Epidemiological aspects of Obstetric Anal Sphincter Injuries

A population-based study in Norway

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Abstract

Aims: Obstetric anal sphincter injuries (OASIS) are serious complications of vaginal childbirth and may result in severe consequences such as dyspareunia, anal- and urinary incontinence. In Norway and other Scandinavian countries, the reported occurrence of these injuries has increased during the past decades. The aims of this thesis were first to validate the registration of OASIS in two Norwegian databases, the Medical Birth Registry of Norway (MBRN) and Patient Administration System (PAS). Secondly, we wanted to investigate risk factors and secular trends of OASIS in Norway in 1967-2004 and whether changes in risk factors over time could explain the trends. Thirdly, we wanted to study the obstetric history of a woman with OASIS in terms of recurrence risk, likelihood of having a subsequent delivery and mode of delivery. Finally, we wanted to assess possible familial aggregation of OASIS among relatives.

Methods: All four papers are historic cohort studies. In paper I, data on OASIS cases occurring at Haukeland University Hospital during 1990-92 and 2000-02 were derived from PAS and MBRN. The registration of OASIS was validated by comparing these two registries with patient hospital records as the gold standard. Papers II-IV were population-based studies based on data from MBRN 1967-2008. We used contingency tables, logistic regression, Cox proportional hazards regression and stratification to explore associations between various exposures and outcomes, to assess interactions and to adjust for confounders.

Results: The sensitivity and specificity of the MBRN database to detect OASIS were 85.3% and 99.5% in 1990–92, 91.8% and 99.7% in 2000–02, respectively. The positive and negative predictive values of OASIS in the MBRN were 91.4% and 99.1% in 1990-92 and 95.4% and 99.4% in 2000–02. The sensitivity and specificity of the PAS database were correspondingly 52.1% and 99.0% in 1990–92 and 84.6% and 98.5% in 2000–02. The positive and negative predictive values of OASIS in PAS database were 75.8% and 97.1% in 1990–92 and 92.7% and 98.9% in 2000-02.

The reported occurrence of OASIS increased from 0.5% in 1967 to 4.1% in 2004. After adjustment for changes in demographic and other risk factors, the increase of OASIS persisted, although significantly reduced. OASIS were associated with maternal age 30 years or more, vaginal birth order 1, previous caesarean delivery, instrumental delivery, diabetes type 1, gestational diabetes, induction of labour by prostaglandin, large maternity units, birth weight 3,500 g or more, head circumference 35 cm or more and African or Asian women's country of birth. Only in birth order 1 with instrumental delivery, episiotomy seemed to protect perineum against OASIS; otherwise it either increased the risk of OASIS or gave no protection against OASIS.

Women with a history of OASIS in the first and the two first deliveries had four and ten fold increased risk of OASIS in the subsequent delivery, respectively. Population-attributable risk percentage of OASIS in second and third delivery due to previous OASIS was 10% and 15%, respectively. Recurrence of OASIS was high in large maternity units, in forceps delivery and with birth weight 3,500 g or more in the current delivery. However, instrumental delivery did not further increase the excess recurrence risk observed in heavy newborns.

A man who fathered a child whose delivery was complicated by OASIS in one woman was more likely to father another child with OASIS delivery in another woman, if the mothers delivered at the same maternity unit.

The subsequent delivery rate was not different in women with and without previous OASIS, whereas women with previous OASIS were more often scheduled to caesarean delivery.

The risk of OASIS was increased two fold if a woman's mother or sister had sustained OASIS and to a less extent if her partner's mother or sister had sustained OASIS, and not if her brother's partner had sustained OASIS.

Conclusions: The validity of the registration of OASIS in MBRN is sufficiently high to justify epidemiological studies on OASIS based on data from this registry. The risk of OASIS increased noticeably in 1967-2004 in Norway. Changes in observed risk factors could only partially explain this increase. Most of observed risk factors such as birth order 1 and high maternal age were non-modifiable and women with such risk factors should be paid more attention at delivery for minimising their risk of OASIS. Instrumental delivery was a dominant risk factor, but the majority of OASIS cases occurred in non-instrumental vaginal deliveries. Consequently, training in both instrumental and non-instrumental deliveries with focus on reducing the speed of the birth, support of perineum and axis of birth canal should be an essential part of the national and local training programme for birth attendants.

Women with a history of OASIS had a high recurrence risk in second and third delivery. Therefore, emphasis should be placed on counselling women after an initial OASIS. A history of OASIS had little or no impact on subsequent delivery rate. However, women with previous OASIS more frequently had planned caesarean delivery.

Our findings in paper IV suggest that maternal and to a less extent paternal factors contribute to the risk of OASIS. The higher maternal than paternal recurrence of OASIS indicate maternal rather than paternal genetic susceptibility for OASIS. These observations must be cautiously interpreted since bias due to unmeasured confounding may have impacted the findings.

List of publications

This thesis is based on four papers, which will be referred to by Roman numerals as follows:

I. Baghestan E, Børdahl PE, Rasmussen S, Sande AK, Lyslo I, Solvang I. **A validation of the diagnosis of obstetric sphincter tears in two Norwegian databases, the Medical Birth Registry and the Patient Administration System.** Acta Obstet Gynecol Scand 2007;86(2):205-209.

II. Baghestan E, Irgens LM, Børdahl PE, Rasmussen S. **Trends in risk factors for obstetric anal sphincter injuries in Norway.** Obstet Gynecol 2010;116(1):25-34.

III. Baghestan E, Irgens LM, Børdahl PE, Rasmussen S. **Risk of recurrence and subsequent delivery after obstetric anal sphincter injuries.** BJOG 2012;119(1):62-69.

IV. Baghestan E, Irgens LM, Bordahl PE, Rasmussen S. **Familial risk of obstetric anal sphincter injuries: registry-based cohort study.** Submitted in May, 2011.

Contents

1. Abbreviations

BMI	Body Mass index
CI	Confidence interval
Cm	Centimetres
DRG	Diagnosis-related groups
EAS	External anal sphincter muscle
EAUS	Endoanal Ultrasonography
G	Grams
HR	Hazard ratio
IAS	Internal anal sphincter muscle
ICD	International Classification of Disease
LMP	Last menstrual period
MBRN	Medical Birth Registry of Norway
OASIS	Obstetric anal sphincter injuries
OECD	Economic Cooperation and Development
OR	Odds ratio
PAS	Patient Administration System
RCOG	Royal College of Obstetrics and Gynaecology
RCT	Randomised Controlled Trial
SINTEF	Stiftelsen for Industriell og Teknisk Forskning

VBAC	Vaginal Birth After Caesarean

2. Definitions

Birth order: The classification of a given pregnancy or birth from the first to the current, including late abortions and stillbirths.

Vaginal birth order: Birth order, with the exclusion of previous caesarean deliveries.

Parity: The classification of a woman by the number of children she has previously delivered, including late abortions and stillbirths.

Overt OASIS are clinically recognised OASIS at the time of delivery.

Occult OASIS are OASIS cases not been recognised at the delivery, but detected by EAUS (Endoanal Ultrasonography).

Sensitivity is the proportion of actual positives which are correctly identified as such.

Specificity is the proportion of negatives which are correctly identified as such.

Positive predictive value or precision rate is the proportion of subjects identified as positives who are correctly identified.

Negative predictive value is the proportion of subjects identified as negatives who are correctly identified.

3. Introduction

Giving life to another human being is likely the most meaningful act anyone can perform in a lifetime. As obstetricians, we are responsible to promote the health and well-being of infant and mother during pregnancy, childbirth and postpartum period.

Even though maternal mortality and morbidity have improved significantly in recent decades, a number of women still suffer from pregnancy- and birth related complications. Third- and fourth degree perineal injuries are serious birth complications and may result in short- as well as long-term problems such as perineal pain, dyspareunia, urinary- and faecal incontinence. The reported occurrence of these injuries has gradually increased in several countries including Norway, and birth injuries are listed as one of the indicators for patient safety in OECD (Economic Cooperation and Development).[1] The fact that the result of primary repair is not always optimal calls for more research to prevent sphincter injuries. In order to minimise the occurrence of these injuries, knowledge of risk factors is fundamentally important. The overall aim of the present thesis was to provide such knowledge to birth attendants by using a large nationwide data set.

3.1 Historical Perspective

The earliest evidence of perineal injury sustained during childbirth was found in the mummy of queen Henhenit, wife of pharao Mentuhotep II (2061 BC – 2010 BC).[2] Her pelvis had an abnormal shape and the delivery resulted in rupture of vagina into the bladder, and the lower bowel was found protruding from the anus. These severe injuries probably led to her death.[2,3] The first reported surgical treatment of perineal tears is by the Persian physician, astronomer and philosopher Abu Ali Husain ebn Abdallah Ebn-e Sina (latin: Avicenna) (980-1037) in his Al Qanoun fi al Tibb (The Canon of Medicine).[4] He recommended a form of crossed suture for the repair of perineal injuries.

The introduction of the obstetric forceps in Europe in the 18th century led to an interest in female anatomy and physiology and the introduction of obstetrics as a medical topic. André Levret of Paris (1703-80) described the pelvic channel as curved and introduced the pelvic curve of the forceps, which resulted in considerably fewer perineal tears.[5] William Smellie (1697-1763), the father of British midwifery, described in his pioneering "Treatise on the Theory and Practice of Midwifery" in 1751 obstetric sphincter tears and what caused them. He gave 260 years ago this precise account "This laceration is frequently occasioned from the excessive largeness of the child's head; from the rigidity of the fibres in women who are near the borders of forty when their first children are born; from the accoucheur's neglecting to slide the perineum over the head when it is forcibly propelled by the pains, or from his omitting to keep up the head with the flat of his hand that it may not come too suddenly along; from too great violence used in laborious or preternatural labours; and from the operator's incautious manner of thrusting in his hand".[6] Smellie described the necessities of diagnosing and treating the tears because of the severe consequences for the women if untreated.

In later midwifery literature, emphasis on perineal ruptures, their prevention and treatment varies. The man-midwife Fielding Ould (1710-89) is credited with the oldest written description of episiotomy. In his "Treatise of Midwifery" in 1742,[7] he recommended an incision from the vaginal outlet toward the anus of women undergoing extremely difficult deliveries, "…there must be an Incision made towards the Anus with a Pair of crooked Probe-Szisars; introducing one Blade between the Head and Vagina…..After the Delivery the Wound must be taken Care of: if the Incision so near the Rectum as to weaken its Contraction, the Wound must be united by a Stitch…" Ould did not coin the incision episiotomy, a term introduced by Carl R. Braun of Wien (1822-91) in a textbook of midwifery in 1857.[8] Braun did, however, consider the necessity of an episiotomy to be rare, in 1-2 ‰ of deliveries. The main prevention of perineal rupture was according to Braun the Ritgen grip, named after the German obstetrician Ferdinand von Ritgen (1787-1867) who described it in 1828.

In Scandinavian midwifery literature since the 18th century the description of perineal tears, prevention, treatment and consequences varies. The broadest description of this was given by Schønberg's textbook in 1899,[9] thereafter it has been given more modest considerations. Schønberg[9] described methods of supporting the perineum and credited several obstetricians of the 18th century for these techniques.

3.2 The Perineum

When seen from below, the perineum (regio perinealis) is diamond-shaped and is enclosed antoriorly by the pubic arch, laterally by the ischiopubic rami, ischial tuberosities and sacrotuberous ligaments, and posteriorly by os coccygis. The perineum is divided in two triangular parts by a line drown between the ischial tuberosities. The anterior part is bigger and constitutes the urogenital triangle; the posterior part is the anal triangle. The urogenital triangle is further divided into two compartments, the superficial perineal compartment and the deep perineal compartment. The perineal membrane separates these compartments.

The superficial compartment contains the m. transversus perinei superficialis, m. bulbospongiosus, and m. ischiocavernosus. The deep compartment contains m. transversus perinei profundus, the compressor urethrae and the m. urethrovaginalis (Figure 1).

3.3 Centrum tendineum perinei

Centrum tendineum perinei or perineal body (Figure 1) is the pyramidal fibromuscular structure occupying the area between ostium vaginae and anus. This area acts like a centre to which muscles like the external anal sphincter muscle (EAS), m. bulbospongiosus, the superficial and deep transverse perineal muscles, and the levator ani muscles are attached (Figure 1).

In clinical practice, the term perineum is referred to the centrum tendineum perinei.

