.2	Between 1 and 3 years	
Glazener [73]	435	Women with any report of SCD	35.0	1 year	
		Women with any report of SCD	34.0	2 years	
Halaska [65]	85	Prolapse recurrence	16.9	1 year	
Jacquetin [66]	90	POP-Q stage II	14.9	1 year	
		POP-Q stage III	1.1	1 year	
		POP-Q stage II	16.5	3 years	
		POP-Q stage II	15.9	5 years	
Karmakar [92]	158	Recurrence (same compartment)	9.5	53 weeks[3]	
Lamblin [93]	33	POP-Q stage >2	0	1 year	
Liang [102]	174	Recurrent prolapse	5.2	1 year	
Lo [94]	124	Recurrent prolapse	3.5	1 year	TVM3 implanted; RIVM
		Recurrent prolapse	6.6	1 year	TVM4 implanted; RIVM
Lo [95]	65	POP stage 2 posterior compartment	3.1	1 year	
Morling [103]	13133	Prolapse	3.0	During 5-year FU	Unspecified mesh
		Prolapse	2.0	During 5-year FU	Retropubic mesh
		Prolapse	2.0	During 5-year FU	Transobturator mesh
Önol [78]	74	POP stage II anterior compartment	2.7	41.2±19.3 months[2]	
		POP stage ≥III anterior compartment	0	41.2±19.3 months[2]	
		POP stage ≥II posterior compartment	0	41.2±19.3 months[2]	
		POP stage ≥II apical compartment	0	41.2±19.3 months[2]	

Reference	Study population (n)	Complication	Complication rate	Follow-up period[a]	Remark
Ow [30]	161	Prolapse same compartment	16.7	1 year	TVM5 implanted[4]
		Prolapse same compartment	25.0	>1 year	TVM5 implanted[4]
		Re-operation for prolapse	4.6	1 year	TVM5 implanted[4]
		Re-operation for prolapse	7.4	>1 year	TVM5 implanted[4]
		Prolapse same compartment	5.7	1 year	TVM6 implanted[5]
		Prolapse same compartment	7.5	>1 year	TVM6 implanted[5]
		Re-operation for prolapse	3.8	1 year	TVM6 implanted[5]
		Re-operation for prolapse	7.5	>1 year	TVM6 implanted[5]
Papcun [107]	47	Recurrent POP	4.3	1 year	
Rapp [79]	42	De novo rectocele	3.0	2 years	
		POP-Q stage II or III – anatomical site specific recurrence	10.0	2 years	
		Prolapse recurrence	3.0	2 years	
Rogowski [69]	114	POP-Q anterior stage II	7.7	18±2 months[2]	TVM1 implanted
		POP-Q anterior stage III	1.9	18±2 months[2]	TVM1 implanted
		POP-Q anterior stage IV	0	18±2 months[2]	TVM1 implanted
		POP-Q anterior stage II	4.8	18±2 months[2]	TVM2 implanted
		POP-Q anterior stage III	4.8	18±2 months[2]	TVM2 implanted
		POP-Q anterior stage IV	0	18±2 months[2]	TVM2 implanted
Sayer [81]	110	Further prolapse surgery	1.7	22 months	
Stanford [70]	142	New prolapse	3.5	2 years	
Svabik [84]	36	POP-Q grade II	16.0	1 year	
		Prolapse (anatomical failure, clinically)	3.0	1 year	

Reference	Study population (n)	Complication	Compli-cation rate	Follow-up period[a]	Remark
Vaiyapuri [33]	169	Recurrent cystourethrocoeles	6.5	2 years	
		Recurrent vault prolapse	1.4	2 years	
		Recurrent uterine descent	1.4	2 years	
Weintraub [53]	79	Recurrence of prolapse symptoms	13.9	85 months [79-104][1]	
Zhang [99]	206	Symptomatic recurrence POP	2.1	1 to 5 years	
Zhang [104]	48	POP-Q anterior stage II	18.8	1 year	
		POP-Q apical stage II	2.1	1 year	
		POP-Q posterior stage II	2.1	1 year	
		POP-Q anterior stage II	26.7	2 years	
		POP-Q apical stage II	3.3	2 years	
		POP-Q posterior stage II	3.3	2 years	

Abbreviations: FU – follow-up, POP – pelvic organ prolapse, POP-Q – pelvic organ prolapse quantification, SCD – something coming down, SSLF – sacrospinous ligament fixation, TVM – transvaginal mesh, ULS – uterospinal ligament fixation

