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PREVENTION OF STRIAE GRAVIDARUM

A thesis submitted to the College of Medicine, Nursing and Health Sciences,
National University of Ireland Galway, in fulfilment of the requirements for the
degree of Doctor of Philosophy

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Declaration

I, Miriam Brennan declare that this work is submitted to fulfil the requirement of the degree of Doctor of Philosophy, at the National University of Ireland Galway. I have not obtained a degree in the National University of Ireland Galway, or elsewhere, on the basis of the work detailed in this thesis. I am the author of this thesis and the principal author of the four included papers. Contributions by others are included under 'Contributions to Research'.

Signature: 

Date: December 2019

Abstract

Introduction

Striae gravidarum, or stretch marks, are a common physiological skin change occurring during pregnancy. They improve postpartum, but do not disappear fully. While their cause remains unclear, many associated risk factors have been identified. In addition to their physical effect, they are known to cause other symptoms and to affect women psychologically. They are seen commonly as an aesthetic or cosmetic issue and by some as disfiguring, and can be distressing for women. Further, there is a growing body of evidence of their effects on women's quality of life. Many women apply one or more of the many topical products available to their skin in efforts to prevent striae gravidarum, but many of these products have not been evaluated and there is a dearth of high-quality evidence of effectiveness on any of the topical products used by women.

The thesis aims are:

1. to systematically review the evidence of the effectiveness of topical preparations in the prevention and reduction in severity of striae gravidarum;
2. to survey women on their use of skin products to prevent or reduce the development of striae gravidarum, and
3. to undertake a pilot randomised trial to evaluate the feasibility of conducting a large trial on the effectiveness of a moisturising oil (commercially available) compared to no treatment for the prevention and reduction in severity of striae gravidarum.

Methods

This thesis includes four papers. A Cochrane systematic review and meta-analysis was undertaken to evaluate the evidence for the effectiveness of topical preparations in the prevention and reduction of striae gravidarum (Question 1, Chapter 2). This was followed by a cross-sectional descriptive survey, which identified the topical products commonly used (Question 2, Chapter 3). The protocol for the pilot randomised trial to evaluate the feasibility of conducting a large trial on the effectiveness of a moisturising oil compared to no treatment (Question 3, Chapter 4) followed. It was informed by the findings of the survey and the literature. However, despite amendments to the protocol and a

collaborative effort to recruit women, recruitment was difficult. This prompted exploration of the factors influencing recruitment to the trial (Question 4, Chapter 5).

Results

The Cochrane systematic review and meta-analysis found that there was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment, and that there was no statistically significant average mean difference in the severity of stretch marks. Similarly, there was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients and there was no statistically significant difference in the severity of stretch marks. The review concluded that there is a clear need for robust, methodologically rigorous randomised trials involving larger sample sizes to evaluate the effects of topical preparations on the development of stretch marks in pregnancy.

In the cross-sectional descriptive survey, most respondents (n = 589, 78.2%) indicated that they used a product to prevent or reduce the development of stretch marks during their current pregnancy. A large range of products was used, and more than one-third of women (n = 210, 36.5%) had used two or more products. Furthermore, a majority of women, 68.3% (n = 514), indicated that they would consider participating in a future trial of a product to prevent or reduce stretch marks in pregnancy.

The pilot trial experienced significant challenges with recruitment and therefore no summative evaluation was possible. From participants' response to the pilot trial which was investigated in the qualitative study, it is not possible to conduct a definitive randomised controlled trial to evaluate the effectiveness of a moisturising oil (commercially available) compared to no treatment. The qualitative descriptive study found that striae gravidarum prevention is important to women; many knew what product they were going to use, had purchased it

and in some cases had started using it. In relation to influences on trial participation, the possibility of being randomised to the non-intervention or control group was a deterrent for many women.

Conclusion

Striae gravidarum prevention is important to women, and many make their product choice out of the healthcare setting, influenced by friends and family. Although this thesis identified the need for robust, methodologically rigorous randomised trials involving larger sample sizes to evaluate the effects of topical preparations, the pilot trial identified challenges with undertaking such a study, while the qualitative study highlighted issues that must be overcome before embarking on this course of research.

List of Publications from the Thesis

Published Papers

Brennan, M., Young, G. & Devane, D. (2012) Topical preparations for preventing stretch marks in pregnancy. *Cochrane Database of Systematic Reviews*, Issue 11. Art. No.: CD000066.

DOI: [10.1002/14651858.CD000066.pub2](https://doi.org/10.1002/14651858.CD000066.pub2).

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD000066.pub2/full>.

Brennan, M., Clarke, M. & Devane, D. (2016) The use of anti stretch marks' products by women in pregnancy: A descriptive, cross-sectional survey. *BMC Pregnancy and Childbirth*, **16**(1), 276. <https://doi.org/10.1186/s12884-016-1075-9>.

Brennan, M., Clarke, M., Newell, J. & Devane, D. (2018) Prevention of striae gravidarum: study protocol for a pilot randomised controlled trial. *Trials*, **19**(1), 553. <https://doi.org/10.1186/s13063-018-2898-7>.

Under Review

Brennan, M., Clarke, M., Devane, D. & Dowling, M. A qualitative study of the factors influencing recruitment to a pilot trial on the prevention of striae gravidarum. Submitted to *BMC Pregnancy and Childbirth*.

Contributions to Research

This thesis consists of four papers, three of which have been published and a fourth one which has been submitted for publication and is under review. The first paper presented in chapter 2 is a Cochrane Systematic Review. I led this review. The study design followed the design guidelines from the Cochrane Handbook (Higgins & Green, 2011). Literature searching was undertaken by the Trials search co-ordinator. Reference lists of all the identified studies were checked by all authors and led by Miriam Brennan (MB); one extra study was retrieved. Literature selection was done by MB and agreed by Declan Devane (DD) and Gavin Young (GY). Quality appraisal of the literature was undertaken by MB, DD & GY. All data was extracted independently by MB and checked by DD and GY. Analysis and interpretation was by MB, DD & GY. MB drafted the manuscript. All data was entered into the Review Manager Software (RevMan2011) by MB and checked for accuracy by MB, DD and GY. MB led on the reviewers' feedback and final review was approved by all authors (MB, DD & GY).

The second paper presented in chapter 3 is a descriptive, cross-sectional survey. I led this study. The study design was conceived by MB, DD & Mike Clarke (MC). Literature searching to inform the study was done by MB. The data collection questionnaire was developed by MB. Feedback at the different stages of development were given by DD. Testing of the questionnaire for content validity was led by MB and supported by DD. MB developed and prepared the study information pack (letter of invite, participant information sheet). The applications for ethical approval to the Clinical Research Ethics Committee for Galway University Hospitals and the Research Ethics Committee of the National University of Ireland were prepared by MB and approved by DD. The requests for further information or changes to the ethics' applications were attended to by MB and approved by DD. Extensions to the data collection period were attended to by MB with DD's support. MB was responsible for data collection and assisted with it. MB did the data entry in SPSS and undertook the descriptive analysis. Inferential statistical analysis was supported by Davood Roshan (DR). The manuscript was prepared by MB and MC and DD reviewed the manuscript at each stage, editing sections accordingly. All authors (MB, DD and MC) approved

the final version of the manuscript. MB submitted the manuscript and MB attended to the requests by the reviewers, for amendments and additional analysis with the support of DD.

The third paper is a protocol for a pilot randomised controlled trial and is presented in chapter 5. I led this study. MB, DD and MC conceptualised and designed the study. MB undertook the associated literature searching and review. MB prepared the study protocol and was supported by DD, MC and John Newell (JN). MB prepared the intervention product and all of the data collection and case report forms under the supervision of DD. MB developed and prepared the study information pack (letter of invite, participant information leaflet). The application for ethical approval to the Clinical Research Ethics Committee for Galway University Hospitals was prepared by MB and approved by DD. The request for further information from the ethics committee was attended to by MB and supported by DD. Extensions to the data collection period were attended to by MB with DD's support. MB was responsible for participant recruitment, over the data collection period. MB led on meetings and contacting key personnel to advise how recruitment could be improved. MB was supported by DD and MC in trying to address the recruitment challenges. MB drafted the manuscript under the supervision of DD. JN advised and supported the writing of the statistical analysis section. DD and MC reviewed and revised the final manuscript. MB revised the manuscript following feedback from DD, MC and JN. All authors (MB, DD, MC and JN) approved the final version of the manuscript. MB submitted the manuscript to the journal. MB attended to the reviewers' requests for clarification and amendments, with the support of DD.

The fourth paper is a qualitative study of the factors influencing recruitment to the pilot trial on the prevention of striae gravidarum and is presented in chapter 5. I led this study. MB, DD and MC conceptualised the study. MB undertook the associated literature searching and review. MB led on the development of the interview guide and all authors (MB, MC, DD and Maura Dowling (MD)) contributed to its development. MB developed and prepared the study information pack (letter of invite, participant information sheet) and the consent form with the support of DD. The application for ethical approval to the Clinical

Research Ethics Committee for Galway University Hospitals was undertaken by MB under the supervision of DD. Participant recruitment, follow up and data collection was undertaken by MB. Data analysis was undertaken by MB under the supervision of MD. MB prepared the initial manuscript draft and MD, DD and MC reviewed and contributed to subsequent drafts. MB submitted the manuscript to the journal. All the authors (MB, MC, DD and MD) saw and approved the final version of this article. MB will attend to reviewer requests for amendments as needed, with the support of DD.