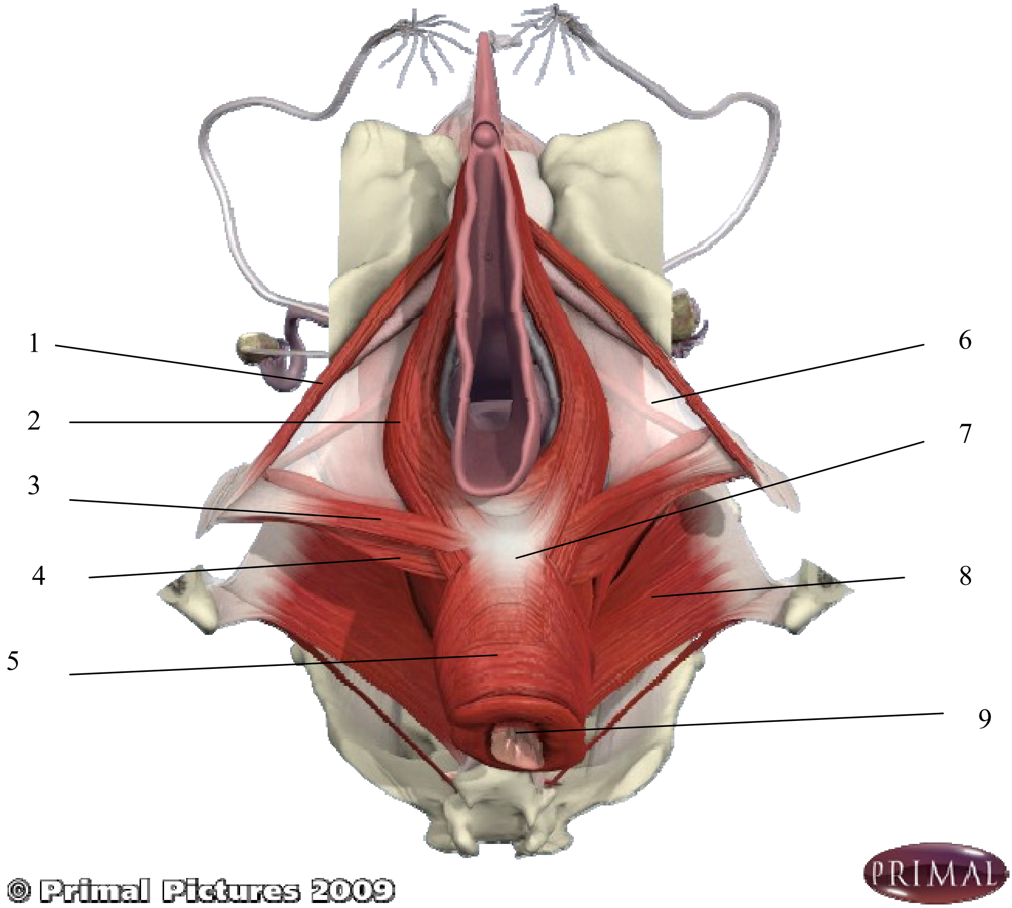

Figure 1. The muscles of the perineum (images courtesy and copyright: Primal Pictures Ltd). 1. M. ischiocavernosus, 2. M. bulbospongiosus, 3. M. Transversus perinei superficialis, 4. M. Transversus perinei profundus, 5. External anal sphincter muscle (EAS), 6. Perineal membrane, 7. Centrum tendineum perinei (Perineal body), 8. M. illiococcygeus, 9. Anal canal

3.4 The anal canal

The anal canal is approximately 4 cm long and starts at the anorectal ring (strong muscular ring that represents the upper end of the levator-EAS complex around the anorectal junction) and terminates at the anal verge. This is the surgical definition of the anal canal and it differs from the anatomical anal canal which extends from the dentate line to the anal verge and is approximately 2 cm long.[10,11] The dentate line (Figure 2) represents the junction between the upper mucosal segment and the lower cutaneous segment of the anal canal. Above the dentate line, the innervation is autonomic; hence no sensitivity for pain, while below the dentate line the innervation is somatic with sensitivity for pain. Embryologically, the dentate line represents the junction between the endoderm and ectoderm.

3.5 The anal sphincter complex

The anal sphincter complex consists of the EAS and internal anal sphincter muscle (IAS) separated by the conjoint longitudinal coat (Figure 2).

The EAS is approximately 4 cm long muscle that surrounds the IAS as a cylinder and starts and terminates slightly more distally than IAS (Figure 2). EAS is a striated muscle and has somatic innervation by the pudendal nerve. Structurally, the EAS is divided into three parts: the subcutaneous, superficial and deep. The deep part of EAS fuses with the lower edge of puborectalis muscle.[3]

The IAS is a thickened continuation of the circular smooth muscle of the bowel. It starts approximately 12 mm above the EAS and ends with a well-defined rounded edge (5 mm thick) 6-8 mm above the anal margin at the junction of the superficial and subcutaneous part of the EAS (Figure 2). The IAS is a smooth muscle and has autonomic innervation.[3]

The conjoined longitudinal muscle is a continuation of the longitudinal muscle layer of the rectal wall and is located in the intersphincteric space between the EAS and IAS (Figure 2).

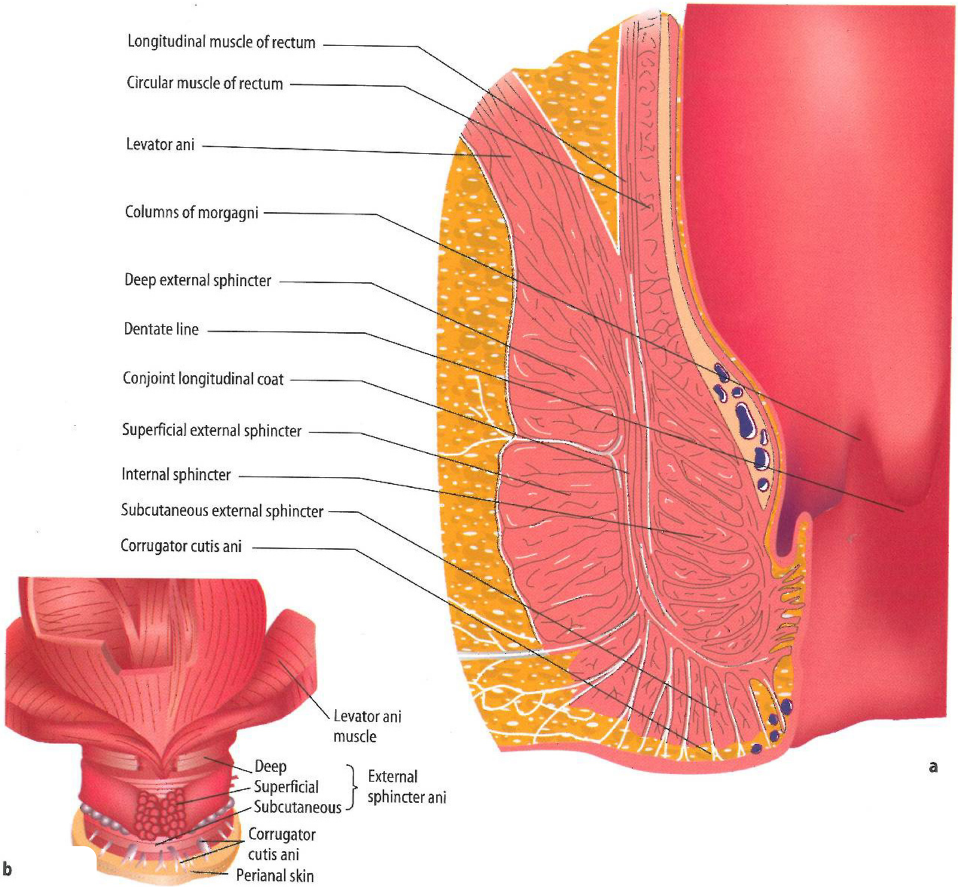

Figure 2. a Coronal section of the anorectum b Anal sphincter and levator ani. From reference 4, with kind permission of Springer Science and Business Media.

3.6 Anal incontinence

Anal incontinence is involuntarily loss of flatus and / or faeces causing social and hygienic inconvenience. Symptoms of anal incontinence can be classified into four grades; grade 1 implies full continence, grade 2 incontinence to flatus, grade 3 incontinence to liquid stools and grade 4 incontinence to solid stools.[12] Faecal urgency is defined, as sudden compelling desire to defecate that is difficult to defer.[13]

The physiology of anal continence is complex and the anal sphincter and other pelvic floor muscles, pudendal nerve, puborectalis muscle and the anorectal angle, the anal cushions, the volume and consistency of stools, colonic transit time, rectal distensibility, anal sensation and mental function, all contribute to the maintenance of anal continence.[3,14] Abnormalities of any of these factors, alone or in combination, can lead to incontinence.[3]

The IAS is responsible for 55% of the resting tone in the anal canal, while EAS accounts for 30% of the resting tone.[14] The haemorrhoidal plexus contributes with 15% of the resting tone of the anal canal (the figures represent only an estimate).[14] A disruption of IAS will lead to passive incontinence (unrecognised anal leakage), while dysfunction of the EAS will result in urge incontinence (involuntary but recognised passage of flatus or faeces).[14]

The constant tone in the puborectal muscle pulls the muscle forward which creates the anorectal angle. The tone of the muscle keeps solid stool in the rectum.[14]

3.7 Obstetric anal incontinence

In adult women, vaginal delivery is considered the most important risk factor for anal incontinence.[15-17] Our knowledge of factors involved in anal incontinence after childbirth is limited. This is possibly due to the complexity of mechanisms involved in continence and because clinical research concentrates predominantly on anal sphincter function alone.[3] Studies on anal incontinence after childbirth provide conflicting results. This might be due to lack of consistency in the definitions of anal incontinence or to differences in methods of assessment, study design, classification, follow-up or study population.[18]

The physiological evaluation of women whose continence has been compromised by childbirth has revealed two predominant factors: structural and neurogical.[3] Isolated neuropathy as a cause of incontinence is less common (about 10%) than structural sphincter damage, which to date is considered the main pathogenetic mechanism.[3,17-19] The risk of anal incontinence after clinically recognised OASIS is about 30% and depends on the grade of OASIS,[16,20-22] and any subsequent vaginal delivery may further increase the risk.[17,20,23] Most of the symptoms are mild or infrequent, e.g. flatus incontinence. Frank faecal incontinence after OASIS has been reported as 0-17%.[19-21,24,25]

However, anal incontinence is also observed after vaginal delivery without OASIS and after caesarean delivery.[26-28] This fact reflects the complexity of the aetiology of anal incontinence.

Developments in endoanal ultrasonography (EAUS) examination techniques have improved the detection of OASIS and occult OASIS. Sultan et al.[22] showed in a prospective study that 3% of primiparous women had clinically diagnosed OASIS, whereas 33% of those who delivered vaginally developed a sphincter defect visible in the EAUS examination (occult OASIS) that was not identified at delivery. They found a significant association between the detected sphincter defect in EAUS and the development of bowel symptoms. Since this pioneer study in 1993, many subsequent studies have explored occult sphincter defects and their relationship to symptoms of anal incontinence.[29-33] The significance of these occult injuries has not been fully established. Although a defect may be found in an EAUS examination, the majority of these women have no symptoms of anal incontinence.[25] There is some conflicting evidence whether occult injuries may predispose women to incontinence later in life.[34-37] Oberwalder et al. estimated that the probability of faecal incontinence associated with an anal sphincter defect was 76.8-82.8%.[25]

First degree: laceration of the vaginal epithelium or perineal skin only.

Second degree: involvement of the perineal muscles but not the anal sphincter.

Third degree: disruption of the anal sphincter muscles which should be further subdivided into:

> **3a:** <50% thickness of external sphincter torn.
>
> **3b:** >50% thickness of external sphincter torn.
>
> **3c:** internal sphincter also torn.

Fourth degree: a third degree tear with disruption of the anal epithelium as well.

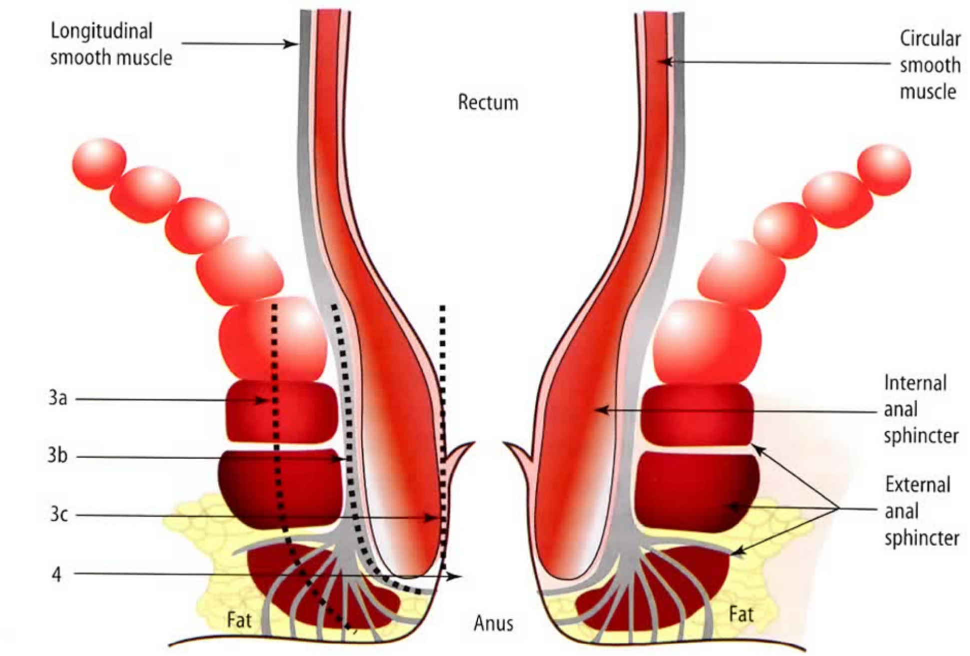

Figure 3. Classification of third- and fourth-degree anal sphincter injuries. From reference 4, with kind permission of Springer Science and Business Media.

3.8 Classification of obstetric perineal injuries

In the international classification system ICD-10, perineal injuries are divided into four degrees. First degree injuries are defined as injuries involving vaginal epithelium or perineal skin only. Second degree involves the perineal muscles, but not the anal sphincter muscles (Figure 3).

Third degree injuries are injuries of anal sphincter muscles and have previously been divided into partial and complete injuries of EAS. In 1999, Sultan[3] proposed a more detailed classification of third degree injuries which has been adapted by Royal college of Obstetrics and Gynaecology (RCOG) and also internationally (Figure 3).[38,39] Sultan subdivided third degree injuries into: 3a with disruption of less than 50% of EAS, 3b involves more than 50% of EAS and 3c involving both EAS and IAS. Forth degree injuries are third degree tears with disruption of the anal epithelium as well.

3.9 Occurrence of OASIS

There is a wide variation in the occurrence of clinically recognised (overt) OASIS in the literature, ranging from 0.1% to 17%.[40,41] The occurrence differs not only between countries, but also within the same country the occurrence differs between hospitals.[42,43] The variation in the reported overt cases of OASIS might be caused by reporting the occurrence in different populations, e.g. in all deliveries, only in vaginal deliveries, in nulliparous or multiparous women. The type of episiotomy also seems to influence the incidence of OASIS. Centres using midline episiotomy have higher incidence of OASIS.[40,44] Pirhonen et al [45] reported a marked difference in the occurrence of OASIS between Sweden (2.69%) and Finland (0.36%) and concluded that this variation might be due to the difference in the manual control of the baby's head when it is crowning. The routines of registration and accuracy of diagnosis might also influence the incidence of OASIS. Fernando et al.[46] surveyed 672 consultants in active obstetric practice and reported that 33% classified a complete or partial external sphincter tear as second degree. Groom et al.[47] demonstrated that the overall rate of OASIS rose from 2.5% to 9.3% when all second degree tears were re-examined by an experienced research fellow.