[a] Period after surgery when complications are reported/follow-up period

[1] Median period [range]

[2] Mean period ± standard deviation

[3] Mean period to diagnosis

[4] A group of different TVMs used

[5] A group of different TVMs used

Table 5.5 Overview of publications reporting incontinence as complication

Reference	Study population (n)	Complication	Compli-cation rate (%)	Follow-up period[a]	Remark
Barros-Pereira [63]	100	New-onset incontinence	3.0	1 year	TVM1 implanted
		New-onset incontinence	2.0	1 year	TVM2 implanted
Bjelic-Radisic [32]	726	Clinical SUI	19.0	1 year	
		Latent SUI	2.0	1 year	
Chang [105]	104	Urge urinary incontinence	10.5	1 year	
Damiani [6]	58	Stress incontinence	16.7	2 years	
		Urge incontinence/overactive bladder	13.3	2 years	
		Mixed incontinence	0	2 years	
		De novo or worsening incontinence	13.3	2 years	
de Landsheere [87]	524	Urinary incontinence	6.9	13 months[1]	
		De novo SUI	4.4	16 months [1-60][2]	
		Recurrent SUI	0.4	23 months [3-43][2]	
de Tayrac [72]	111	SUI	1.2	1 year	
		SUI	2.5	3 years	
		Anal incontinence	3.5	1 year	
		Anal incontinence	1.3	3 years	
Fan [34]	47	De novo SUI	11.0	23±12 months[3]	Vault prolapse group
		De novo USI	6.0	23±12 months[3]	Vault prolapse group
		De novo SUI	21.0	32±15 months[3]	Uterus and pelvic floor
		De novo USI	14.0	32±15 months[3]	Uterus and pelvic floor
		De novo SUI	20.1	21±12 months[3]	Uterus and pelvic floor and hysterectomy group
		De novo USI	13.0	21±12 months[3]	Uterus and pelvic floor and hysterectomy group
Fünfgeld [64]	289	Urinary incontinence	1.1	Between 1 and 3 years	
		Fecal incontinence	0.7	Between 1 and 3 years	

Reference	Study population (n)	Complication	Compli-cation rate (%)	Follow-up period[a]	Remark
Glazener [73]	435	Urinary incontinence	8.0	1 year	
		Urinary incontinence	6.0	2 years	
		Fecal incontinence	25.0	1 year	
		Fecal incontinence	27.0	2 years	
Halaska [65]	85	De novo SUI	35.1	1 year	
Kdous [106]	105	De novo SUI/de novo urge incontinence	2.0	3 years	
Khandwala [75]	157	De novo SUI	8.2	1 year	
		De novo urge urinary incontinence	11.2	1 year	
Lo [35]	114	Occult USI	7.9	3 years	FU unclear
		Overt USI	13.2	3 years	FU unclear
Morling [103]	13133	Incontinence	7.0	During 5-year FU	Unspecified mesh
		Incontinence	4.0	During 5-year FU	Retropubic mesh
		Incontinence	5.0	During 5-year FU	Transobturator mesh
Nüssler [77]	356	Urinary incontinence - worsened	22.0	1 year	FU unclear
		De novo urinary incontinence	16.0	1 year	FU unclear
Önol [78]	74	Persisted stress incontinence	5.4	41.2±19.3 months[3]	
Rapp [79]	42	De novo SUI	5.0	2 years	
		Some degree of persistent SUI	15.0	2 years	
Rogowski [69]	114	De novo SUI	11.5	18±2 months[3]	
		De novo SUI	14.5	18±2 months[3]	
Rudnicki [80]	79	De novo SUI	5.3	1 year	
		De novo urge urinary incontinence	1.3	1 year	
Stanford [70]	142	De novo SUI	4.2	2 years	
Svabik [84]	36	De novo SUI	36.0	1 year	
		Total SUI	44.0	1 year	

Reference	Study population (n)	Complication	Compli-cation rate (%)	Follow-up period[a]	Remark
Vaiyapuri [33]	169	De novo SUI De novo urge urinary incontinence	10.1 8.0	2 years 2 years	
Weintraub [53]	79	SUI	1.3	85 months [79-104][2]	

Abbreviations: FU – follow-up, SUI – stress urinary incontinence, TVM – transvaginal mesh, USI – urodynamic stress incontinence
[a] Period after surgery when complications are reported/follow-up period
[1] Median period
[2] Median period [range]
[3] Mean period ± standard deviation

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