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I wish to extend my appreciation to the members of my Graduate Research Committee (GRC) Professor Declan Devane, Professor Mike Clarke, Professor Kathy Murphy and Professor Dympna Casey who supported, advised and guided me at my annual reviews.

For their roles and contribution to the Cochrane systemic review, I would like to thank Professor Declan Devane and Dr Gavin Young. I would also like to re acknowledge my appreciation to the different people who helped with the review and who are identified and acknowledged in Chapter 2, paper 1. They include those who helped with the translations of non-English language papers for the review, an author of the original version of the review and those who reviewed and commented on the review.

My sincere gratitude to all those who helped and supported me and who contributed to the three other studies and who are acknowledged in each of the papers. They include Professor Mike Clarke and Professor Declan Devane, both who assisted me with the three other papers (survey, pilot trial and qualitative study), Professor John Newell who helped me with the pilot trial (paper 3) and Dr Maura Dowling who supported me during the qualitative study (paper 4). All gave generously of their time and offered helpful and encouraging support at the different stages, for which I am very appreciative. I am very grateful to the women who helped me at the different stages of this thesis as without them it would not have been possible. They include those that helped with the development and testing of the survey questionnaire, those who participated in the survey and those who did the qualitative interviews. I also wish to include the maternity advocacy groups who helped me with the on-line survey (paper 2)

and the midwifery students who helped me with data collection for the survey (paper 2). Others include the midwifery and administrative staff at the Antenatal Clinic, the staff at the Ultrasound Department and the midwifery managers in the Maternity Unit of Galway University Hospital.

I wish to extend my appreciation to my colleagues in the School of Nursing & Midwifery at the National University of Ireland Galway and my clinical colleagues in Galway University Hospital who supported me and offered words of encouragement at the different stages of this PhD journey. They include the Heads of School, midwifery and nursing lecturers, research staff, administrative staff, clinical placement coordinators, practice development officers, who were all helpful at the different stages of this journey. I am very grateful for the help which was always forthcoming when sought out or indeed volunteered in many cases.

To my family I wish to say a big thank you.

Finally thank you Fred. I really appreciated the continuous support, encouragement and motivating words. You helped me in so many ways and made completion of this PhD possible.

Dedication

I would like to dedicate this thesis to my parents John and Carmel.

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Funding was awarded through a number of scholarships from the School of Nursing and Midwifery, National University of Ireland Galway, towards the costs associated with this thesis.

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List of Abbreviations

AIMS Ireland	Association for Improvements in the Maternity Services-Ireland
BMI	Body mass index
CENTRAL	Cochrane Central Register of Controlled Trials
CI	Confidence interval
HPRA	Health Products Regulatory Authority
HRQoL	Health related quality of life
ICC	Intracluster correlation co-efficient
ISRCTN	International Standard Registered Clinical/social sTudy Number
MD	Mean difference
RR	Risk ratio
SMD	Standardised mean difference
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
SPSS	Statistical Package for the Social Sciences
Tau²	tau-squared
TSC	Trial Steering Committee
WHO	World Health Organization
WMA	World Medical Association
X²	Chi ² / Chi-square test

Chapter 1: Introduction

This chapter provides an introduction and background to the thesis on the prevention of striae gravidarum, with explanation of the research questions, relevant literature and methodology, concluding with an outline of the thesis structure.

1.1 Overview of striae

Pregnancy is associated with many changes to the skin (Cunningham *et al.*, 2014; Murray, 1990) in association with the endocrine, metabolic and immunologic (Muzaffar *et al.*, 1998), mechanical and blood-flow changes (Papoutsis & Kroumpouzou, 2007) occurring during pregnancy. Striae gravidarum, or stretch marks, are a common physiological change to the skin during pregnancy (Muzaffar *et al.*, 1998). They are classified as benign skin changes (Ikram *et al.*, 2018) and are the most common connective tissue change in pregnancy (Lawley & Yancey, 1999), affecting up to 90% of women (Vaughan Jones, 2007). However, prevalence can range between 50% and 90% (Chang *et al.*, 2004).

Striae gravidarum develop commonly in the second half of pregnancy (Buchanan *et al.*, 2010; Cunningham *et al.*, 2014), most commonly by the sixth and seventh month (Wong & Ellis, 1984), though they can occur as early as the first trimester (Chang *et al.*, 2004). They appear as '*reddish slightly depressed streaks*' (Cunningham *et al.*, 2014:51), which, in the multigravid woman, will co-exist with the '*glistening, silvery lines*' that testify to previous striae occurrence (Cunningham *et al.*, 2014:51). Although they exhibit marked improvement (Murray, 1990) as they '*fade postpartum*' (Atwal *et al.*, 2006:965) and are less evident (Winton & Lewis, 1982), they do not disappear fully (Atwal *et al.*, 2006; Murray, 1990; Vaughan Jones, 2007; Young & Jewell, 1996).

Striae gravidarum are found most frequently on the abdomen but can occur on the thighs and breasts (Cunningham *et al.*, 2014) and, while usually symptomless (Papoutsis & Kroumpouzou, 2007), they can be associated with pruritus (Lerdpienpitayakul *et al.*, 2009; Muzaffar *et al.*, 1998), which can be mild to moderate (Papoutsis & Kroumpouzou, 2007) or indeed profound in the

presence of severe striae (Chang *et al.*, 2004). A burning sensation is also reported (Lerdpienpitayakul *et al.*, 2009).

1.2 Aetiology and risk factors for striae

Described as a '*mystery*' by Zheng *et al.*, in 1985, the cause of striae gravidarum remains unclear (Atwal *et al.*, 2006; Errickson & Matus, 1994; Kasielska-Trojan *et al.*, 2015; Lawley & Yancey, 1999; Murray, 1990). Some attribute them to the '*hormonal milieu*' primarily (Winton & Lewis, 1982) while others say that the hormones create a '*unique milieu*' for their development (Chang *et al.*, 2004:882). At a microscopic level, research has focused on changes in the dermal elements, and striae may be related to the effects of stretching or tension on the dermal extracellular matrix involving the elastin and collagen elements. According to Shuster (1979:161), they are always associated with stretching and occur in skin where '*the connective tissue is partially mature with a critical titre of rigid cross-linked collagen and "elastic" unlinked collagen*'. Others report that there may also be changes in the elastin network important in skin elasticity, as a result of persistent strain on the dermal tissue, and this may be related to a deficiency in cutaneous fibrillin (Watson *et al.*, 1998). Even moderate strain may be enough to damage the elastic fibre network (Watson *et al.*, 1998). More recent research suggests that there may be '*ineffective repair of collagen disrupted by intense skin stretching*' (Wang *et al.*, 2018:749).

While the cause remains unclear, many risk factors have been found to be associated with striae, albeit inconsistently (Atwal *et al.*, 2006; Kasielska-Trojan *et al.*, 2015). For example, maternal age, maternal body mass index, maternal weight gain, and neonatal weight were found to be independently and significantly associated with striae by Atwal *et al.* (2006) in their large observational study (n=309) involving white primiparous women in the UK. In relation to maternal age, where the most significant association was found ($p < 0001$), striae were more common in younger women (< 20 years) compared to older women, which they relate to possible increased fibrillin fragility. Furthermore, young maternal age, increasing maternal weight gain and increasing birth weight in the baby were also associated with severe striae. In a seminal study undertaken in the US using 'self-reported survey data', Chang *et*

al. (2004:884) found that a personal history of striae, family history and race were significantly indicative of the development of striae gravidarum, and more so than weight gain or changes in BMI during pregnancy. They highlight how their findings contradict earlier findings (Davey, 1972; Poidevin, 1959) while also identifying study limitations such as the self-reported data and recall errors. Similarly, in a later Turkish study, Durmazlar & Eskioğlu (2009) report how family history, maternal weight gain and maternal age were associated significantly with the presence and severity of striae; however, neither personal history nor infant weight was significantly associated with striae. In keeping with Atwal *et al.* (2006), the baby's weight, height and head circumference were also identified by Ghasemi *et al.* (2007) as being significantly associated with striae gravidarum.

More recently, lower maternal age, higher preconception BMI, family history, birthing a male infant and a lower educational level were significantly predictive of striae development in Turkish primiparous women (n=211) participating in an observational study considered by the authors as the largest of its type (Ersoy *et al.*, 2016). Kasielska-Trojan *et al.* (2015) found that family history of striae gravidarum, lack of a chronic disease, BMI before pregnancy and birth weight were all independent predictors for striae gravidarum in their study involving postnatal primiparous and multiparous women. Furthermore, women who had a history of breast striae were at increased risk of developing striae gravidarum in contrast to those with striae on their thighs, which decreased the risk. Environmental factors have also been considered a risk factor for striae gravidarum (Narin *et al.*, 2015). Specifically, Narin *et al.*, (2015) found that the development of striae gravidarum was significantly more common in higher-altitude geographical areas.