The prevalence of occult OASIS has been estimated between 12% and 35% after vaginal delivery.[22,29,30,32,48] However, for a long time it was not established whether these injuries were truly occult or represented overt OASIS either wrongly classified or missed. Andrews et al.[49] reported in a prospective study that the occurrence of OASIS rose from 11% to 25% in primiparous women when they were re-examined by an experienced research fellow with both digital and EAUS examination. Additionally, 87% and 27% of OASIS were not identified by midwives and doctors respectively. Only 1.2% of injuries was truly occult and was recognised by EAUS at the time of delivery. Therefore, the variation in the reported occurrence of overt OASIS might also be a consequence of the differences in registration, diagnostic skills, and obstetric practice.

In recent years, a gradual increase in the occurrence of OASIS has been reported in several countries including Norway.[41,50,51] In 2003–04, the Norwegian Board of Health made an extensive inspection of maternity wards in Norway and reported a high incidence of OASIS (0.5% to 6.0% among 26 maternity units).[52] Several units were criticised for a high incidence as well as for the management of the injuries. After consultation with the Ministry of Health and Social Affairs, a National Advisory Committee for Obstetrics was set up to develop a national strategy to reduce the number of OASIS.[53] As part of this programme a multicentre interventional study was designed with focus on the management of manual assistance of the foetal head during the last part of labour.[54] Only 4 hospitals were included in this study, but many other maternity units focused on the reduction of the number of OASIS on their own initiatives. This national attention has been rewarding and the occurrence of OASIS was reduced from 4.3% in 2004 to 2.5% in 2009.[55]

3.10 Risk factors for OASIS

To prevent OASIS, the knowledge of risk factors, particularly modifiable, is crucial. Many studies have previously reported on risk factors of OASIS. However, most of them are small hospital-based studies or have included first delivery only.[20,51,56-64] There is a number of factors interacting during childbirth; hence, it is not possible to point out a single causal factor for OASIS. Consequently, in the analyses of risk factors for OASIS, the consideration of confounding variables is very important. To date, it has not been possible to use a risk scoring system to predict OASIS.[65]

Risk factors for OASIS may be divided into maternal, foetal and obstetric risk factors.

3.10.1 Maternal risk factors

To my knowledge, previous studies consistently agree that OASIS particularly occur in the first vaginal delivery.[20,56,63,66] Women delivering vaginally after a previous caesarean delivery (VBAC) represent a particular group of women who are parous but not vaginally delivered. These women's risk of OASIS has previously been investigated in a few studies,[60,66,67] reporting a risk not different from nulliparous women.[60,66] However, they might have higher risk of OASIS compared to nulliparous women.[67]

In previous studies, high maternal age has been reported with conflicting results.[56,61,62] Additionally, some studies have shown that ethnic background appears to be associated with OASIS,[60,68,69] with Asian women having the highest risk. Ekeus et al.[51] found that compared to Swedish women, both Asian and African women giving birth in Sweden were at higher risk of OASIS. This finding was in conflict with previous studies suggesting that African-American women had lower risk of OASIS compared to white women.[60,68,69]

Other maternal factors such as BMI (body mass index), smoking, marital status and the level of education have previously been investigated without finding any association with OASIS.[51,70,71] In a recent Norwegian study, the authors observed an association between pre-gestational physical inactivity and OASIS.[71]

3.10.2 Fetal risk factors

Foetal weight over 4,000 g, large head circumference, gestational age more than 42 weeks and occiput posterior position and deflexion of the foetal head have been associated with OASIS in a series of studies.[20,51,56,57,63,72]

3.10.3 Obstetric risk factors

Instrumental vaginal deliveries, particularly forceps deliveries, are associated with OASIS,[56-58,70,72] as are epidural analgesia, induction of labour, stimulation of labour with oxytocin, prolonged first and second stage of labour and fundal pressure.[20,51,56,58,72] However, none of those factors have consistently been reported to be associated with OASIS

3.11 Episiotomy

Episiotomy (perineotomy) is the most frequently performed obstetric procedure. The use of episiotomy expanded in the 1920s when a shift to hospital deliveries took place and the physicians became more involved in normal uncomplicated deliveries.[73] The purpose of this incision is to increase the space available for vaginal delivery, allow better healing and prevent pelvic floor relaxation.[3,74] Episiotomy was used routinely, particularly in nulliparous women, until the 1980s when more evidence against routinely use was at hand.[75] Even though agreement about restricting the use of episiotomy is generally growing,[76] the rates of episiotomy differ widely around the world, from 9.7% in Sweden to almost 100% in Taiwan.[77]

A Cochrane review including 6 randomised controlled trials (RCTs) of episiotomy[78] has indicated that restrictive rather than routine episiotomy caused less posterior perineal trauma, less suturing and fewer healing complications. There is no evidence that routine episiotomy prevents urinary incontinence 3 years postpartum.[79] Additionally, in the literature there are conflicting results whether episiotomy protects against or increases the risk of OASIS.[56-58,60,72]

If episiotomy is not advised in all deliveries, what is the appropriate episiotomy rate, which type of episiotomy should be preferred and what are the indications for performing an episiotomy? RCTs comparing routine- and restrictive use suggest that a rate of 20-30% is reasonable for restrictive use of episiotomy.[80,81] Midline episiotomies are more frequently performed in North America as it is believed that they are easier to repair, result in better healing and less dyspareunia.[3,74] However, midline rather than mediolateral episiotomies have been reported to increase the risk of OASIS,[44,82-84] Additionally, one study showed a 50% relative reduction in risk of OASIS for every 6 degrees away from the perineal midline that an episiotomy was cut.[85]

Thus, there is no convincing evidence that episiotomy should be performed routinely and when it is performed, a mediolateral episiotomy with a wide angle is preferred. Appropriate indications for episiotomy include foetal asphyxia, high birth weight, breech delivery, shoulder dystocia and forceps delivery.[74] Still, the final rule is, to cite the authoritative 'Williams textbook', that "there is no substitute for surgical judgment and common sense".[74]

3.12 Recurrence of OASIS

The risk of the recurrence of OASIS in the same woman is a debated issue and previous studies have shown contradictory results,[44,66,86-93] the majority reporting that prior OASIS result in increased risk of recurrent OASIS.[44,66,87,89-93] However, Dandolu et al. and Edwards et al.[86,88] found no increased risk of OASIS in women with prior OASIS. The authors assumed that the conflicting results were caused by selection- and reporting bias and different obstetric practices in the respective countries. However, in contrast to other authors, Dandolu et al. and Edwards et al.[86,88] included women with

OASIS in birth order 1 in the reference group, and thus probably underestimated relative risks due to a too high risk of OASIS in the reference group.

Thus, even though OASIS is rare in women of birth order 2 or more, women with prior OASIS are reported to have increased risk of OASIS in a subsequent delivery. Still, all previous studies have investigated the recurrence risk of OASIS in women of birth order 2 or in a mixed population with non-specified birth order. Hence, knowledge about the recurrence risk beyond birth order 2 is lacking.

3.13 Studies involving families

Family studies include intergenerational studies and studies of siblings. Not only genetic variants and their associated phenotypes but also socioeconomic, environmental and behavioural characteristics may be passed on across generations.[94] Because the outcomes of interest often are rare, cohorts used in intergenerational studies require large numbers.[95] The Medical Birth Registry of Norway (MBRN) with almost 100% ascertainment of all births over a 40-years period provides a unique data set for intergenerational studies. In recent years, MBRN has been used in many studies focusing on the occurrence of familial aggregation of pregnancy complications and adverse outcomes.[96-102]

There are several studies suggesting that there is a genetic basis for the development of female pelvic floor disorders including pelvic organ prolapse and urinary incontinence.[103-106] However, knowledge on aggregation of OASIS in relatives is scarce. Such knowledge is important from an aetiological, epidemiological and clinical point of view.

The fact that OASIS tends to recur within the same woman suggests that there might be a genetic predisposition for OASIS, possibly involving both maternal and foetal genes, thus increasing aggregation of OASIS among relatives. Among possible genetic pathways 1) genes, expressed in the mothers could increase their susceptibility to OASIS 2) genes passed on from the mother or the father acting in the foetus could increase the risk of OASIS in the mother as well.[107] However, environmental factors may also be involved.

4. Aims of the thesis

The specific aims of this thesis were to:

1. validate the registration of OASIS in the Medical Birth Registry of Norway (MBRN) and Patient Administration System (PAS) with the individual hospital records as "golden standard"
2. investigate risk factors for OASIS in a large population based data set covering an extended period of time
3. assess to what extent changes in the prevalence of risk factors over time could account for secular trends in OASIS
4. investigate the risk of recurrence of OASIS in subsequent deliveries
5. study the effect of instrumental delivery, inter-delivery interval, maternal age and size of maternity unit on the recurrence of OASIS in the same woman
6. estimate the proportion of OASIS cases attributable to a history of OASIS
7. assess the paternal contribution to OASIS
8. assess the likelihood of having a further delivery after OASIS
9. investigate the aggregation of OASIS in relatives.

5. Materials and methods

5.1 Data sources

The databases used in this thesis are presented:

5.1.1 The Medical Birth Registry of Norway (MBRN)

MBRN was established in 1967 by the Directorate of Health to monitor maternal and perinatal health problems and to contribute to identification of their causes.[108] Run by the University of Bergen until 2002, it was integrated into the Norwegian Institute of Public Health. Based on compulsory notification of all live births and stillbirths in Norway after 16 weeks of gestation, MBRN comprises records of more than 2,200,000 births. The standardised notification form comprises demographic variables, as well as data on maternal health, reproductive history, complications during pregnancy and delivery, and pregnancy outcome. The form is completed by the midwives and attending physicians, and forwarded to MBRN within the ninth day postpartum or at discharge from delivery department. Additionally, since 1999 MBRN receives a notification form for all infants transferred to a neonatal care unit, including data on birth defects and other neonatal diagnoses.[108] The notification form remained almost unchanged until 1999 (Appendix 1), when a revised version was introduced (Appendix 2).

In recent decades, data from MBRN have been an essential source in epidemiological and clinical research.[109] The validity of birth outcomes is considered to be high.[108,110] Previously performed studies including validation of MBRN-variables comprise birth defects,[111-113] maternal diabetes, epilepsy and asthma,[114,115] unexplained antepartum death,[116] rheumatic disease[117] and caesarean delivery.[118] MBRN was the main source in the present thesis.

5.1.2 Record linkage

Run by Statistics Norway, the Central Population Registry was established in 1964 and comprises personal data on every permanent resident in Norway. The individuals are identified by the national identification number. MBRN is routinely linked to the Population Registry by mother's national identification number to obtain the infant's and father's identification numbers. These record linkages ensure almost complete ascertainment in MBRN of all births in the country. Very few MBRN records are not matched by routine linkage. The non-matched cases (80-100 births annually) are mainly due to refugees and foreign citizens giving birth in Norway before receiving their national identification number. Data on non reported births are then collected directly from the delivery units.[109]

Additionally, data on level of education and country of birth are provided by linkage between MBRN and Statistics Norway.

5.1.3 The Patient Administration System (PAS)

Established in 1972, PAS at Haukeland University Hospital contains the patient's name, address, national identification number, contacts with the hospital, admission and discharge (Aksland, A. IKT, Haukeland University Hospital, personal communication, March 23, 2011). Diagnoses at discharge based on ICD 8, ICD 9 and ICD 10 codes are recorded in PAS. Additionally, all procedure codes for treatments are also registered in this database. Partially since 1991 and completely from 1999, diagnoses and procedure codes registered in PAS have provided the basis for financing of the health services by DRG (Diagnosis-Related Groups) in Norway.

5.1.4 Birth logs

In our department, all births are registered manually by midwives in a separate birth log. Since 1927, these logs have been archived in the maternity unit at Haukeland University Hospital. Each birth is registered in the birth log with mother's name and date of birth, the date and time of delivery, birth weight and Apgar score, the mode of delivery and delivery complications such as OASIS.

5.2 Study designs and populations

Data in this thesis are collected from recorded information stored in national registries. Therefore the studies could be considered as historical cohort studies.

Paper I: A validation of the diagnosis of obstetric sphincter tears in two Norwegian databases, the Medical Birth Registry and the Patient Administration System

This study was a validity study in which all cases of OASIS occurring at the Department of Obstetrics and Gynaecology at Haukeland University Hospital in 1990-92 and 2000-02 were identified in the midwives' birth logs. We then received a file from MBRN where all OASIS cases from our department in the respective periods were identified. Similarly, we received a list from PAS with all OASIS cases registered either by diagnosis or procedure codes in the respective years. Table 1 shows diagnosis and procedure codes used to identify OASIS-cases in PAS.

Table 1. Diagnosis and procedure codes in the Patient Administration System (PAS), 1990–92 and 2000–02

1990-92		
Diagnosis codes (ICD-9)	664.2	Perineal tears, third degree
	664.3	Perineal tears, fourth degree
Procedure code (CO)	7720	Suture of tear (sphincter/cervix/deep vaginal)
2000-02		
Diagnosis codes (ICD-10)	O70.2	Perineal tear, third degree
	O70.3	Perineal tear, fourth degree
Procedure code (NCSP)	MBC33	Suture of perineal tear, third or fourth degree

ICD: International Classification of Disease
CO: Classification of Operation
NCSP: Nordic Classification for Surgical Procedures

We also scrutinised lists from PAS including all perineal tears sutured by a doctor, irrespectively of the classification of the tear, in case the diagnosis was set wrong. In our department, OASIS are handled by the doctors, while first- and second degree injuries are mainly handled by midwives. We then linked all three data sets and provided a database with all OASIS cases registered in any of these data sets. The medical records of all patients with OASIS registered in this database were reviewed. Perineal tears as recorded in the medical records, including the procedure record of the surgical repair, constituted the "golden standard".

Paper II: Trends in risk factors for obstetric anal sphincter injuries in Norway

The main data source in this historical cohort study was a standard data file with the birth as the unit of analysis, covering all births in Norway from 1967 to 2004. All vaginal births of a singleton and vertex-presenting fetus weighing 500 g or more were included. Women with their first birth before 1967 and births subsequent to OASIS were excluded, leaving 1,673,442 births for study.

Paper III: Risk of recurrence and subsequent delivery after obstetric anal sphincter injuries

This study is a population-based cohort design with a longitudinal approach. All births of a woman registered in MBRN in 1967-2004 were linked by the national identification number, providing sibship files with the mother as the unit of analysis. The analyses were restricted to mothers with singleton, vertex-presenting infants weighing 500 g or more who had their first delivery after 1967, altogether 828,864 mothers. In order to compare subsequent rates of OASIS after vaginal births with and without OASIS, women with previous caesarean delivery were excluded.

In order to increase sample size in analyses of paternal contribution to the recurrence of OASIS, 48,392 pairs of first to second, second to third, third to fourth, and fourth to fifth singleton vertex-presenting vaginal deliveries with birth weight 500 g or more with the same father and different mothers were identified. 18,579 (in 11,372 fathers) pairs of births took place at the same maternity units, whereas 29,813 (17,986 fathers) pairs of births took place in different maternity units.

Because caesarean delivery may influence further delivery rates,[119,120] when subsequent delivery rates from first to second and second to third births were calculated, mothers with caesarean delivery in previous births (first and first or second, respectively) were excluded. The classification of caesarean deliveries into emergency and planned in the MBRN was introduced in 1988. Consequently, analyses of planned caesarean delivery were restricted to the period 1988-2004. In the calculation of subsequent total delivery rate and planned caesarean delivery rate after the first and the second delivery, each mother was observed until the end of the observation period (31. December 2004). Data on mothers who did not have a subsequent delivery were treated as censored observations with censored time equal to the last date of registration (31. December 2004)

Paper IV: Familial risk of obstetric anal sphincter injuries: registry-based cohort study

The main analytical files in this study were:

1) Generational file based on all births in Norway in 1967-2005. Births were linked to the mother's and father's own birth records by their national identification numbers.

2) A file based on all births in Norway in 1967-2008 among full sisters and full brothers. Consecutive births among full sisters and brothers when they became parents were linked using their national identification numbers.

Figure 4 and 5 show the study populations in those files.

From the generational file we also identified 25,568 pairs of sisters whose mother did not have OASIS. This enabled us to assess the relative risk between sisters.

The number of fathers with data on their own births was considerably lower than the number of mothers, because they were on average 2 years older. Thus, fewer of their births were recorded in the Medical Birth Registry from 1967; 55% of mothers were born during 1967–1971, whereas 63% of fathers were born during the same period.

Additionally, 7% of the fathers were unknown (not reported by the mother) and could not be identified.

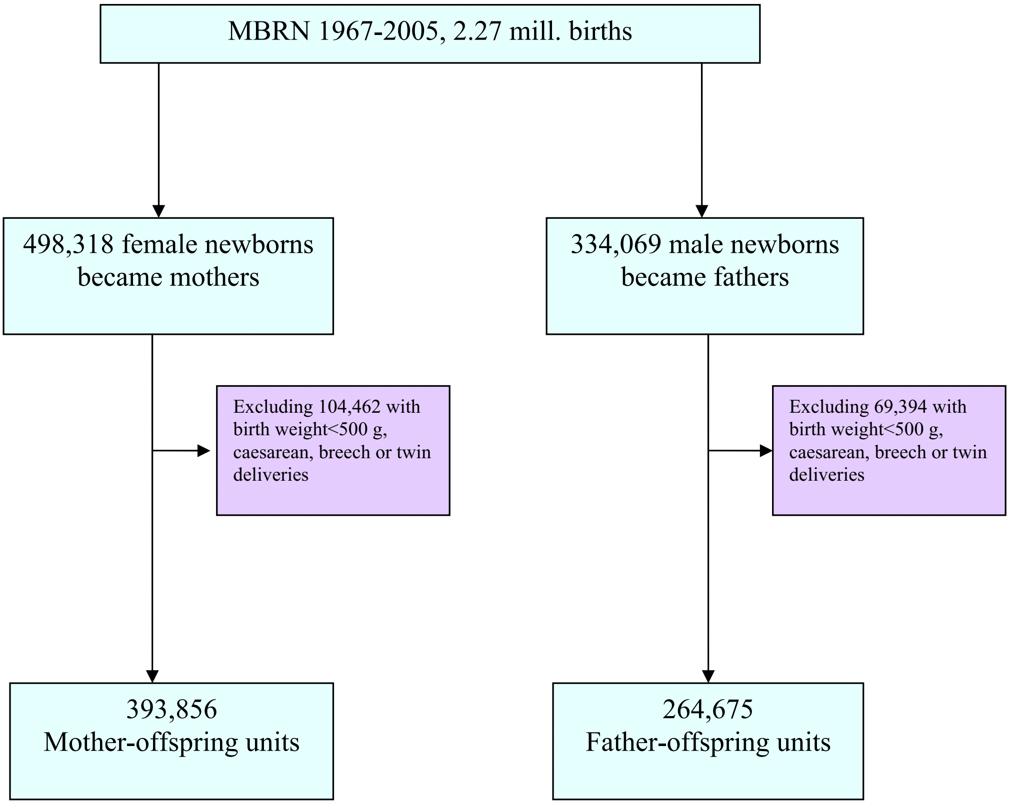

Figure 4. Flow charts of study population in paper IV, generational file, Norway, 1967-2005.

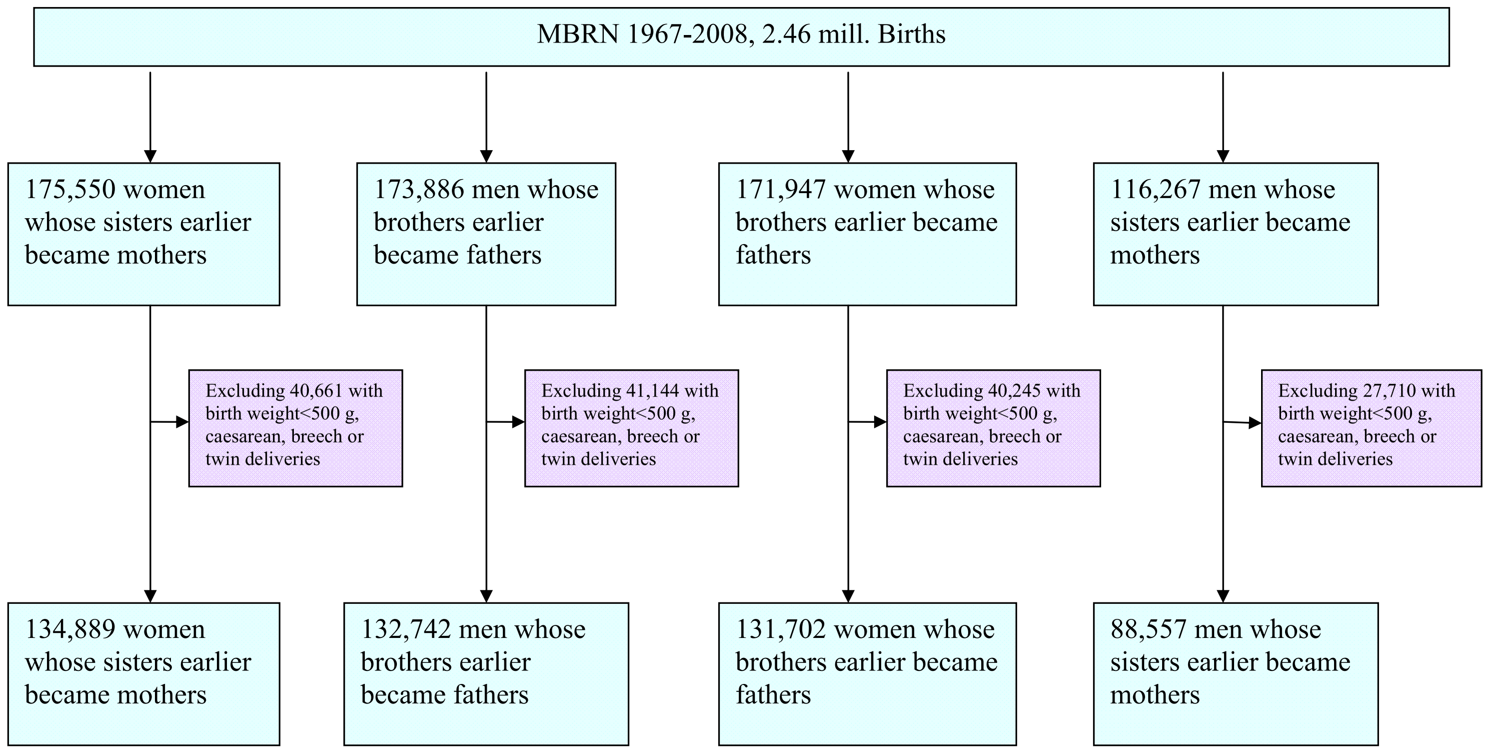

Figure 5. Flow charts of study population in paper IV, full sisters and brothers, Norway, 1967-2008

5.3 Outcomes and independent variables, including possible confounders

OASIS was the main outcome variable in all four papers. OASIS was classified according to international classification of diseases (ICD) and included 3rd degree (ICD-10: O70.2) involving sphincter muscle and 4th degree (ICD-10: O70.3) involving rectal mucosa. This classification was used both in MBRN and in PAS. In 1967–1998, OASIS was notified to the MBRN as plain text and coded as a dichotomous variable. From 1999 onwards OASIS has been notified as a dichotomous variable by checking of a box.

Year of delivery was categorised differently in each paper:

Paper I: 1990-1992 and 2000-2002.

Paper II: 1967–1977, 1978–1987, 1988–1998 and 1999–2004.

Paper III: 1967-1974, 1975-1982, 1983-1990, 1991-1998 and 1999-2004.

Paper IV: For the analysis in the generational file: before 1996, 1996-2000, and 2001-2005; for pairs of siblings 1967-1977, 1978-1988, 1989-1998 and 1999-2008.

The registration of *maternal age* is almost complete in MBRN since mothers' year of birth is a part of the national identification number. Maternal age at birth was categorised as less than 20, 20–24, 25–29, 30–34, 35–39, 40 years or older, unknown. There were only 6 cases of missing or unknown maternal age in paper II.

Birth order was recorded as 1, 2, 3, or 4 or greater, based on number of previous deliveries reported by the mother at birth.

In order to assess the 'pure' effect of a previous vaginal birth, we introduced the variable *'vaginal birth order'* based on the number of previous vaginal deliveries (1, 2, 3, 4, 5, 6, 7 or greater).

Previous caesarean or vaginal delivery: In paper II, deliveries were grouped according to history of vaginal birth or caesarean delivery as: 1) first vaginal delivery without previous caesarean delivery (first birth) 2) first vaginal delivery after one or more previous caesarean deliveries (previous caesarean only) 3) delivery after one or more caesarean and vaginal deliveries (previous vaginal and caesarean) 4) delivery after one or more vaginal deliveries without previous caesarean delivery (previous vaginal only).

Mother's country of birth was obtained by linkage of records in MBRN to Statistics Norway and was in the present study categorised into: European, African, Asian, North American, Latin American, Oceanian and unknown. In paper II, there were 1,785 (0.1%) cases with unknown country of birth.

Diabetes type 1, type 2 and gestational diabetes were notified as yes or no. Data on maternal diabetes were collected in MBRN before 1999, but the classification of pre-gestational diabetes into type 1 and type 2 were reported in MBRN from 1999. We therefore chose to select data only from 1999 onwards. The registration of diabetes in MBRN has previously been validated.[114] The authors found that the sensitivity of the registration of diabetes type 1 in MBRN in the period 1999-2004 was 88%. Positive predictive values for gestational and pre-gestational (type 1 and type 2) diabetes in 1998 were 89.4% and 79.5%, respectively.[114]

Smoking at the end of pregnancy (yes or no), was notified to MBRN since 1999.

Marital status was classified as married, cohabiting and single. Cohabiting was introduced in the MBRN after 1982. Thus, cohabitants were previously notified as single. Marital status may influence the further delivery rate; therefore we adjusted the analyses of subsequent delivery rate in paper III for this variable.

Mother's education level was derived from the register of Level of Education, run by Statistics Norway. This variable was used in paper II and was categorised as shorter than 8, 8–10, 11–12, 13–17, 18 years or longer, or unknown which was recorded for 36,312 (2.2%) women in paper II.

Size of maternity unit was based on number of deliveries per year and was classified as: less than 49, 50–499, 500–999, 1000–1999, 2000–2999, 3000 or greater, home transport or unknown. There were 12,342 (0.7%) cases either reported as home-, transport or unknown in paper II.

Instrumental delivery was categorised in paper II as forceps, vacuum, both vacuum and forceps and non-instrumental. In paper III and IV, it was categorised as forceps or vacuum.

Episiotomy (yes or no) was recorded since 1999. The type of episiotomy was not specified in MBRN. However, mediolateral episiotomy is traditionally performed in Norway.

Induction of labour by vaginal prostaglandin application (yes or no) was recorded in MBRN in both old and revised notification forms. However, in the revised notification from 1999 onwards, the method for induction of labour is specified by checking boxes and is thus probably more reliable. For this reason, we chose to select data on this variable only from 1999 onwards.

Epidural analgesia classified as yes or no. This variable was notified to the MBRN as plain text and coded as a dichotomous variable in 1967-98. From 1999 onwards, epidural analgesia is notified as a dichotomous variable by checking of a box.