Farahnik *et al.* (2017) report from their literature review, involving 11 studies, that younger maternal age, maternal and family history of striae, greater pre-pregnancy and pre-delivery maternal weight, and higher infant birth weight were the most significant risk factors identified for striae development. Finally, in the most recent study addressing risk factors for striae in primigravid women, Kocaöz *et al.* (2019) found increased risk in those without social security, who

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sleep nine hours or more a day, have a BMI of greater or equal to 30 kg/m² and have a family history of striae. Risk factors for striae are examined commonly in the literature but findings are, as discussed, inconsistent, thus making it difficult to identify risk factors consistently associated with striae gravidarum (Korgavkar & Wang, 2015). To help identify who is at risk of developing stretch marks, Korgavkar & Wang (2015) identified a list of attributes; they state that women with one or more of the attributes listed may be at increased risk of developing stretch marks (see Table 1) and should be a focus in prevention efforts.

Table 1.1 Risk factors potentially associated with development of striae gravidarum – Korgavkar & Wang (2015)

(Permission to include table granted by Korgavkar & Wang and John Wiley and Sons)

Maternal factors prior to pregnancy
Family history of striae
Personal history of breast or thigh striae
Young age
Baseline weight
Body mass index > 26
Alcohol intake
Light skin colour
Race ^a
Maternal factors during pregnancy
Increased weight gain
Increased body mass index at delivery
Increased abdominal and hip girth
Low serum vitamin C level
Low serum relaxin level
Low water intake
Neonatal factors
Increased gestational age at delivery
Increased birthweight
Increased height and head circumference
^a <i>Depending on the study, both nonwhite and white race have been associated with increased risk.</i>

Some authors refer to risk factors for striae development as both modifiable and non-modifiable (Kasielska-Trojan *et al.*, 2015), where the modifiable factors are considered important in maternal education, particularly until effective preventative means are identified (Osman *et al.*, 2008). This is echoed in the later literature where some highlight that knowledge of these risk factors is key

in efforts to prevent striae; for example, in making lifestyle changes such as restricting weight gain (Kocaöz *et al.*, 2019).

Women ask frequently about their risks for striae development (Kasielska-Trojan *et al.*, 2015; Osman *et al.*, 2007). However, Korgavkar & Wang (2015) highlight the lack of evidence in support of the efficacy of lifestyle changes in either preventing or reducing the severity of striae gravidarum. One study examined diet and exercise and their effects on striae distensae (Schwingel *et al.*, 2003). Researchers in this Japanese study involving 80 non-pregnant, obese women enrolled in a weight-loss programme (diet or diet plus aerobic exercise programme, or diet plus resistance exercise programme), found that the degree of striae was not affected by the weight loss irrespective of the exercise programme undertaken (Schwingel *et al.*, 2003). The authors highlight the need for more research on this topic (Schwingel *et al.*, 2003). Nevertheless, some authors suggest that telling women about risk factors for striae gravidarum as part of health education for women may be helpful in preventing striae gravidarum; for example, informing young women of the risk factors for striae such as pre-pregnancy weight and weight gain during pregnancy (Picard *et al.*, 2015). However, there is an absence of evidence on the effectiveness of such strategies on preventing or reducing the severity of stretch marks.

1.3 Effects of striae in the context of other changes in pregnancy

Striae gravidarum are one of many cutaneous or skin changes occurring in the '*altered physiological milieu*' of pregnancy (Elling & Powell, 1997:35), some of which recede after pregnancy or persist in a less obvious form (Elling & Powell, 1997), as in the case of striae. Physiological skin changes in pregnancy have been classified as pigmentary (eg, melasma and linea nigra), vascular (eg, Spider nevi, palmer erythema), structural (eg, striae gravidarum), appendageal (eg, sweat gland activity with sweating, sebaceous gland activity with greasy skin, hair changes) and miscellaneous (eg, mucus membrane changes with gingivitis) (Elling & Powell, 1997) and all can '*cause significant cosmetic distress*' for women (Geraghty & Pomeranz, 2011:771). This is in contrast to the pathological changes or specific dermatomes of pregnancy, which are rare (Beard & Millington, 2012; Geraghty & Pomeranz, 2011) but some of which can

cause extreme pruritus or skin blistering and in some cases increase the risk of negative foetal events (Geraghty & Pomeranz, 2011). One example of a dermatome of pregnancy that is associated with an increased risk of an adverse foetal outcome is Pemphigoid gestationis. Another is intrahepatic cholestasis of pregnancy, which, though not primarily a skin condition, affects the skin and may be associated with adverse foetal outcomes (Geraghty & Pomeranz, 2011). However, most of the dermatomes of pregnancy clear up after pregnancy, except in the case of pre-existing conditions which have flared up or newly presenting ones (Geraghty & Pomeranz, 2011).

Other physiological changes affect other body organs such as cardiac, respiratory, gastro-intestinal, musculoskeletal and renal systems, among others (Tan & Tan, 2013). Due to these changes, many women experience '*inconvenient*' but non-life-threatening disorders (Patrick, 2017:317), sometimes referred to as the minor disorders of pregnancy (Bharj & Daniels, 2017; Patrick, 2017). All can be a source of worry for women during pregnancy (Bharj & Daniels, 2017). They include nausea and vomiting, heartburn, pica, constipation, varicosities, and backache (Patrick, 2017). While the numbers of women affected by the different minor disorders varies according to the different sources consulted, nausea and backache affect similar percentages of women to striae during pregnancy (Bharj & Daniels, 2017); up to 85% and 90% of women have been affected by both these conditions respectively. Furthermore, both nausea and vomiting (though less common) have been described as distressing for women (Matthews *et al.*, 2015) or as adversely affecting the woman's quality of life (NICE, 2008), as is the case with backache. This was evident in a systematic review involving 37 articles that identified nausea and vomiting and backache among other factors as associated with poorer quality of life for women during pregnancy (Lagadec *et al.*, 2018). Although skin changes were not identified in this review, others have made the link with quality of life and striae (Mosbeh, 2019; Nusrat *et al.*, 2019; Yamaguchi *et al.*, 2012).

1.4 Affects of striae on women during pregnancy

Most writers comment on the effects of striae gravidarum on women. They are identified frequently as a common aesthetic (Atwal *et al.*, 2006) or cosmetic (Bahrami *et al.*, 2012; Ersoy *et al.*, 2016; Lerdpienpitayakul *et al.*, 2009; Muallem & Rubeiz, 2006; Osman *et al.*, 2007) issue occurring in pregnancy, which may be attributed to their permanency (Ersoy *et al.*, 2016). Mosbeh (2019) suggests that their permanency could affect women psychologically and thus affect quality of life. Some writers note how striae gravidarum can be '*disfiguring*' for women (Buchanan *et al.*, 2010; Chang *et al.*, 2004). Striae are, in general, known to be very distressing for those affected (Kang *et al.*, 1996), presenting '*a significant psychological burden*' (Al-Himdani *et al.*, 2014:527) or impact (Liu *et al.*, 2014) and this also applies to striae gravidarum (Farahnik *et al.*, 2017). They can affect women's perception of themselves (Osman *et al.*, 2008), affect women psychologically (Soltanipour *et al.*, 2014), causing '*psychological distress*' (Yamaguchi *et al.*, 2014:595) or '*disturbance*' (Nusrat *et al.*, 2019:117), which some suggest may relate to the physical symptoms of pruritus (Chang *et al.*, 2004; Lerdpienpitayakul *et al.*, 2009). Earlier literature refers to them as causing permanent distress to women (Mallol *et al.*, 1991). Lack of self-confidence may also be present (Narin *et al.*, 2015). The effect on women is not a new development; striae have concerned women greatly since ancient times, with ancient Egyptian writings referring to many treatments for striae (Farahnik *et al.*, 2017; Salter & Kimball, 2006).

Prior to the work of Yamaguchi *et al.* (2012), which focused on quality of life in relation to striae gravidarum, few had focused on their psychological effects (Kocaöz *et al.*, 2019). There is now a body of evidence emerging in relation to striae gravidarum and quality of life (Mosbeh, 2019; Nusrat *et al.*, 2019; Ogrum & Dogru, 2019). Although striae gravidarum did not affect general quality of life (QOL), they were found to affect women's dermatology-specific quality of life based on scores obtained on the emotion scale of Skindex-29 (instrument for quality of life in dermatology patients) used by Yamaguchi *et al.* (2012) in a study involving Japanese women. This was particularly so for multiparous women. The researchers compared the effect of striae gravidarum on quality of life in

Japanese women to quality of life in those with other chronic skin diseases (Yamaguchi *et al.*, 2012).