Birth weight was categorised as less than 2500, 2500–2999, 3000–3499, 3500–3999, 4000–4499, 4500–4999, 5000 g or greater. The quality of data on birth weight is considered to be high in the MBRN. Peaks at rounded weights (nearest 50 or 100 g) are found. A very small number of births are registered with weights that are obviously erroneous, such as records with weights below 100 g and above 7000 g (four cases). In the present study, we have excluded births with weights less than 500 g, and misclassification of birth weight has unlikely any implications for the results.

Head circumference was not recorded in the early period of registration. The registration was consistent after 1980. Thus, we chose to select data from 1980 onwards. Head circumference was categorised as less than 33, 33–34, 35–36, 37–38, 39–40, 41 cm or greater or unknown. There were 11,217 (0.7%) missing data in paper II.

Gestational age was estimated by subtracting the first day of LMP (last menstrual period) from the date of birth. From 1999, gestational age based on ultrasound dating was available and was used when data on the LMP were lacking (7.2%). This variable was categorised as less than 37, 37–38, 39–40, 41–42, 43 weeks or more, unknown. There were 96,327 (5.7%) missing data in paper II.

Inter-delivery interval was defined as the number of years between two deliveries and was in paper III classified as less than 5 years, 5-9 years and 10 years or more.

Infant death within one year classified as yes or no, included all foetal death from 16 weeks' gestation plus live births that died within the first year of life. Since previous studies[120,121] have shown that perinatal loss influence subsequent delivery rate, we adjusted the analysis on subsequent delivery rate in paper III for this variable.

Caesarean delivery was excluded in all four papers with exception of analyses of subsequent delivery rate in paper III. When subsequent delivery rates from first to second and second to third births were calculated, mothers with caesarean deliveries in previous births (first and first or second, respectively) were excluded.

Caesarean delivery was notified to the MBRN throughout the whole period, but the classification of caesarean deliveries into emergency and planned was introduced in the MBRN from 1988. In paper III, planned caesarean deliveries included those that were planned, irrespective of how they were performed (planned or emergency caesarean or vaginal delivery). Caesarean delivery has previously been validated in the MBRN with satisfactory result.[118]

Breech deliveries were excluded in paper II, III and IV. Most previous studies on risk factors of OASIS have excluded breech deliveries. Vaginal breech deliveries are particularly rare in many countries where breech presentation is regarded as an indication for caesarean delivery. In order to make our results comparable with previous studies, we excluded breech deliveries from papers II, III and IV. In 2008, breech presentation occurred in 4.5% of all deliveries in Norway and 33% of them were delivered vaginally.[122] Because vaginal breech deliveries are not rare in our country, we wanted to assess the risk of OASIS in breech delivery in paper II. Before we excluded breech deliveries from the study population in that paper, we studied the risk of OASIS in breech deliveries. The results are presented in this thesis in the section with supplementary results.

In these analyses, breech deliveries were categorised into assisted breech deliveries without forceps to after-coming head and breech deliveries with forceps to after-coming head. Non-instrumental vertex vaginal deliveries were the reference group. Only vaginally delivered breech presentations were included in the analyses.

5.4 Methods

Paper I: The *sensitivity* was calculated as the proportion of OASIS cases diagnosed in the medical records that were recorded as OASIS in MBRN or PAS.

The *specificity* was calculated as the proportion of those cases not diagnosed as OASIS in the medical records that were not recorded in MBRN or PAS.

The *positive predictive value* was calculated as the proportion of all cases recorded as OASIS in MBRN or PAS who truly were OASIS (identified in the medical records).

The *negative predictive value* was calculated as the proportion of all cases not recorded as OASIS in MBRN or PAS who truly were not OASIS (not identified in the medical records).

Paper II: The relative risk of OASIS was estimated by odds ratio (OR) and defined as the odds of OASIS in an exposed group to the odds of OASIS in an unexposed group of women.

Paper III: The odds ratio (OR) of recurrence of OASIS in second and third delivery was defined as the odds of OASIS among women having already had an OASIS relative to the odds of OASIS in those without a previous OASIS.

Population-attributable risk percentages were estimated as 100 × (incidence in the population–incidence in the non-exposed group) / incidence in the population, on the assumption of a causal relationship between an initial and a subsequent OASIS. Exposed third deliveries were those with either OASIS in the first or second delivery.

The subsequent delivery rate was defined as the percentage of all women who had a delivery (second or third) subsequent to first or second delivery.

Planned caesarean delivery rate was defined as the percentage of all women who had a planned caesarean delivery, irrespective of how the delivery was performed (planned or emergency caesarean or vaginal delivery), subsequent to a first or second delivery.

Paper IV: The recurrence rate of OASIS from mothers to daughters was defined as the likelihood of OASIS in daughters whose mothers had OASIS.

The recurrence rate of OASIS from mothers to sons' partners was defined as the likelihood of OASIS in women whose mothers-in-law had OASIS.

The recurrence rate between sisters was defined as the likelihood of OASIS in women whose sisters earlier had OASIS.

The recurrence rate between brothers' partners was defined as the likelihood of OASIS in partners of men whose brothers' partners earlier had OASIS.

5.5 Statistics

In all four papers, the statistical analyses were carried out with SPSS (SPSS Inc., Chicago, IL) and the MlWin program (Centre for Multilevel Modelling, University of Bristol, UK).

ORs and 95% confidence intervals (CIs) were calculated by logistic regression (paper II-IV). For proportions, CIs were calculated with the score method (paper I).[123]

Logistic regression models were used to estimate effects, adjust for confounding and evaluate interaction between factors. Additionally we used Cox proportional hazard regression models and stratification to adjust for possible confounders.

When analysis included two or more births in the same woman or man's partner (papers III and IV), we used multilevel logistic regression analysis in order to avoid biased risk estimates and standard errors caused by the nested structure of data (births nested within women).

5.6 Ethical consideration

Paper I was approved by the local ethics committee and the Data Inspectorate of Norway.

The regional committee for medical research ethics approved the study protocol for paper II-IV (REK Vest no 247.09).

6. Main results

Paper I: At the Department of Obstetrics and Gynaecology at Haukeland University Hospital, there were 13,381 and 12,380 vaginal births in 1990-92 and 2000-02, respectively. We identified a total of 774 and 813 cases of OASIS in those respective periods. Because of the lack of medical records or incorrect registration, 10 cases were excluded.

The incidence of OASIS was 5.8% in 1990–92; 5.6% were third degree and 0.2% fourth degree injuries. In 2000–02 the total incidence was 6.6%; of these 5.9% were third and 0.7% fourth degree injuries, respectively. We found no significant increase in third degree perineal tears between the two three-year cohorts. There was, however, a significant increase of fourth degree sphincter injuries ($p<0.001$), and also a significant increase in the total incidence of OASIS ($p<0.001$).

In 1990-92, 772 cases of OASIS were recorded in MBRN, 660 of these cases were true OASIS (confirmed by the medical records). In 2000-02, 782 cases of OASIS were recorded in MBRN, 746 of these cases were true OASIS.

In 1990-92, 532 cases of OASIS were recorded in PAS; only 403 of these cases were true OASIS. In 2000-02, 742 cases of OASIS were recorded in PAS, 688 of these cases were true OASIS.

Based on this data, we calculated the sensitivity, specificity, positive predictive value and negative predictive value of the registration of OASIS in MBRN and PAS (Table 2).

Table 2: The validity of the registration of obstetric anal sphincter injuries in the Medical Birth registry of Norway (MBRN) and Patient Administrative System (PAS) in 1990-92 and 2000-02, on the basis of medical record review.

	1990-92		**2000-02**	
	MBRN	**PAS**	**MBRN**	**PAS**
	% (95% CI)	**% (95% CI)**	**% (95% CI)**	**% (95% CI)**
Sensitivity	85.3 (82.6-87.6)	52.1 (48.6-55.6)	91.8 (89.7-93.5)	84.6 (82.0-85.9)
Specificity	99.5 (99.4-99.6)	99.0 (98.8-99.1)	99.7 (99.6-99.8)	98.5 (99.4-99.6)
Positive predictive value	91.4 (89.1-93.2)	75.8 (71.9-79.2)	95.4 (93.7-96.7)	92.7 (90.6-94.4)
Negative predictive value	99.1 (98.9-99.3)	97.1 (96.8-97.4)	99.4 (99.3-99.5)	98.9 (98.7-99.1)

CI: Confidence interval

Paper II: The occurrence of reported OASIS increased from 0.5% in 1967 to 4.1% in 2004 in Norway. OASIS was more frequent in forceps and vacuum deliveries than in non-instrumental deliveries and in all three categories the same trend was observed. After adjusting for several risk factors, the increase of OASIS persisted, although reduced significantly from 7.1 fold to 5.6 fold.

OASIS was significantly associated with year of delivery, maternal age over 30 years, vaginal birth order 1, previous caesarean delivery, instrumental delivery, episiotomy, diabetes type 1, gestational diabetes, induction of labour by prostaglandin, large maternity unit, birth weight 3,500 g or more, head circumference 35 cm or more and African and Asian country of birth. No or marginal associations were observed with diabetes type 2, gestational age, epidural analgesia, smoking and level of maternal education.

Regardless of vaginal birth order, the highest crude occurrence of OASIS by maternal age was observed in mothers 25–34 years of age (Figure 3 in paper II).

In vaginal birth order 1 deliveries, our data indicated no protection against OASIS of episiotomy when it was used in non-instrumental deliveries (OR 1.0, 95% CI 1.0–1.1), but in instrumental deliveries the use of episiotomy was protective against OASIS (OR 0.8, 95% CI 0.8–0.9). In vaginal birth order 2+ deliveries, we found a higher risk of OASIS when episiotomy was used in non-instrumental deliveries (OR 1.3, 95% CI 1.2–1.5), and no significant protective effect of episiotomy against OASIS in instrumental deliveries (OR 0.8, 95% CI 0.6–1.1).

Paper III: The occurrence of OASIS in second deliveries subsequent to deliveries with OASIS was 5.6%, and without OASIS 0.8% (adjusted OR 4.2, 95% CI 4.2-4.9) (Figure 6). Additionally, forceps deliveries, birth weight greater than 3,500 g and maternity units with 3,000 deliveries or more per year were associated with recurrence of OASIS in the second delivery

A history of OASIS in the first or second delivery increased the occurrence in the third delivery. The ORs and absolute risks were highest in women with no OASIS in first delivery but OASIS in second delivery and women with OASIS in both first and second deliveries (adjusted ORs 9.3, 95% CI 7.2-11.8 and 10.6, 95% CI 6.2-18.1, respectively, Figure 6).

Population-attributable risk percentage of OASIS in second and third delivery due to previous OASIS was 10% and 15%, respectively.

A man who fathered a birth with OASIS was more likely to father a subsequent birth with OASIS in another woman who gave birth in the same maternity unit (adjusted OR, 2.1, 95% CI 1.2-3.7) (Table 4). Adjusting for birth weight or head circumference had negligible effect. However, if the deliveries took place in different maternity units, the recurrence risk was not significantly increased (adjusted OR 1.3, 95% CI 0.8-2.1) (Table 4).

Subsequent delivery rates in women with and without previous OASIS were non-different. However, women with a history of OASIS were more frequently scheduled to caesarean delivery subsequently.

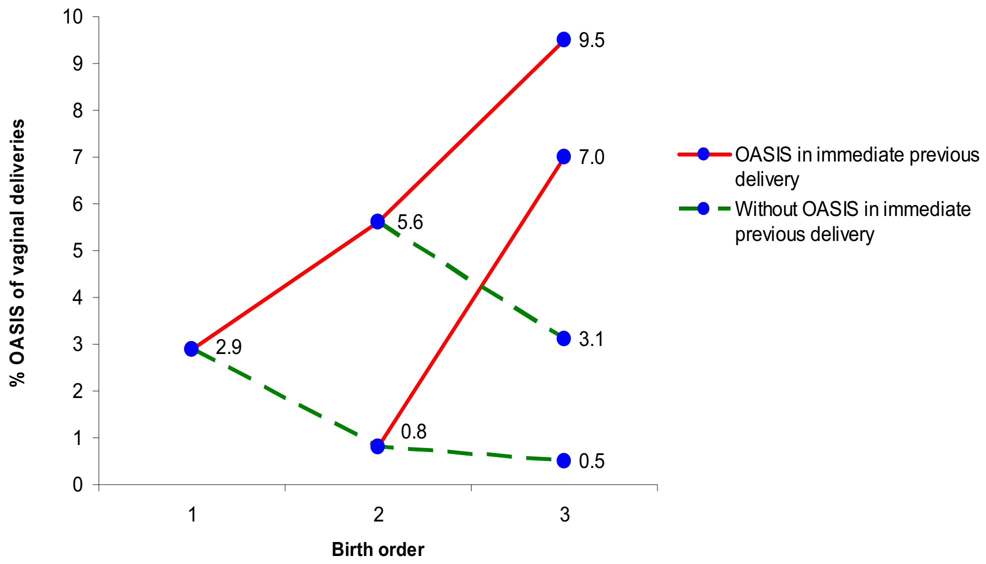

Figure 6. Risk of obstetric anal sphincter injuries (OASIS) by birth order and OASIS in previous deliveries, Norway 1967-2004.

Paper IV: Women who were born in a delivery complicated by OASIS had twice the risk of having OASIS in their own delivery compared to women with no family history of OASIS (adjusted OR 2.0, 95% CI 1.7-2.5). For men who were born in a delivery complicated by OASIS, the risk of OASIS in their partner was moderately increased (adjusted OR 1.4, 95% CI 1.1-1.8). Stratifying data for first or second generation's birth order did not alter the results. No significant time trends in odds ratios were observed.