More recently, in Pakistan, Nusrat *et al.* (2019) found that women with severe striae gravidarum had significantly higher scores on emotion of Skindex-16 (dermatology-specific QOL questionnaire) in comparison to those with absent or mild striae. Mosbeh (2019) found that women with severe striae had statistically significantly higher median scores in the three domains (symptoms, emotions and functioning) of the Skindex-16 QOL questionnaire compared to women with mild striae gravidarum. He also noted a statistically significant correlation between Skindex-16 QOL and Davey's scores in this study undertaken in Egypt with 200 women. Ogrum & Dogru (2019) used the Skindex-29 questionnaire to evaluate the impact of striae gravidarum on 153 Turkish women's quality of life and found that the emotion and symptom score of primiparae with severe striae gravidarum was significantly higher (i.e. worse) than women without striae ($p = 0.001$; $p = 0.028$, respectively). Furthermore, women with striae who applied a cream or lotion had higher symptom and emotion scores than those who did not use one ($p < 0.001$; $p = 0.038$, respectively). They conclude that striae gravidarum may lead to psychological and physical effects among women but particularly in primiparae with severe striae and may negatively affect their quality of life (Ogrum & Dogru, 2019). In a similar vein, Kocaöz *et al.* (2019) report how women's body image declined in the presence of striae and their increasing severity. Striae gravidarum were also identified, along with other specific pregnancy changes, as affecting women's body dissatisfaction in an Australian qualitative study (Watson *et al.*, 2016), which used individual structured interviews with 19 pregnant women.

1.5 Prevention of striae

Prevention of striae gravidarum is important to many women (Salter & Kimball, 2006) because, if they develop, they remain for life (Ersoy *et al.*, 2016). Prevention is executed mainly through the use of creams and lotions to moisturise the skin (Yamaguchi *et al.*, 2014). There is a wide range of products available purporting to prevent or minimise the development of stretch marks (Brennan *et al.*, 2016) and many women use one or more of the commonly

available anti-stretch mark creams or lotions in efforts to prevent or reduce the development of stretch marks. In one recent large Irish survey involving 753 pregnant women (Brennan *et al.*, 2016) (Chapter 3), most respondents (78%, n=589) indicated that they used a product to prevent or reduce the development of stretch marks during the current pregnancy and over one-third (37%, n=210) had used two or more products. This is similar to a Japanese study involving both primiparae and multigravidae where 77.7% (n=138/179) of women used a product in efforts to prevent striae gravidarum (Yamaguchi *et al.*, 2012).

Osman *et al.* (2007) report that 61% (n=67) of women used a cream or lotion to try to prevent striae gravidarum while 17% (n=19) had used more than one. Others reporting product use to prevent striae gravidarum are Lerdpienpitayakul *et al.* (2009), where 70% (n=190) of women used a product. Kocaöz *et al.* (2019) report that 50% (n=172) of participants used an intervention including a product with or without massage to prevent striae gravidarum.

Bahrami *et al.* (2012) report that 32% (n=71) used a product (lotion, cream or oil) to try to prevent striae, while 2.2% (n=5) had used more than one product. Similar proportions (3.3%, n=7) were also using two products (oil and cream) in a Turkish prospective observational study undertaken by Ersoy *et al.* (2016), while multiple product use was also evident from Kocaöz *et al.* (2019) (rates are not provided). Although the rates for multi-use of products when available are lower than in Brennan *et al.* (2016), some women do seem to be using more than one product in efforts to try to prevent striae gravidarum and are not committing exclusively to one, for reasons that are unclear. Furthermore, preventative steps in the form of applying a moisturising product may preserve quality of life in women with striae gravidarum during pregnancy, as suggested by Yamaguchi *et al.* (2014). Their cross-sectional study involving primiparae and multiparae (n=156) found that, while striae gravidarum may impair emotional quality of life, those with striae who took preventative steps demonstrated the same level of emotional quality of life as those without striae (Yamaguchi *et al.*, 2014).

1.6 Products to prevent striae gravidarum and their effectiveness

Products used by women to prevent striae gravidarum include various oils (almond, cocoa, olive, baby oil), cocoa butter creams and lotions, vitamin E products, and specific branded products like Bio-oil. While many products purport to prevent the development of striae gravidarum (Summers & Lategan, 2009), most have not been well evaluated. Products that have been evaluated include some that are available commonly; for example, cocoa butter lotion and cream and olive oil, and others that are less well known or not so commonly available: for example, Velastisa Anti-Stretch Marks ISDIN (a commercially available cosmetic product: specific anti-stretch mark cream containing hydroxyprolisilane-C, rosehip oil, Centella asiatica triterpenes and vitamin E) (García Hernández *et al.*, 2013) and Trofolastin (commercially available) (Mallol *et al.*, 1991). Both trial products contained Centella asiatica, a medicinal plant from East Asia which has been found to have a number of clinical applications, for example in wound healing (Brinkhaus *et al.*, 2000). Studies involving both animal and in vivo human fibroblasts indicate that it may stimulate the fibroblasts (Brinkhaus *et al.*, 2000). Changes seen included increased collagen synthesis (Brinkhaus *et al.*, 2000). Centella asiatica is also reported to suppress glucocorticoid activity (Mallol *et al.*, 1991).

There is growing interest in the literature in Centella asiatica, since Mallol *et al.*'s double-blind, placebo-controlled, randomised trial involving 80 women found that significantly fewer women developed striae gravidarum following daily application of Trofolastin (contains Centella asiatica in addition to other ingredients) from the end of the 12th week of pregnancy to the day of labour compared to women who applied a placebo cream (contains excipient part of the active cream) (32%, n=14 versus 56% n=22) (Mallol *et al.*, 1991). Furthermore, those women with striae from puberty were given the best protection from the cream in comparison to those with striae from a previous pregnancy. With respect to severity, striae that developed newly in the current pregnancy were less severe in the treated group (p=0.014). However, this was not the case in the later double-blind, placebo randomised controlled trial (García Hernández *et al.*, 2013) where there was no difference in the overall incidence of striae gravidarum in those that applied Velastisa Anti-Stretch Marks

ISDIN (containing *Centella asiatica* triterpenes) compared to those who applied a placebo. However, in women without prior striae gravidarum, the overall incidence of stretch marks during pregnancy was significantly lower in the treated group (5.6% versus 35%, $p = 0.031$ OR: 9.2 [95% CI: 1.0–83.3]). Further, they found that the severity of striae increased significantly during the study in the control group (17.8%, $p = 0.001$), in contrast to the treated group (6.3%, ns) while in those women that developed new stretch marks during the study, the difference in severity was significantly higher in the control group than in the treated group (0.47 [0.57] versus 0.14 [0.60], $p = 0.031$) (García Hernández *et al.*, 2013). The authors conclude that the cream is '*effective in reducing severity of striae during pregnancy, prevents the appearance of new striae and halts progression of those already present*' (p.233).

Both Mallol *et al.* (1991) and García Hernández *et al.* (2013) have limitations. Mallol *et al.* had a high attrition rate (20%) and there was lack of clarity around randomisation, while García Hernández *et al.* identify the type of placebo used as the main limitation of the study. It is reported as having '*emollient and moisturising properties*', with similar cosmetic properties to the study cream and '*has been proposed as an option to prevent the appearance of striae gravidarum*' (García Hernández *et al.*, 2013:236). This placebo with similar constituents and emollient properties lacked the active ingredients of *Centella Asiatica*, rose hip oil and hydroxyprolisilane-C. These active ingredients are identified as stimulating the fibroblasts (*Centella Asiatica* and rose hip oil) while the hydroxyprolisilane-C is needed for the regeneration of the collagen and elastic fibres (García Hernández *et al.*, 2013). Despite the limitations, these are considered promising results (Antoszewski *et al.*, 2015) with reviewers concluding that *Centella asiatica* should be investigated further (Korgavkar & Wang, 2015), and Korgavkar & Wang (2015:612) suggest the need for thoroughly planned controlled studies to establish the '*specific efficacy of centella*' in the prevention of striae gravidarum.

Another ingredient identified in the literature as active is Hyaluronic acid, which is known to be important in maintaining skin tone (Wierrani *et al.*, 1992). Products containing Hyaluronic acid that have been investigated to date are

Alphastria (de Buman *et al.*, 1987) and Verum (Wierrani *et al.*, 1992). However, according to Korgavkar & Wang (2015), the evidence for the prevention of striae gravidarum is weak and further research is required. Both of these trials involved small samples (n=50 and n=90 respectively) (Wierrani *et al.*, 1992; De Buman *et al.*, 1987), with the inclusion of a placebo in one (de Buman *et al.*, 1987) and no treatment in the other (Wierrani *et al.*, 1992).

In the Wierrani *et al.* study (1992), significantly more women developed striae gravidarum in the no-treatment group compared to the group using the massaged Verum ointment; similarly, significantly fewer women developed striae gravidarum in the Alphastria group compared to the placebo groups in the de Buman *et al.* study (1987). Both of these studies have limitations: for example, the small sample sizes and lack of methodological clarity (eg, it is unclear how randomisation was undertaken in both studies).