Sisters who delivered subsequently to a sister with a history of OASIS had almost twice the risk of having OASIS compared with women with no family history of OASIS (adjusted OR 1.7, 95% CI 1.5-1.9). If OASIS occurred in one brother's partner at delivery, the risk of OASIS in next brother's partner was only marginally increased (adjusted OR 1.2, 95% CI 1.0-1.4). Adjusted OR of recurrence from a sister to her brother's partner was 1.3 (95% CI 1.2-1.5). However, there was no increased recurrence from a brother's partner to his sister (adjusted OR 1.1, 95% CI 0.9-1.3). There was no time trend in recurrence of OASIS between sisters or brother's partners. However, recurrence between brother's partners decreased with time and was not significant from 1978 onwards.

In the subgroup of sisters with no history of OASIS in their mother, we found the same adjusted relative recurrence risk of OASIS between sisters (adjusted OR 1.7, 95% CI 1.4-2.1).

Except for year of delivery, effects of adjustments were generally small or negligible.

7. Supplementary results

Paper II: In this paper we wanted to analyse the risk of OASIS in breech deliveries. The reason for excluding breech deliveries in paper II and not presenting these data in the paper is discussed on page 43-44.

Compared with non-instrumental vertex vaginal deliveries, the risk of OASIS was decreased in breech deliveries without forceps to after-coming head (adjusted OR 0.8, 95% CI 0.7-0.9) (Table 3). When the breech deliveries were performed with forceps to after-coming head the risk of OASIS increased with almost two-fold (adjusted OR 1.9, 95% CI 1.6-2.3) (Table 3).

Table 3. Risk of obstetric anal sphincter injuries (OASIS) in breech deliveries with and without forceps to after-coming head, Norway, 1967-2004

Mode of delivery	**No. of deliveries**	**No. (%) of OASIS**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**
Non-instrumental vertex vaginal deliveries	1,548,940	21,563 (1.4)	Reference	Reference
Breech with forceps	5,947	129 (2.2)	1.6 (1.3-1.9)	1.9 (1.6-2.3)
Breech without forceps	23,359	192 (0.8)	0.6 (0.5-0.7)	0.8 (0.7-0.9)

OR: Odds ratio, CI: Confidence interval
Adjusted for year of delivery, vaginal birth order, maternal age, birth weight and the size of maternity unit.

Paper III: Table 4 shows recurrence of OASIS in the immediate subsequent delivery according to change of partner and maternity unit between deliveries. These data are presented in paper III, but the table is not presented in the paper.

Table 4. Maternal and paternal recurrence of obstetric anal sphincter injuries (OASIS) in a subsequent delivery by change of parenthood and maternity unit in four pairs of delivery (first to second, second to third, third to fourth, and fourth to fifth), Norway 1967–2004.

Previous delivery	Subsequent delivery				
OASIS	**"Parenthood"**	**Change of maternity unit**	**Total**	**OASIS**	
				N (%)	**Adjusted odds ratio (95% CI) †**
No	Same mother and father	No	422,942	2,992 (0.7)	Reference
Yes		No	8,492	491 (5.8)	6.5 (5.9-7.2)
No		Yes	193,749	1,753 (0.9)	Reference
Yes		Yes	3,871	246 (6.4)	5.6 (4.9-6.4)
No	Same mother, different father	No	17,243	140 (0.8)	Reference
Yes		No	257	10 (3.9)	4.7 (2.5-9.1)
No		Yes	23,672	254 (1.1)	Reference
Yes		Yes	394	21 (5.3)	4.7 (3.0-7.5)
No	Same father, different mother	No	18,313	415 (2.3)	Reference
Yes		No	266	15 (5.6)	2.1 (1.2-3.7)*
No		Yes	29,357	852 (2.9)	Reference
Yes		Yes	456	20 (4.4)	1.3 (0.8-2.1)*

CI: Confidence interval.

†: Adjusted for year of delivery (1967-82, 1983-98 and 1999-2004) and maternal age (less than 20, 20-29, 30-34, 35-39 and 40 years or older) in the current delivery

*: Additionally adjusted for maternal birth order in the subsequent delivery

8. Discussion

8.1 Validity of the study

The validity of a study is usually evaluated by two components:

1) The validity of the conclusions drawn as they relate to the members of the source population (internal validity).

2) The validity of the conclusions drawn as they relate to people outside the source population (external validity or generalisability).[124]

8.1.1 Internal validity

Internal validity is a prerequisite for the external validity. Violations of internal validity can be classified into selection bias, information bias and confounding.[124]

Selection bias may occur when the relation between exposure and outcome is different in the study population and those who are not participating in the study.[124] Notification in MBRN (papers I-IV) is mandatory and not depending on OASIS. Therefore, our study would most likely not be affected by selection bias.

In paper I, the validation was based on data from one hospital (Haukeland University hospital). This could introduce selection bias into this study, since the registration and diagnostic routines might possibly vary at different maternity units. However, our findings were confirmed by Drøyvold et al. who included nine different maternity units.[125] This matter is discussed further on page 58.

In paper III, we followed up women with respect to reproductive career. Loss of follow-up could occur in women who emigrated or died. However, by logistic regression adjusted for year of delivery, we found no significant differences in emigration (0.3-1.6%) or death (0.5-1.7%) between groups defined as OASIS or not in first and second deliveries. For the same reason, in paper IV emigration or death would likely not significantly affect the results.

With the exception of analyses for subsequent delivery rates after OASIS, we excluded caesarean deliveries from our studies. It is possible that women with severe OASIS and potentially higher recurrence risk were delivered by caesarean in the subsequent delivery and thus were excluded from our population in paper III. The exclusion of these women could influence our results by reducing the recurrence rate. In a supplementary analysis, we included caesarean delivery into the study population, but this did not significantly alter the results (data not shown).

Information bias may arise due to errors in the information or classification of collected subjects.[124] Such bias is often referred to as misclassification when the variable is measured on a categorical scale. If the misclassification of the exposure or outcome is not dependent on the other variables, the misclassification is referred to as non-differential.[124] Differential misclassification occurs if the misclassification of the exposure or outcome depends on the other, and it can exaggerate or underestimate an effect.[124]

OASIS was the main outcome and the fundament of this thesis. Hence, we started this work by validating the registration of OASIS in MBRN and PAS (paper I). In paper I, 25.5% of cases reported with OASIS in 1990-92 and 3.2% of cases in 2000-02 lacked procedures records. These cases were however qualified as OASIS, because there were other information in the medical record that made the correct classification possible. In most of these cases, OASIS was recorded by doctors in the partogram or in some cases there was a record of postpartum control. In MBRN, we found a high validity of the registration of OASIS and this finding was afterwards confirmed by Drøyvold et al.[125] However, it is possible that particularly in the early study period, OASIS were underreported to the MBRN. This lack of registration might be due to poor registration- or diagnostic routines. Due to the high specificity, it seems reasonable to believe that most OASIS cases in MBRN are true cases. Thus, the relative risk estimates are most likely not biased.

In papers III and IV, a record of prior OASIS in a woman or perhaps also in a first degree relative could introduce a differential misclassification caused by increased diagnostic attention during delivery which might increase relative risks estimates of recurrence.

In papers III and IV, we investigated a potential contribution of fathers to the risk of OASIS. MBRN comprises no information about false paternity. However, a Norwegian genetic study suggested that less than 5% of infants in Norway have incorrect registered paternity information (Min Shi, as referred in[126]). This low level of misclassification would likely not influence the estimated paternal effects in our study.

Instrumental delivery might introduce a differential misclassification. In Norway, non-instrumental deliveries are attended usually by midwives, whereas instrumental deliveries are conducted by doctors. In a prospective interventional study, Andrews et al.[49] showed that midwives missed 26 of 30 cases of OASIS, while doctors missed 8 of 29 cases. It is possible that OASIS has been diagnosed more frequently in instrumental deliveries, because doctors examined them immediately after delivery. In this case, misclassification of OASIS would be differential and the effect of instrumental delivery exaggerated.

Confounding is a situation in which one (confounding) factor causes an outcome falsely attributed to another factor. A confounder is associated with the exposure in the source population, as well as a risk factor for the outcome and not be intermediate in the chain of causation between the exposure and outcome variable.[124]

OASIS is most likely the end-product of many factors during pregnancy and childbirth. The complexity of risk factors represented a great challenge in our studies. It is only possible to control for confounders that are known or can be measured. Since our study was based on data that already were registered, we could not control for potential confounders not registered in MBRN. Episiotomy has only been notified to MBRN since 1999. The routines for management of manual assistance of the foetal head during the last part of labour, the experience of birth-attendant, the indication for instrumental delivery, angle of episiotomy and duration of second stage of labour are possible additional factors that are not registered in MBRN. Still, there is a wide range of registered variables of good quality in MBRN that allowed us to assess the effects of a series of factors working together. In the present studies we used stratification, multivariate logistic regression and Cox proportional hazard regression to assess the effects of confounders.

Effect modification also called interaction, exists if the estimate of the effect of an exposure on an outcome varies according to the level of a third variable.[124] In the present thesis, effect modification was evaluated by stratification or by including an interaction term in multivariate analyses.

8.1.2 External validity (generalisability)

Paper I was conducted at Haukeland University Hospital which is a referral hospital with approximately 5,000 deliveries per year and was limited to the periods 1990-92 and 2000-02. This study indicated a high validity of recording of OASIS in MBRN. Drøyvold et al.[125] published similar results from nine Norwegian hospitals including both referral and community hospitals.

Papers II-IV were based on Norwegian population and the findings in these studies are applicable to the population in Norway. The results in paper II and III are generally consistent with most previous studies. The increase in the occurrence of OASIS is reported in other Nordic countries.[41,50,51] The results of these papers thus should apply to other populations than Norwegian with similar health care system and rate of OASIS.

In paper II we found an excess risk of OASIS in African and Asian mothers compared to European women. This finding applies to African and Asian women giving birth in Norway and we do not know if this could be applicable to African and Asian women in general.

Results in paper IV may to a larger extent be explained by biological mechanisms, and are likely more applicable to other populations.

8.1.3 Precision

Precision of a study is reduced to the extent random errors occur. In general, precision can be improved by either modifying the study design or increasing the study size, of which the latter is the principal way of increasing the precision in epidemiological studies.[124]

In paper I we included OASIS in two different time periods (1990-92 and 2000-02). We could have increased the sample size by including a larger cohort, but this was considered being time-consuming, and the cohorts were large enough for the aim of this study with relatively narrow confidence intervals.

In papers II-IV, we used data from MBRN. These studies had large sample sizes, and the estimates of associations were precise with narrow confidence intervals. On the other hand, some analyses were precluded by small sample sizes in subgroups, e.g. we wanted to assess the risk of OASIS in births where both parents were born in OASIS complicated deliveries (paper IV). This analysis was hampered by few cases and therefore was not included in this thesis.

Hopefully in the future, it would be possible to increase the sample size by linkage to other Nordic Medical Birth Registries.

8.2 Discussion of the results

8.2.1 The validation of the registration of OASIS in MBRN and PAS

OASIS was notified to MBRN as plain text during 1967-98 and coded as a dichotomous variable. In the revised notification form from 1999, OASIS has been notified as a dichotomous variable by checking of a box. For that reason, we validated the registration of OASIS in two different time periods, before and after the revision.

We found a high precision of MBRN-data during 2000-02. The sensitivity and positive predictive value of MBRN were lower during 1990-92, but still high enough to be reliable. The validation of the registration of OASIS in PAS was low in 1990-92 and much improved in 2000-02. This study was the first in Norway to investigate the reliability of OASIS registration in MBRN and PAS. However, the study was restricted to the Haukeland University Hospital which is a referral hospital with approximately 5,000 births per year and the results may not be applicable to all hospitals providing obstetric care. This publication was followed by a report from Drøyvold et al. at SINTEF[125] (Stiftelsen for industriell og Teknisk Forskning) who studied the validity of OASIS in MBRN and PAS in nine Norwegian hospitals during 1999-2000. Our data from 2000 was a part of this study. This study confirmed our finding that MBRN had a high validity (87.3% sensitivity). Additionally, they stratified their results by type of hospital and found no difference in validation of the registration of OASIS in the MBRN between referral and community hospitals. The validation of the registration of OASIS was lower in PAS (68.2% sensitivity) and differed significantly between referral and community hospitals (65.7% and 91.1%, respectively).[125] We found a higher sensitivity in PAS during 2000-2002 (84.6%) than Drøyvold et al. possibly due to the fact that Drøyvold et al. used only diagnosis codes to find OASIS-cases in the PAS, but in our study, we used both diagnosis and procedure codes.

Jander et al.[127] found only 6% of OASIS-cases registered at a referral hospital not being registered in the Medical Birth Registry of Sweden.

The validity of the registration of OASIS in PAS has been studied in two previous studies in USA,[128,129] showing sensitivities 76.6% to 90.0%.

8.2.2 The incidence of OASIS

The occurrence of OASIS at Haukeland University Hospital (paper I) increased significantly from 5.8% in 1990-92 to 6.6% in 2000-02. In paper II, we investigated the occurrence of OASIS in Norway and found an increase in the occurrence from 0.5% in 1967 to 4.1% in 2004 (Figure 7). The observed high occurrence in paper I was consistent with our finding in paper II that the occurrence of OASIS was associated with the size of maternity unit and was highest at maternity units with more than 3,000 deliveries per year (Figure 8), as this is the case at Haukeland University Hospital.

Possible explanations for the increase of OASIS during 1967-2004 include 1) improved routines for the registration of OASIS in the MBRN, 2) improved diagnostic attention and routines, 3) changes in obstetric and demographic risk factors.

Paper 1 indicates that the registration of OASIS in the MBRN was satisfactory in 1990-92 and further improved in 2000-02. We have no information about the validity of the registration before 1990. Changing to the revised notification form in 1999 may have improved the recording of OASIS in the MBRN. Additionally, in 1997-99 financial incitements for correct coding (DRG) were implemented in the Norwegian health care. If these two events have influenced the registration of OASIS, we would observe a sudden increase around the time period these events took place. The reported occurrence of OASIS in instrumental deliveries increased from 7.2% in 1995-1998 to 12.6% in 1999-2004 (Figure 9) which may be explained by improved registration and coding routines. However, the overall occurrence of reported OASIS increased from 2.4% to 3.8% in the respective periods (Figure 7). In our study population, the majority of OASIS cases (71.6%) occurred in non-instrumental deliveries which likely were less influenced by changes in coding system or notification form.