Cocoa butter lotion has not been found to be effective in preventing striae when compared to a placebo lotion (Osman *et al.*, 2008), nor has cocoa butter cream in two randomised placebo controlled trials (Osman *et al.*, 2008; Buchanan *et al.*, 2010). While the results for olive oil are inconsistent, Taavoni *et al.* (2011) concluded, from their randomised trial involving the application of olive oil versus no treatment in a group of 70 nulliparous women between 18-20 and 28 weeks' gestation (phase 1), that there was no significant difference between the intervention and control groups in relation to the incidence of striae gravidarum. This was also the outcome in a later-phase trial (undertaken by some of the same researchers) where women were followed up until 38-40 weeks' gestation (delivery time) (Soltanipoor *et al.*, 2012). This concurs with the findings from the prospective observational study by Poidevan (1959) who suggests that olive oil may actually increase women's risk of getting striae instead of preventing them. Contrasting with these are the findings of Davey's (1972) observational study which found that there was a lower rate of striae in women who massaged their abdomen with olive oil.

Another oil that has been evaluated is bitter almond oil. Timur Taşhan & Kafkasli (2012) conducted a post-test quasi-experimental study with 141 primiparous

women in Turkey, comparing oil only versus oil with a 15-minute massage versus a control group that did not undertake any specific prophylactic action. They found that the frequency of striae gravidarum was lower in the bitter almond oil and massage group compared to the bitter almond oil group only and the control group ($p < 0.05$). The authors report that the massage positively affected the participants' skin and that bitter almond oil might have increased the positive effect (Timur Taşhan & Kafkasli, 2012).

Others have reported in their observational studies on the effects of topical products in general, for example Madlon-Kay (1993) and Murphy *et al.* (1992). However, the search for an effective product to prevent striae gravidarum has yielded little success (Buchanan *et al.*, 2010; Farahnik *et al.*, 2017) and no product has been identified consistently as effective in the prevention of striae gravidarum, which is also the case in relation to striae distensae (Al-Himdani *et al.*, 2014).

In light of the paucity of research and the anecdotal information on the effectiveness of many of the products (Taavoni *et al.*, 2011), researchers commonly recommend the need to investigate the effectiveness of the creams and lotions used commonly by women to prevent stretch marks (Bahrami *et al.*, 2012; Taavoni *et al.*, 2011). Some argue that prevention of striae has received little attention from researchers (Taavoni *et al.*, 2011) and clinicians, and indeed that it gets little attention in the medical text books or literature (Madlon-Kay, 1993; Osman *et al.*, 2008), despite the psychological and economic strain for women (Osman *et al.*, 2008). This could also be said in relation to midwifery textbooks (King *et al.*, 2019; Macdonald & Johnson, 2017; Marshall & Raynor, 2014) which usually devote only a short paragraph or so to the topic. Furthermore, some are critical of how textbooks communicate that striae gravidarum are of significant concern without any supporting evidence (Yamaguchi *et al.*, 2012). The degree of attention from both researchers and clinicians contrasts sharply with pregnant women who give great attention to it (Madlon-Kay, 1993; Taavoni *et al.*, 2011). There is a view that striae gravidarum are '*a cosmetic nuisance and overlooked by practitioners as clinically insignificant*' (Farahnik *et al.*, 2017:82). This was highlighted by Salter & Kimball

(2006) previously and contrasts sharply with the approach to either nausea and vomiting or backache.

In summary, striae gravidarum are a common physiological skin change occurring in pregnancy. They may cause symptoms such as pruritus or can be symptomless, and while they fade postnatally they never disappear totally. While their exact cause is still unclear, both non-modifiable and modifiable risk factors have been identified, with the latter being suggested for inclusion in health education for women during pregnancy. Many have identified how striae are a cosmetic or aesthetic issue and that they cause distress to women, although the evidence in support of this is not always clear. Striae gravidarum have been shown to affect women's quality of life similarly to other chronic skin diseases and to affect their body image. Although they are not a health risk, many women try to prevent them by applying some of the many commercially available topical products to their skin during pregnancy, independent of their clinician's advice and despite many of these products lacking evidence of effectiveness. Further, women frequently use one or more of the many marketed products purporting to prevent or minimise the development of striae gravidarum often in absence of evidence to support their effectiveness or lack of knowledge of product evaluations. There have been calls for further research into the effectiveness of topical preparations used by women. This is particularly significant in the context of the perception that striae gravidarum is a neglected topic due to its clinical insignificance from a medical perspective, though of huge importance to many women during pregnancy.

Given the many women affected by striae gravidarum, the dearth of research on this topic compared to other commonly occurring physiological changes in pregnancy, and particularly in view of the importance of the topic for women, this PhD study addresses the prevention of striae gravidarum in primigravid women.

1.7 Study aims

The aims of this study are:

1. to systematically review the evidence of the effectiveness of topical preparations in the prevention and reduction in severity of striae gravidarum;
2. to survey women on their use of skin products to prevent or reduce the development of striae gravidarum, and
3. to undertake a pilot randomised trial to evaluate the feasibility of conducting a large trial on the effectiveness of a moisturising oil (commercially available) compared to no treatment for the prevention and reduction in severity of striae gravidarum.

1.8 Research questions

1. What is the current evidence in support of the use of topical preparations for the prevention of striae gravidarum?
2. What are the topical products used commonly by women during pregnancy to prevent or reduce the development of striae gravidarum?
3. Is it feasible to undertake a large trial on the effectiveness of a moisturising oil (commercially available) compared to no treatment for the prevention and reduction in severity of striae gravidarum?

Due to challenges in recruitment to the pilot randomised controlled trial (as detailed in Chapter 5), I explored the factors influencing women's decision to participate in the pilot trial by means of a qualitative descriptive study, which sought to answer the question:

4. What are the factors influencing recruitment of women to the pilot trial on the prevention of striae gravidarum?

1.9 Outline of the thesis

This thesis comprises six chapters, including three papers published in peer-reviewed journals. The fourth paper is under review. Due to the independent nature of the papers, there is an unavoidable element of repetition. The research questions are addressed in Chapters 2, 3, 4 and 5.

Chapter 1 introduces the thesis, with an explanation of the background, the research questions, and relevant literature and methodology, and concludes with an outline of the thesis.

Chapter 2 presents the Cochrane systematic review and meta-analysis undertaken to evaluate the evidence base for the effectiveness of topical preparations in the prevention and reduction of striae gravidarum (Question 1).

Chapter 3 presents the cross-sectional descriptive survey, which identified the topical products used commonly by women during pregnancy to prevent or reduce the development of striae gravidarum (Question 2).

Chapter 4 presents the protocol for the pilot randomised trial to evaluate the feasibility of conducting a large trial on the effectiveness of a moisturising oil (commercially available) compared to no treatment for the prevention and reduction in severity of striae gravidarum (Question 3).

Chapter 5 presents the qualitative descriptive study exploring factors influencing recruitment of women to the pilot trial on the prevention of striae gravidarum (Question 4).

Chapter 6 presents the overall discussion of the thesis and its contribution in the context of knowledge generation or development on the prevention of striae gravidarum. Finally, implications for practice and further research are outlined.

Given the thesis-by-publication structure of this thesis, references are placed at the end of respective chapters to aid the reader's journey through the thesis.

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Chapter 2: Paper 1

2.1 Introduction

This chapter presents paper 1; the Cochrane systematic review and meta-analysis undertaken to systematically review the evidence of the effectiveness of topical preparations in the prevention and reduction of striae gravidarum. It addresses question 1 i.e. What is the current evidence in support of the use of topical preparations for the prevention of striae gravidarum? The original review 'Creams for preventing stretch marks in pregnancy' (Young & Jewell, 1996) was updated substantially and conclusions changed.

2.2 Paper 1

Topical preparations for preventing stretch marks in pregnancy

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2.3 Abstract

Background

Striae gravidarum (stretch marks developing during pregnancy) occur in 50% to 90% of women. They appear as red or purple lines or streaks that fade slowly to leave pale lines or marks on the skin. The abdomen, breasts and thighs are commonly affected. The exact cause of stretch marks is unclear and no preparation has yet been shown to be effective in preventing the development of stretch marks. They are a source of significant anxiety for women, impacting on their quality of life.

Objectives

To assess the effects of topical preparations on the prevention of stretch marks in pregnancy.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 October 2011) and reference lists of retrieved reports.

Selection criteria

We included randomised controlled trials and quasi-randomised controlled trials comparing topical preparations (with active ingredients) with other topical preparations (with active ingredients), with a placebo (that is, preparations without active ingredients) or with no treatment for the prevention of stretch marks in pregnant women.

Data collection and analysis

Three review authors independently assessed trial eligibility and trial quality, and extracted data. Data were checked for accuracy. The primary outcome was the presence of stretch marks and the secondary outcome was the severity of stretch marks.

Main results

We included six trials involving 800 women. Of the six trials, we judged the risk of bias for three as 'low risk' for random sequence generation, blinding of participants and personnel, blinding of outcome assessment, completeness of outcome data and selective reporting.