During the past two decades, EAUS has revealed unrecognised or occult OASIS.[22,32,33] Studies have suggested that increased vigilance and appropriate examination[47,49] probably along with higher demands for documentation, may have improved the diagnostics and thus increased the occurrence of registered OASIS.

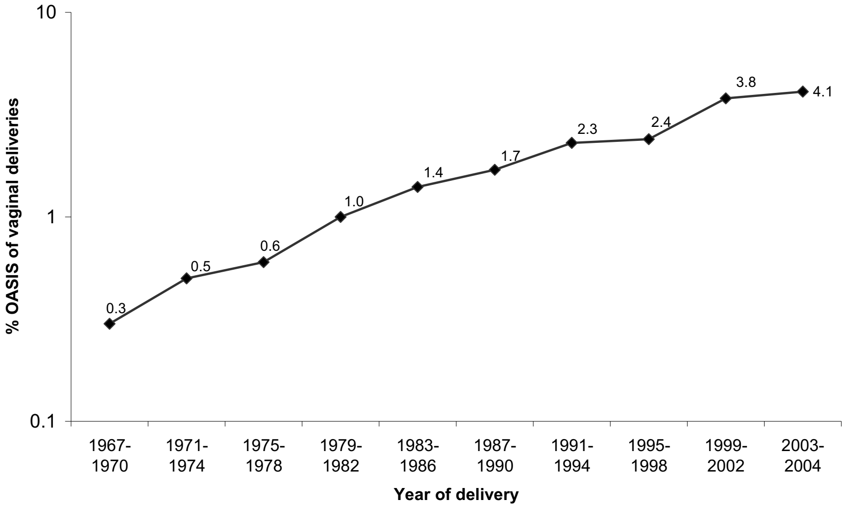

Figure 7. The occurrence of obstetric anal sphincter injuries (OASIS) by year of delivery, 1967-2004, Norway (semi logarithmic scale).

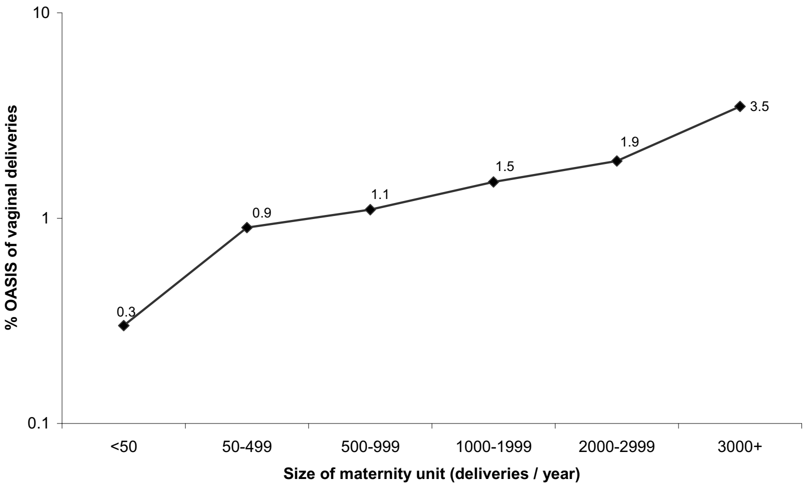

Figure 8. The occurrence of obstetric anal sphincter injuries (OASIS) by the size of maternity unit, 1967-2004, Norway (semi logarithmic scale).

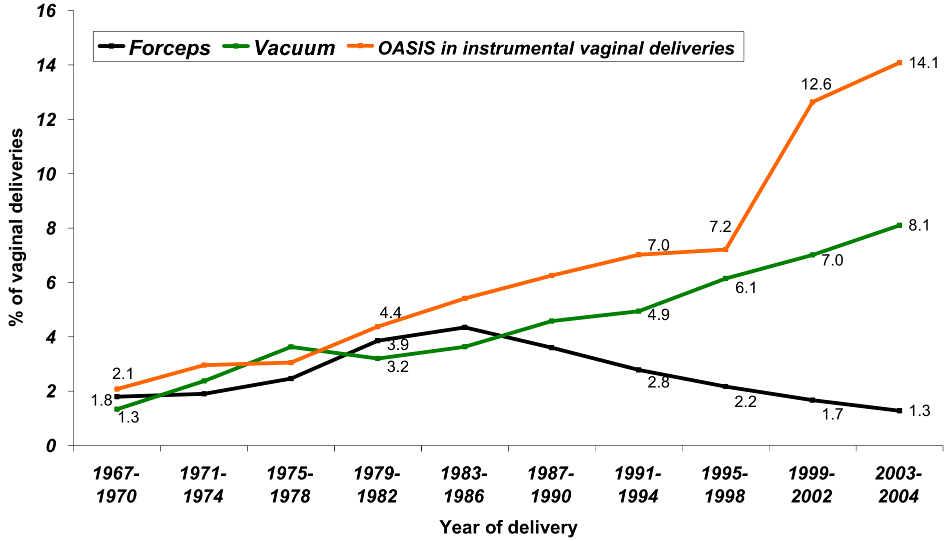

Figure 9. Trends in use of forceps, vacuum and the occurrence of obstetric anal sphincter injuries (OASIS) in instrumental deliveries by year of delivery, 1967-2004, Norway

In paper II, we studied changes in demographic and obstetric risk factors during 1967-2004 (Table 1, paper II). Except a little decrease during 1970s, the total numbers of births in Norway were stable in the study period (Figure 10). The proportion of women of birth order 1 over 30 years of age increased by 25%. Caesarean deliveries increased from 2% to 15%. The proportion of infants weighing 4,000 g or more increased by 5%. Instrumental deliveries increased from 3.2% to 9.5%, but an increase was only observed in vacuum deliveries. Forceps deliveries, however, decreased in the same period (Figure 9). The proportion of African and Asian mothers in Norway increased by 30%. However, after adjustments for these factors, the trend in OASIS persisted, although it was reduced significantly. Therefore, our results indicate that only some of the increase may be caused by these changes.

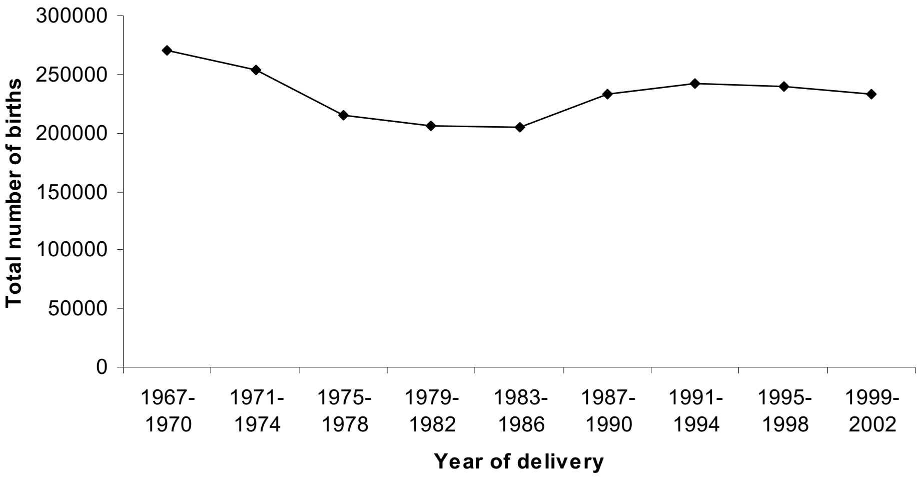

Figure 10. The total numbers of births in Norway, 1967-2002

Further, the 'hands off' practice promoted from the 1960s and 1970s [130] may have contributed to the increased occurrence of OASIS. One might also speculate that the concomitant shift in Norway from delivery unit- to university college-based midwife training may have changed the management of the second stage of labour. Such information was not recorded in the MBRN.

Finally, improved registration and diagnosis routines may have contributed to false increase in the reported number of OASIS. However, the increased occurrence seems at least to some extent to be true and may result from changes in obstetric routines not accounted for in the present study.

8.2.3 Risk factors for OASIS

In paper II, we investigated risk factors for OASIS.

As in previous reports,[60,62,64,66,67] our study suggested that birth order 1 is a dominant risk factor for OASIS. Whereas previous vaginal delivery reduces the risk of OASIS, our results indicated that regardless of previous vaginal delivery, previous caesarean delivery increases the risk. In separate analyses (not shown) we found that women with previous caesarean delivery were delivered more frequently instrumentally in the subsequent vaginal delivery. Thus, the excess risk of OASIS might be caused by instrumental vaginal delivery. We therefore stratified our results for instrumental delivery and found no significant excess risk associated with previous caesarean delivery in instrumental deliveries although the effect of previous caesarean was still significant in non-instrumental deliveries (Table 3, paper II). This observation may be explained by the effect of the instrumental delivery or the effect of the indication for the previous caesarean delivery. The risk of OASIS in vaginal births subsequent to caesarean delivery has been studied before,[60,66,67] but only one of these studies[60] compared women with previous vaginal delivery with and without earlier caesarean delivery as well. Consistent with the present study, Handa et al. and Richter et al.[60,67] reported higher risk estimates of OASIS in women who had had a previous caesarean delivery. However, Lowder et al.[66] reported no excess risk of OASIS in women with a previous caesarean, possibly because they adjusted for the effects of instrumental delivery. The excess risk after a previous caesarean delivery might be attributed to the indication for the caesarean delivery which may persist in the next pregnancy. The lower risk of OASIS in multipara probably relates to perineum being stretched in previous vaginal delivery and our results indicate that pregnancy per se does not cause such an effect.

The association between maternal age and risk of OASIS has been suggested before, but not consistently.[51,56,62,127] In our study, regardless of birth order, the risk for OASIS increased with maternal age until 30 years (Figure 3, paper II). In birth order 3 or more the increase continued above the age of 30. A possible explanation could be the loss of elasticity of the perineal tissue in older women.

In agreement with other studies,[51,56,58,64,127] the risk of OASIS was fourfold higher in forceps deliveries and twofold in vacuum deliveries compared with non-instrumental deliveries. The higher risk in forceps than in vacuum deliveries persisted after adjusting for possible confounders like year of delivery, maternal age and vaginal birth order. Vacuum is generally thought to be less traumatic to the perineum than forceps.[131] Both vacuum and forceps deliveries are complex procedures and require experience and knowledge with birth attendants performing those. We can not then, rule out the possibility that the more frequent use of vacuum has contributed to developing better technique and more skilled birth attendants and consequently less birth trauma in vacuum deliveries compared with forceps deliveries. Additionally, because forceps is less likely to fail achieving a vaginal birth,[131] it might contribute to the higher risk of OASIS in two ways; 1) forceps is selected in more complicated vaginal deliveries such as occiput posterior 2) forceps is more likely to be performed successfully and not being converted to an emergency caesarean delivery.

Midline episiotomy has been associated with OASIS,[82,127,132] but the association with mediolateral episiotomy, as generally used in Norway, is less consistent.[56,57,62,72,85] In paper II, we noted an overall increased risk of OASIS associated with episiotomy. However, our results suggest that episiotomy in birth order 1 with non-instrumental delivery had no effect on OASIS, but had a 'protective' effect in instrumental deliveries. Consistent with our study, several studies have reported a 'protective' effect of mediolateral episiotomy in instrumental vaginal delivery.[72,132,133] Additionally, because of lack of data on the recognised individual variation in the angle and size of mediolateral episiotomy,[57,85,134] our results are not conclusive.

In our study, African and Asian mothers in Norway had a higher risk of OASIS as compared with European women. Our finding that Asian women have a higher risk is supported by other studies.[51,60,66,67,132] Consistent with our study, Ekeus et al.[51] have found a higher risk of OASIS in African mothers in Sweden. However, other studies,[60,68,69] mainly from USA have found lower risk of OASIS in African women. These contradictories might be due to differences in the origins of African women in Scandinavian countries and USA. African women in our study population were mainly from Somalia, Eritrea and Ethiopia where 80% of women have been infibulated.[135] This might account for the higher risk of OASIS. One may speculate that the higher risk in African and Asian women is also caused by difficult communication with the birth attendants.

We found almost a twofold risk for OASIS in maternity units with 3,000 or more births per year as compared to hospitals with 1,000–1,999 births per year. Larger maternity units in Norway are referral hospitals; they treat more complicated patients and have higher rates of instrumental deliveries. Hence, we adjusted the effect of size of maternity unit for instrumental delivery, but the results remained. Consistent with our results, a Norwegian study[42] found significant differences in the occurrence of OASIS in non instrumental deliveries between 5 hospitals and speculated that the differences could be caused by different perineal protection handling techniques. A recent Finnish population-based study[136] found up to seven-fold inter-hospital differences in the rates of OASIS and concluded that this is due to the differences in Finnish obstetric care including the rate of episiotomy. In this study, we found no major differences in episiotomy rate between maternity units during 1999 to 2004. With the exception of maternity units with less than 50 deliveries per year, which had an episiotomy rate of 11%, the rate ranged from 18.6% to 22.8% (data not shown).

Risk of OASIS in breech delivery is presented in this thesis in supplementary results section. We found a decreased risk of OASIS in breech assisted delivery without use of forceps, compared with non-instrumental vertex vaginal deliveries, but the risk was increased in breech assisted deliveries with forceps to after-coming head. However, compared to risk of OASIS in forceps deliveries with cephalic presentation, the risk of OASIS in breech deliveries with forceps to after-coming head was low. Not many studies of OASIS include breech deliveries,[51,137] and we are not aware of any study distinguishing between breech assisted deliveries with and without forceps to after-coming head.