There was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment (average risk ratio (RR) 0.74; 95% confidence interval (CI) 0.53 to 1.03; five trials, 474 women; random-effects model, $\text{Tau}^2 = 0.09$, $I^2 = 65\%$) (Analysis 1.1).

Results were consistent with the main effects when we performed a sensitivity analysis excluding studies judged to be at high risk of bias for random sequence generation, allocation concealment or more than 20% missing data for a given outcome (average RR 0.81; 95% CI 0.60 to 1.10; four trials, 424 women; random-effects model, $\text{Tau}^2 = 0.05$, $I^2 = 57\%$).

There was no statistically significant average mean difference in the severity of stretch marks (standardised mean difference (SMD) -0.31; 95% CI -1.06 to 0.44; two trials, 255 women; $\text{Tau}^2 = 0.26$, $I^2 = 87\%$).

There was no statistically significant difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients (average RR 0.51; 95% CI 0.16 to 1.60; two trials, 305 women; $\text{Tau}^2 = 0.53$, $I^2 = 74\%$). There was no statistically significant difference in the severity of stretch marks (mean difference (MD) -0.20; 95% CI -0.53 to 0.13; one trial, 206 women; heterogeneity not applicable).

Authors' conclusions

We found no high-quality evidence to support the use of any of the topical preparations in the prevention of stretch marks during pregnancy. There is a clear need for robust, methodologically rigorous randomised trials involving larger sample sizes to evaluate the effects of topical preparations on the development of stretch marks in pregnancy. In addition, it is important that preparations commonly used by women to prevent and treat stretch marks are

evaluated within the context of robust, methodologically rigorous and adequately powered randomised trials.

Plain language summary

Topical preparations for preventing stretch marks in pregnancy

Stretch marks commonly develop during pregnancy, particularly in the third trimester. They affect 50% to 90% of women. They appear as red lines or streaks that fade slowly after the pregnancy to leave pale lines on the skin. The abdomen, breasts and thighs are most often affected. They do not disappear entirely, therefore any treatment which prevents them would be welcomed by many women. In this review, we identified randomised controlled trials and quasi-randomised controlled trials that compared topical creams, lotions and ointments containing active ingredients with placebo or no treatment, and topical preparations with active ingredients versus other topical preparations.

We included six trials (involving 800 women) in this review. We found that the application of a skin preparation to the areas affected by stretch marks during pregnancy did not prevent the development of stretch marks in the women during pregnancy. Only three trials (involving 461 women) looked at the severity of the stretch marks and did not show a clear difference. The preparations used included Alphastrin, Trofolastin, Verum, olive oil and cocoa butter, which all contain vitamin E; Alphastrin and Verum also have hyaluronic acid. Of the six trials, we judged three to be at low risk of bias. All trials were relatively small, with four of the six trials each including less than 100 women. The trials were also different in terms of when the women first started to use the topical applications, ranging from the first trimester to the first 20 weeks.

2.4 Background

The following review is an update of the review 'Creams for preventing stretch marks in pregnancy' (Young 1996).

2.4.1 Description of the condition

Striae distensae (stretch marks), or striae gravidarum as they are known in pregnancy (Cunningham 2010), are considered to be the most common connective tissue change in pregnancy (Lawley 1999). Rates of occurrence of striae gravidarum vary (Salter 2006), with reported rates ranging between 50% and 90% (Osman 2007). In primiparous women incidences of 52% (Atwal 2006), 61% (Osman 2007) and 87.7% (Ghasemi 2007) have been reported, while a rate of 71.1% was found in a study involving both primigravidae and multigravidae (Muzaffar 1998). Striae gravidarum seem to affect all racial groups (Buchanan 2010). Although once considered to be more common in white than in black or Asian women (Wong 1984; Wong 1989), more recently non-white women were seen to be at greater risk (Chang 2004). Striae gravidarum are common during the first pregnancy (Salter 2006) and usually present during the third trimester (Atwal 2006; Cunningham 2010). However, there have been reports in women under 24 weeks' gestation and of women first developing them in a second pregnancy (Chang 2004).

Striae have been defined as 'visible linear scars' (Burrows 2004: 46.6) that have evolved through recognised stages (Kang 1996) similar to the stages of tissue healing (Kang 1998; Salter 2006) or scar formation (Elson 1990). They manifest as 'reddish slightly depressed streaks' (Cunningham 2010: 111) or 'reddish purple linear macules' (Horn 2007: 947). They often fade gradually (Kang 1996; Kang 1998; Papoutsis 2007; Salter 2006) leaving glistening (Cunningham 2010), white depressed (Elson 1990) or pale wrinkled lines (Watson 1998) on the skin, from about six months following birth (Murray 2009). These glistening lines are commonly seen on multiparous women in addition to the reddish striae of the current pregnancy (Cunningham 2010). These benign skin changes (Atwal 2006) commonly occur on the abdomen but are also seen on the breasts and thighs (Cunningham 2010; Horn 2007; Osman 2008; Salter 2006; Thomas 2004), hips and buttocks (Horn 2007; Osman 2008) and groin and axillae

(Papoutsis 2007). Striae have been reported as ranging in severity and have been graded as mild, moderate or severe by some authors (Atwal 2006; Osman 2007; Osman 2008). Atwal 2006: 966 developed and used a numerical system that captured the severity of striae, focusing on the number of striae present and the degree of erythema, or redness. A score of zero to three represented no striae or 'no significant striae', four to nine was considered 'mild', 10 to 15 as 'moderate' and greater than 16 represented 'severe striae'. Other criteria for assessing the severity of striae gravidarum include degrees of 'scaling, burning or stinging, or pruritus' (Kang 1996:520).

While attracting much discussion and debate over the years (Nigam 1989), the exact cause or origin of striae gravidarum remains in doubt (Ghasemi 2007; Lawley 1999; Osman 2007; Osman 2008; Wong 1984) and is understood poorly (Burrows 2010), with researchers disagreeing about their histopathological origins (Zheng 1985). Nevertheless, several risk factors have been identified. Early researchers attributed the development of striae to stretching (Wilks, 1861 cited by Poidevin 1959) and the stretch theory was accepted widely as the cause of striae gravidarum up until the middle of the last century (Poidevin 1959) when it became evident that other factors such as increased adrenal cortical activity may be involved (Poidevin 1959).

From his study of 116 primigravid women, Poidevin 1959 concluded that striae development was not solely reliant on stretching and that striae gravidarum should not be referred to as stretch marks. Poidevin 1959 proposed the existence of a 'striae factor' for each woman and while not identifying what this 'striae factor' may be, he found a clear relationship between the reduced glucose tolerance in pregnancy, a sign of adrenocortical hyperactivity, and the development of striae. This link between increased adrenocortical hormonal activity and striae gravidarum has been suggested by others (Liu 1974; McKenzie 1971). Liu 1974 asserts that striae gravidarum only develop in oestrogen and relaxin primed connective tissue, in response to stretching. Further, increased corticosteroid levels in pregnancy (Venning 1946) are thought to be a contributing factor. Oestrogen, relaxin and corticosteroids are thought to promote the formation of a type of mucopolysaccharide ground substance which

promotes separation of the collagen fibrils (Bryant 1968) and the formation of striae gravidarum in response to stretch (Liu 1974). Collagen is responsible for the tensile strength of the skin (Vaugh 2010) and under normal conditions the interfibrillar substance is highly viscous and there is no slipping or separation of collagen fibrils (Archer 2004). In pregnancy, the collagen mechanism is disrupted and irreversible sliding and separation of fibres occurs (Archer 2004). Liu 1974's position on the development of striae gravidarum is challenged by Shuster 1979, who contends that while the hormones of pregnancy may alter the collagen fibrils, there is no evidence to support this. Instead, Shuster 1979 suggests that striae are always due to stretching and, furthermore, only occur in immature connective tissue characterised by a "critical titre of rigid cross-linked collagen and elastic unlinked collagen" (Shuster 1979: 161), which may be a factor in the higher risk of striae in younger women identified in some studies (Atwal 2006; Murphy 1992; Thomas 2004). The stretching factor is supported by Thomas 2004 who suggest that the degree of stretch applied is also influential.

Further insight into the pathogenesis of striae is given by Watson 1998 who suggests that the development of striae is related to changes in the dermal elastic fibres rather than the collagen. They hypothesised that striae may occur in individuals where there is a deficiency in 'cutaneous fibrillin' and can arise in conditions like pregnancy where there is extra stretching on the skin. The extra strain or stretching could be sufficient to tear the elastic fibre network, resulting in the formation of striae (Watson 1998). Perhaps corticosteroids may also be influential here as they are thought to weaken the 'dermal elastic fibres' leading to their tearing (McKenzie 1971: 774). However, it is far from conclusive, as Zheng 1985 suggest that striae are scars and are not due to rupture of the connective tissue in response to stress. They found that the elastic fibres and collagen arrangement were in keeping with a scar. Furthermore, they are characterised by absent rete ridges and a thinning and flattening of the overlying epidermis (Zheng 1985) and are devoid of sweat glands or hair follicles.

While hormonal influences and stress or stretching factors continue to be considered important in the development of striae (Lawley 1999), other risk factors have been associated with the development of striae gravidarum (Salter 2006). Identified risk factors include family history, race, skin type, birthweight,

baseline body mass index, weight gain and inadequate nutrition (Osman 2007), younger maternal age, increased pregnancy weight gain, use of corticosteroids and a genetic susceptibility (Papoutsis 2007). A number of researchers identified younger maternal age as a risk factor for the development of striae (Atwal 2006; Murphy 1992; Thomas 2004) while others found no association with age (Ghasemi 2007). Greater weight gain (Atwal 2006; Murphy 1992) and higher body mass (Thomas 2004) have been identified as significant factors in the development of striae by some researchers while Chang 2004 indicated that weight gain and changes in weight during pregnancy were less predictive of the development of striae than were genetic factors. A personal history of breast or thigh striae and genetic factors were thought to be the most predictive for the development of striae (Chang 2004). Family history was also identified by Osman 2007, where women with a family history of striae gravidarum were more likely to have moderate to severe striae gravidarum compared to those with no family history. Finally, a number of researchers have identified a significant relationship between the development of striae gravidarum and an increased infant birth weight (Atwal 2006; Ghasemi 2007; Murphy 1992).

Striae have been a significant anxiety for women since early times (Salter 2006). They are an aesthetic concern for many women (Atwal 2006; Chang 2004; Ghasemi 2007; Osman 2007; Osman 2008; Rangel 2001) and can also be a source of stress (Chang 2004; Mallol 1991; Salter 2006). They may also cause itching (Horn 2007; Lawley 1999; Martius 1973; Muzaffar 1998; Papoutsis 2007; Salter 2006) or a burning sensation (Salter 2006) for some women. Authors differ in their evaluation of how symptomatic or not they are; some see them as often symptomatic (Salter 2006) while others report them as usually asymptomatic (Papoutsis 2007).

2.4.2 Description of the intervention and how the intervention might work

Many writers refer to the challenges of treating striae (Alster 1997; Elsaie 2009; Papoutsis 2007), while their prevention has attracted somewhat less attention. Some argue that it may not be possible to prevent striae (Cunningham 2010). Yet, there are an abundance of products on the market claiming to prevent striae (Summers 2009). Consequently, over the years women have used many

approaches and preparations to either prevent or treat striae gravidarum, and often at great expense (Salter 2006). It appears that there are no specific treatments for striae (Elsaie 2009; Errickson 1994; Salter 2006) and no preparation has yet been found to be effective in preventing or healing the lines that remain (Papoutsis 2007). Approaches or preparations used in the prevention and treatment include topical preparations, lasers or pulsed light (Elsaie 2009). However, only topical preparations are considered safe to use in pregnancy and the theoretical reasoning for how they are thought to work include:

- stimulation of fibroblastic activity leading to increased production of collagen and fibronectin (Brinkhaus 2000; Elsaie 2009);
- increased blood perfusion through massaging of the area and potential anti-inflammatory effects (Wierrani 1992);
- Increased skin hydration (Elsaie 2009).

2.4.3 Why it is important to do this review

Striae gravidarum affect between 50% and 90% of women (Osman 2007) during pregnancy and usually remain as silvery scar lines on the skin. They are an unwanted consequence of pregnancy, impacting on women's perception of themselves (Osman 2008) and their quality of life (Salter 2006), and are thus of significant concern to women of child bearing age.

There are many unproven products on the market (Burrows 2010) tried by many women. Consequently, many women incur great expense (Salter 2006) trying to prevent or treat striae (Osman 2008). It is important, therefore, to systematically assess the evidence on the effectiveness of these creams and preparations in the prevention of striae. The findings of this review will benefit both women and healthcare professionals. The review will assist women to make informed decisions about their choice of treatment to prevent striae gravidarum and inform healthcare practitioners when advising women on the effectiveness of topical preparation for the prevention of striae gravidarum.

2.5 Objectives

To assess the effects of topical preparations on the prevention of stretch marks in pregnancy.

2.6 Methods

2.6.1 Criteria for considering studies for this review

2.6.1.1 Types of studies

All randomised and quasi-randomised controlled trials comparing topical preparations (with active ingredients) with other topical preparations (with active ingredients), with a placebo (that is, preparations without active ingredients) or with no treatment.

2.6.1.2 Types of participants

Pregnant women prior to 20 weeks' gestation, including women expecting their first or subsequent babies and women experiencing multiple pregnancies.

2.6.1.3 Types of interventions

For the purpose of this review topical preparations are categorised as follows.

Creams or lotions with active ingredients

Creams and lotions are defined as emulsions with moisturising and emollient effects. They can be either be an 'oil-in-water' or a 'water-in-oil' emulsion (Hunter 1973). Viscosity determines whether an emulsion is categorised as a lotion or a cream.

Examples include:

- Trofolastin cream (containing Centella asiatica extract, alpha tocopherol and collagen-elastin hydrolysates) (Mallol 1991);
- Alphastria cream (containing hyaluronic acid, vitamins A and E, allantoin and calcium pantothenate) (de Buman 1987);
- Cocoa butter lotion (containing cocoa butter and tocopheryl acetate (vitamin E) (Osman 2008).

Ointments with active ingredients

Ointments are defined as semi-solid preparations and can be of three types: those that are 'water soluble', those that 'emulsify with water', or those that 'repel water' (Hunter 1973: 412).

Examples include:

- Verum ointment (containing vitamin E, essential free fatty acids, panthenol, hyaluronic acid, elastin and menthol) (Wierrani 1992).

For the purpose of this review, a placebo is a topical preparation without active ingredients, or 'no treatment'.

Comparisons

1. Topical preparations with active ingredients compared with placebo or no treatment
2. Topical preparations with active ingredients compared with other topical preparations with active ingredients

2.6.1.4 Types of outcome measures

Primary outcomes

1. Presence of stretch marks

Secondary outcomes

1. Severity of stretch marks

2.6.2 Search methods for identification of studies

2.6.2.1 Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (31 October 2011). The Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals

reviewed via the current awareness service can be found in the ‘Specialized Register’ section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

2.6.2.2 Searching other resources

We searched the reference lists of all the identified studies and retrieved one trial (Msika 2002).

We did not apply any language restrictions.

2.6.3 Data collection and analysis

For methods used in previous versions of this review, please see Appendix 1. Methods for this update of the review are informed by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

2.6.3.1 Selection of studies

Three review authors (M Brennan, D Devane, and G Young (MB, DD and GY) independently assessed all potential studies identified for inclusion as a result of the search strategy. We would have resolved any disagreements through discussion but this was not necessary.

2.6.3.2 Data extraction and management

We designed a form to extract data. For eligible studies, three review authors (MB, DD and GY) extracted the data using the agreed form. We resolved discrepancies through discussion. We contacted authors from two trials (Horace Fletcher for Buchanan 2010; P Msika for Msika, unknown year) for further information (see notes in Characteristics of included studies). All data were entered into the Review Manager software (RevMan 2011) and checked for accuracy by the three review authors (MB, DD and GY).

2.6.3.3 *Assessment of risk of bias in included studies*

Three review authors (MB, DD and GY) independently assessed the risk of bias for each study using criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). If there had been any discrepancies we would have resolved them through discussion, but this was not necessary.

2.6.3.3.1 Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the method as:

- low risk (any truly random process, e.g. random number table; computer random number generator);
- high risk (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk (insufficient information to permit judgment).

2.6.3.3.2 Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal the allocation sequence and determined whether intervention allocation could have been foreseen in advance of or during recruitment, or changed after assignment.

We assessed the methods as:

- low risk (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk (open random allocation; unsealed or non-opaque envelopes; alternation; date of birth);
- unclear risk (insufficient information to permit judgment).

2.6.3.3.3 Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded or if we judged that the lack of blinding could not have affected the results.

We assessed the methods as:

- low risk, high risk or unclear risk for participants;
- low risk, high risk or unclear risk for personnel.

2.6.3.3.4 Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding could not have affected the results.

We assessed the methods as:

- low risk (no blinding of outcome assessment but the authors judged that the outcome was not likely to be influenced by this);
- high risk (no blinding of outcome assessment and the outcome measurement was likely to have been influenced by this);
- unclear risk (insufficient information to permit judgment; the study did not address this).

2.6.3.3.5 Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total number of randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or was supplied by the trial authors, we re-included the missing data in the analyses we undertook.

We assessed the methods as:

- low risk (20% or less of missing data);
- high risk (more than 20% of missing data);
- unclear risk (insufficient reporting to permit judgment; the study did not address this).

2.6.3.3.6 Selective reporting (checking for reporting bias)

We investigated the possibility of selective outcome reporting bias by identifying the outcomes in the study protocol (if available) and in the methods section of the publication, and by cross-checking to see if these outcomes were reported in the results section of the trial publication(s). PubMed and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (<http://www.who.int/ictpr/en/>) were searched for the study protocols.