8.2.4 The recurrence of OASIS

We investigated the recurrence risk of OASIS in second and third deliveries in paper III. Women who had OASIS in the first delivery had about fourfold excess risk of OASIS in the second delivery with an absolute risk of 5.6% (Figure 6). If women with OASIS in first delivery had a second delivery without OASIS, they still had increased risk of OASIS in third delivery, although with a lower absolute risk (3.1%, Figure 6). The risk in women who had OASIS in the two first deliveries was particularly high (absolute risk 9.5%, Figure 6). Women with OASIS in the second delivery, but not in the first, were nine times more likely to have OASIS in the third delivery, and also with high absolute risks (7%, Figure 6). The last finding was not expected and justifies attention to recurrence of OASIS after a second delivery.

The risk of OASIS decreases with vaginal birth order and OASIS is uncommon in second and third delivery. In our population 1.1% and 0.7% of women sustained OASIS in second and third delivery, respectively and the majority of women sustaining OASIS in second and third delivery did not have a previous OASIS. However, a history of OASIS increased the risk and as much as 10% of all cases of OASIS in the second and 15% of cases of OASIS in third delivery were attributable to a history of OASIS.

To my knowledge, ten studies have previously reported on the recurrence risk of OASIS[44,66,86-93] with conflicting results. Eight of these studies[44,66,87,89-93] have reported increased recurrence risk of OASIS in second delivery, the other two studies[86,88] found no increased risk of OASIS in women with prior OASIS. The last two studies included women with OASIS in birth order 1 in the reference group, and thus probably underestimated relative risks due to the higher risk of OASIS in the first deliveries, concluding that prior OASIS does not increase the recurrence and that the increased recurrence risk found in previous studies could be caused by bias.

We are unaware of any other studies reporting on the recurrence risk of OASIS in the third delivery.

8.2.5 Risk factors for the recurrence of OASIS

In paper III, we assessed the risk factors for the recurrence risk of OASIS in the second delivery. Consistent with another study based on the MBRN,[92] birth weight more than 3,500 g was strongly associated with recurrence of OASIS. Compared to mothers giving birth to infants weighing 3,000-3,499 g, mothers delivering an infant with birth weight of 5,000 g or more had sevenfold increased risk of the recurrence of OASIS with an absolute risk of 28.2%. This indicates that for women with a history of OASIS and high estimated foetal weight, planned caesarean delivery must be considered.[92] However, neither clinical examination using fundal height measurements nor third trimester ultrasound examinations are effective at detecting heavy infants.[138] In our study, women with OASIS in first delivery who gave birth to an infant weighing 4,000 g or more had an excess risk of giving birth to a heavy infant in second delivery (adjusted OR 3.6, 95% CI 2.6-5.2, data not shown). This may help clinicians when they counsel and inform women with previous OASIS.

Consistent with previous studies,[86,88] instrumental delivery, and particularly forceps delivery, was strongly associated with recurrence of OASIS. Vacuum delivery only marginally increased the excess recurrence risk. Therefore, vacuum is likely a better choice than forceps when women with prior OASIS are delivered instrumentally, unless the operator is skilled in forceps delivery.

Although instrumental delivery was strongly associated with recurrence of OASIS, it did not further increase the excess recurrence risk in heavy newborns, likely because the effect of high birth weight is superior to the effect of instrumental delivery. This may be useful information in the clinical decision whether an instrumental delivery of a large infant should be performed in a woman with a history of OASIS.

We found no association of either maternal age or inter-delivery interval with recurrence of OASIS. Our results provide reassurance that recurrence risk in older women is not substantially different from that in younger and that the time to the next pregnancy does not seem to influence recurrence.

The recurrence risk of OASIS was higher in maternity units with 3000 deliveries or more per year. After adjusting for instrumental delivery, which is more common in referral hospitals, the higher risk persisted. However, it cannot be ruled out that the excess risk was due to better registration, diagnostic skills or referral of more complicated pregnancies to larger maternity units.

8.2.6 Do men contribute to the risk of OASIS in their partners?

Most risk factors for OASIS relate to the mother and little is known about a potential paternal influence on OASIS. Paternal genes increasing birth weight and head circumference[97,139] can be passed to the foetus from the father and increase the mother's risk of OASIS. We explored the paternal contribution to the risk of OASIS in papers III and IV.

To achieve a true paternal effect any maternal influence must be avoided. Therefore, in paper III, we selected men who fathered births in different women. We found that a man who fathered a birth with OASIS in one woman was more likely to father a subsequent birth with OASIS in another. We had earlier reported an association between risk of OASIS and the size of maternity unit. Some men who shift partners will possibly move to other parts of the country and, fathering a child at a different maternity unit with a different risk of OASIS. We stratified the results for the change of maternity unit (Table 4). The excess recurrence rate was not present if deliveries took place in different maternity units. However, it would be more appropriate to compare births at the same maternity unit, since the obstetric routines and the routines for registration and diagnostic of OASIS would be equal. We are not aware of any other potential paternal factors than birth weight or head circumference that might influence the risk of OASIS, but adjustment for birth weight and head circumference did not alter the results.

The paternal effect was further studied in paper IV which is discussed later in this section.

8.2.7 Obstetric history after OASIS

In paper III, we investigated whether a history of OASIS would deter a woman from having a subsequent pregnancy or a vaginal delivery. We found no difference in the adjusted subsequent delivery rate in women with and without previous OASIS, whereas women with previous OASIS were more often scheduled to caesarean delivery.

Studies on the quality of life after OASIS, concentrating on anal incontinence as an indicator of life-quality, have reported conflicting results.[35,93,140,141] However, subsequent fertility and mode of subsequent deliveries have not been emphasised. One study based on the Medical Birth registry in Sweden[89] reported reduced crude likelihood of having a second delivery after OASIS (OR 0.68, 95% CI 0.67–0.70). A recent case-control study[93] investigated the subsequent delivery rate in 136 Swedish primiparous women 3-8 years after OASIS. They found that compared to groups of women with caesarean and vaginal delivery without OASIS, significantly more women with OASIS expressed a wish to postpone (33%) or avoid (18%) a subsequent delivery. However, consistent with our results, there was no difference regarding the subsequent delivery rate (60%) in case and control groups and, consistent with our results, women with previous OASIS had often later caesarean delivery.

Previous studies have suggested that having an overall negative birth experience, being single, maternal age over 35,[142] instrumental vaginal delivery, caesarean delivery or perinatal mortality[120,143] influence women's future reproductive behaviour. Those variables might then be potential confounders in our study. To avoid confounding effects, we excluded cases of caesarean deliveries previous to the current delivery and adjusted the results for maternal age, marital status, maternal education level, infant death within one year, instrumental vaginal delivery and year of delivery.

Whether women with a history of OASIS considered avoiding or postponing a subsequent delivery was not possible to investigate in our study. However, previous OASIS did not influence the women's decision to expand their family. The indication of planned caesarean delivery was not registered in MBRN, but it is possible that to some extent, the assurance of a caesarean delivery reduced these women's hesitation of having a subsequent delivery. On the other hand, the excess rate of planned caesarean delivery in women with a history of OASIS, which has been reported to be associated with increased risk of severe maternal and neonatal morbidity and mortality,[144,145] may have influenced the quality of life in women with a previous OASIS.

8.2.8 The aggregation of OASIS in families

We assessed the familial risk of OASIS in paper IV. We found that the risk of OASIS was twofold if the woman's mother or sister had sustained OASIS in a delivery. The increased risk in daughters and sisters was regardless of birth order. The excess risk of OASIS in sisters was observed if their mother's deliveries were not complicated by OASIS. We found a moderately increased risk of OASIS in partners of men who were born in a delivery complicated by OASIS. The risk from in a brother's partner was also increased, but less so, whereas the risk in a brother's sister was not or only marginally increased.

We are unaware of other studies on the risk of OASIS in relatives. Still, several studies have suggested a genetic basis for the development of female pelvic floor disorders (genital prolapse, urinary and faecal incontinence).[103-106] There is also evidence that OASIS is strongly associated with pelvic floor disorders.[146] Van Dongen[147] observed that genital prolapse was much more uncommon in black women compared to white women, suggesting inherent superior quality of connective tissue in black women. Howard et al.[148] found lower genital laceration rate including OASIS in black women. Handa et al.[149] compared bony pelvis and soft tissue structure of African-American and white women by dynamic magnetic resonance imaging (MRI) in 234 primiparous women. They observed greater laxity of pelvic floor and tissue elasticity in African-American women which could be inherited. Magdi[2] suggested that an "elastic index", measured by the extent of abdominal striae, was predictive of perineal laceration. Our study supports a hypothesis that genetic factors might influence the risk of OASIS.

If OASIS is associated with genetically determined tissue elasticity, an excess risk of OASIS may be inherited through maternal susceptibility genes for OASIS. Evidence suggests that OASIS is caused by an interaction between the woman and her foetus. Thus, factors related to the foetus might also be relevant. Consequently, paternal alleles in the foetus might increase the woman's risk of OASIS. A higher risk related to daughters than sons may also be due to the possible contribution of mitochondrial gene susceptibility, which is exclusively transmitted through the maternal line.[107]

Birth weight and head circumference could be influenced by paternal genes and increase the risk of OASIS.[97,139] However, such effects are likely negligible because adjusting for birth weight or head circumference had no effect.

Additionally, environmental factors such as nutritional-, lifestyle- or other environmental factors shared by generations or siblings might explain the observed risk pattern. However, factors such as level of education, smoking and marital status have previously been studied without showing any association with OASIS. BMI has been studied as well without showing a consistent association with OASIS.[51,60,70,71] Even though, a recent Norwegian study has shown increased risk of OASIS in women with low physical activity.[71]

Thus, the similar risk pattern observed between generations and siblings supports a role for genetic susceptibility in OASIS. If the risk pattern were exclusively explained by environmental factors, one would expect higher rates in sisters than in daughters whose births were more spaced in time.

The weaker and inconsistent risk transmitted through the fathers is consistent with the results in paper III.

9. Conclusions and implications

In paper I we found a high validity of the registration of OASIS in MBRN already in 1990-92 and particularly in 2000-02. The validity of the registration of OASIS was low in the PAS database in 1990-92 with a great improvement in 2000-02. The observed validity in MBRN justifies epidemiological studies of OASIS based on data from MBRN.

In paper II, we observed a considerably increase in the occurrence of OASIS in Norway in 1967-2004. Additionally, we explored a number of maternal, obstetric and foetal risk factors for OASIS. The reported increase in the occurrence of OASIS was only partially accounted for by temporal changes in the observed risk factors.

Most of observed risk factors such as birth order 1, high maternal age and diabetes were non-modifiable and women with such risk factors should be paid more attention at delivery for minimising their risk of OASIS. Instrumental delivery was however a dominant risk factor with greatest modifiable potential. Still, the majority of OASIS cases occurred in non-instrumental vaginal deliveries (71,6%). Therefore, training in both instrumental and non-instrumental deliveries with focus on reducing the speed of the birth, support of perineum and axis of birth canal should be an essential part of the national and local training programme for birth attendants.

In paper III, we explored the obstetric history of women after OASIS. We found a high relative and absolute risk of the recurrence of OASIS in second and third deliveries. As expected, women with OASIS in both first and second deliveries had the highest risk of OASIS. Recurrence of OASIS was strongly associated with forceps delivery and birth weight 3,500 g or more in the subsequent delivery. The occurrence of OASIS was generally low in second and third birth, but 10% and 15% of all cases of OASIS in respectively second and third deliveries were attributable to a history of OASIS. A history of OASIS had no impact on subsequent delivery rate. However, women with previous OASIS more frequently had planned caesarean delivery.

Firstly, these findings suggest that clinicians apparently should focus on preventing OASIS in the first delivery. Secondly, women with a history of OASIS should be counselled before or during next pregnancy for planning the mode of delivery. Thirdly, if a vaginal instrumental delivery is imminent, vacuum is likely a better choice than forceps, unless the operator is skilled in the use of forceps.

We additionally found that a man who fathered a child whose delivery was complicated by OASIS in one woman was more likely to father another child with OASIS complicated delivery in another woman, if the mothers delivered at the same maternity unit. The potential genetic paternal effect was further explored in paper IV.

In paper IV, we assessed the aggregation of OASIS from a mother to her daughter and to her son's partner and between siblings when they became parents. There appear to be increased familial aggregation of OASIS. These risks are stronger through a maternal than a paternal line of transmission, suggesting a strong genetic role that shapes aggregation of OASIS within families. These observations must be cautiously interpreted since bias due to unmeasured confounding may have impacted the findings.

Genetic susceptibility, along with other risk factors of OASIS, could help clinicians identifying women at risk and preventing OASIS in vaginal deliveries.

10. Suggestions for future research

The present studies leave of course several unanswered questions that should be addressed in future research. I hope that our research can contribute to and stimulate such research. Some of these issues are listed in the following:

1) Are differences in the occurrence of OASIS geographically or over time due to different diagnostic routines or criteria for diagnosis? Could this variation explain the observed excess risk of OASIS in bigger maternity units?

2) The Norwegian multicentre interventional study has already shown that by replacing forceps with vacuum extraction and focusing on manual support of perineum near the end of the second stage of labour, the occurrence of OASIS was reduced significantly. Could intensive training in forceps deliveries reduce the excess risk of OASIS in forceps deliveries?

3) Several studies have shown that compared with white women, African women have lower risk of OASIS. Still, African women giving birth in Norway and Sweden have excess risk of OASIS. Is this due to properties related to African mothers in Norway or to the management of their birth?

4) What is the risk of urinary- and anal incontinence in women with OASIS? This question could be studied by linking data from MBRN to the Norwegian mother and child cohort study (MoBa) or HUNT.

5) Do women with inherited risk of OASIS have higher risk of developing pelvic floor disorders? This question could be answered by linking data from MBRN to PAS or Norwegian county health survey (HUNT).

6) Does the composition of connective tissue differ in women with and without OASIS?

7) Is the increased recurrence rate between relatives influenced by shared environmental factors?

8) In our studies, the paternal contribution to OASIS in their partner could not be explained by paternal influence on birth weight or head circumference. Are there other genetic or environmental factors contributing to the paternal effect?

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