We assessed the methods as:

- low risk (where it was clear that all of the study's pre-specified outcomes as identified in the study protocol (where available) and in the method's section were reported on; that all expected outcomes of interest to the review were reported on);
- high risk (where it was clear that not all of the study's pre-specified outcomes as identified in the study protocol (where available) and in the method's section were reported on; failure to include a key outcome that would have been expected to have been included);
- unclear risk (insufficient information to permit judgment).

2.6.3.3.7 Other bias (checking for other biases)

We described for each included study any important concerns we had about other possible sources of bias. We assessed whether each study was free of other problems that could put it at risk of bias as follows:

- low risk (study appeared to be free of bias);
- high risk (had at least one important risk of bias, for example related to study design);
- unclear risk (insufficient information to permit judgment).

2.6.3.4 *Measures of treatment effect*

2.6.3.4.1 Dichotomous data

For dichotomous data, we presented the results as summary risk ratio (RR) with 95% confidence interval (CI).

2.6.3.4.2 Continuous data

For continuous data, we used the mean difference for outcomes measured in the same way between trials. We used the standardised mean difference to combine trials that measured the same outcome but used different scales.

2.6.3.5 *Unit of analysis issues*

2.6.3.5.1 Cluster-randomised trials

We did not identify any cluster-randomised trials in our search. In future updates of this review, if we identify any cluster-randomised trials we will include them along with individually randomised trials. We will adjust their sample sizes using the methods described in the *Handbook for Systematic Reviews of Interventions* (Higgins 2011) using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial, or from a study of a similar population. If we use ICCs from other sources we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify cluster-randomised trials and individually-randomised trials we will synthesise the relevant information. We will consider it reasonable to combine the results from both where there is little heterogeneity between the study designs and where we consider that there is unlikely to be an interaction between the effect of the intervention and the choice of randomisation unit. We will acknowledge heterogeneity in the unit of randomisation and perform a sensitivity analysis to investigate the effects of this heterogeneity on the review findings.

2.6.3.6 *Dealing with missing data*

For included studies, we noted the levels of attrition.

For all outcomes we carried out analyses, as far as possible, on an intention-to-treat basis, that is we attempted to include all participants randomised to each group in the analyses, and all participants were analysed in the group to which they were allocated regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

2.6.3.7 *Assessment of heterogeneity*

We assessed statistical heterogeneity in each meta-analysis using the Tau² (tau-squared), I², and X² (Chi²) statistics. We regarded heterogeneity as substantial if:

(a) the I² value was high (exceeding 30%); and

either

(b) there was inconsistency between trials in direction or magnitude of effects (judged visually), or a low (< 0.10) P value in the Chi² test for heterogeneity;

or

(c) the estimate of between-study heterogeneity (Tau²) was above zero.

2.6.3.8 *Assessment of reporting biases*

As there were less than 10 studies included in the meta-analysis we did not investigate publication bias using funnel plots. In future updates of this review, if there are 10 or more studies included in the meta-analysis, we will assess funnel plot asymmetry visually and use formal tests for funnel plot asymmetry. For continuous outcomes, we will use the test proposed by Egger 1997, and for dichotomous outcomes we will use the test proposed by Harbord 2006. If asymmetry is detected in any of these tests or is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

2.6.3.9 *Data synthesis*

We carried out statistical analysis using the Review Manager software (RevMan 2011). As there was clinical diversity in respect of the interventions, that is each trial used a different topical preparation with different active ingredients, we used a random-effects model meta-analysis to produce an overall summary of the average treatment effect across the six included trials. This random-effects summary is treated as the average range of possible treatment effects and therefore the true effect differs in the different trials or varies '...across studies about an overall pooled value' (Riley 2011). For each outcome reported, we presented the results of the random-effects model analyses as the average

treatment effect with its 95% confidence interval, and the estimates of Tau² and I².

2.6.3.10 Subgroup analysis and investigation of heterogeneity

We neither planned nor conducted any subgroup analyses.

In future updates of this review, if we identify substantial heterogeneity we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful and, if it is, use random-effects model analysis to produce it.

We plan to carry out the following subgroup analysis.

1. Parity (nulliparous versus multiparous women).

Subgroup analysis will be restricted to primary outcomes.

We will assess subgroup differences by the interaction tests available within RevMan (RevMan 2011). We will report the results of subgroup analyses quoting the χ^2 statistic and P value, and the interaction statistic I² value.

2.6.3.11 Sensitivity analysis

The previous version of this review (Young 1996) did not include any a priori sensitivity analysis. In this update we undertook a sensitivity analysis by trial quality, by removing from the analysis those studies judged to be at high risk of bias for random sequence generation, allocation concealment, or with more than 20% missing data for a given outcome. In future updates of this review, the criteria for sensitivity analysis will broaden to determine the effect of also excluding trials judged to be at high risk of bias for blinding.

2.7 Results

2.7.1 Description of studies

2.7.1.1 Results of the search

Our updated search identified a total of 13 reports relating to 12 trials (Buchanan 2010; de Buman 1987; Lachmann 2011; Mallol 1991; Martius 1973; Mendez Velarde 2010; Msika 2002; Ortega 1985; Osman 2008; Puder 1965; Taavoni 2011; Wierrani 1992). Eight new potential trials for inclusion were identified (Buchanan 2010; de Buman 1987; Lachmann 2011; Mendez Velarde 2010;

Msika 2002; Ortega 1985; Osman 2008; Taavoni 2011) in addition to the four studies (Mallol 1991; Martius 1973; Puder 1965; Wierrani 1992) included in the previous version of this review (Young 1996). All of the trials were retrieved via the search of the Cochrane Pregnancy and Childbirth Group Trials Register with the exception of two studies (Lachmann 2011; Msika 2002). Msika 2002 was found from searching reference lists of retrieved studies and Lachmann 2011 via communication with Expanscience Laboratories in France during our attempts to get more information on Msika 2002. Other searches did not yield any further potentially eligible studies.

This updated review includes six studies (involving 800 women). Two additional trials (Lachmann 2011; Ortega 1985) are awaiting classification. Despite translating the paper, there was insufficient information on the randomisation process to judge if the study by Ortega 1985 was eligible for inclusion and attempts to contact the authors have been unsuccessful (see Studies awaiting classification). We are awaiting the translated report of Lachmann 2011 from Expanscience Laboratories (France).

2.7.1.2 Included studies

This update includes four (Buchanan 2010; de Buman 1987; Osman 2008; Taavoni 2011) new studies bringing the total number of included studies to six (involving a total of 800 women) (Buchanan 2010; de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011; Wierrani 1992) (see Characteristics of included studies).

Included studies were undertaken in Germany (de Buman 1987), Spain (Mallol 1991), Austria (Wierrani 1992), West Indies (Buchanan 2010), Lebanon (Osman 2008) and Iran (Taavoni 2011) and were conducted mainly in antenatal clinics and medical centres.

Two studies compared topical preparations with active ingredients with placebo, that is Trofolastin (which contains Centella asiatica extract, alpha tocopherol and collagen-elastin hydrolysates) versus placebo cream (Mallol 1991) and cocoa butter lotion versus placebo lotion (Osman 2008). Two studies compared topical preparations with active ingredients with no treatment, that is olive oil versus no treatment (Taavoni 2011) and Verum ointment (which contains vitamin E,

essential free fatty acids (vitamin F), panthenol, hyaluronic acid, elastin and menthol) versus no treatment (Wierrani 1992). One study compared topical preparations with active ingredients with other topical preparations with active ingredients, that is cocoa butter cream versus a similar cream with vitamin E and other constituents but without cocoa butter (Buchanan 2010). Finally, one study included two intervention groups and a placebo group; topical preparations with active ingredients were compared with other topical preparations with active ingredients, and topical preparations with active ingredients were compared with placebo, that is Alphastria cream (which contains hyaluronic acid, vitamin A, vitamin E, allantoin, calcium pantothenate) versus a cream with vitamins and excipients, and Alphastria cream and cream with vitamins and excipients versus a cream with excipients only (de Buman 1987).

2.7.1.3 Excluded studies

For this update, we have added two new excluded studies (Mendez Velarde 2010; Msika 2002) bringing the total number of excluded studies to four (Martius 1973; Mendez Velarde 2010; Msika 2002; Puder 1965) (see Characteristics of excluded studies).

2.7.2 Risk of bias in included studies

We assessed the risk of bias in the included studies (Figure 2.1; Figure 2.2). Overall, the studies were at low or unclear risk of bias across most domains (Figure 2.1). No study was at low risk of bias across all seven domains, while three studies (Buchanan 2010; Mallol 1991; Osman 2008) were at low risk of bias across five of the seven domains and one study (Taavoni 2011) was at low risk of bias across four of the seven domains. All of the included studies were at unclear risk of bias for allocation concealment except for Wierrani 1992, which was at high risk of bias (Figure 2.2). Details of risk of bias within domains and across studies are given below.

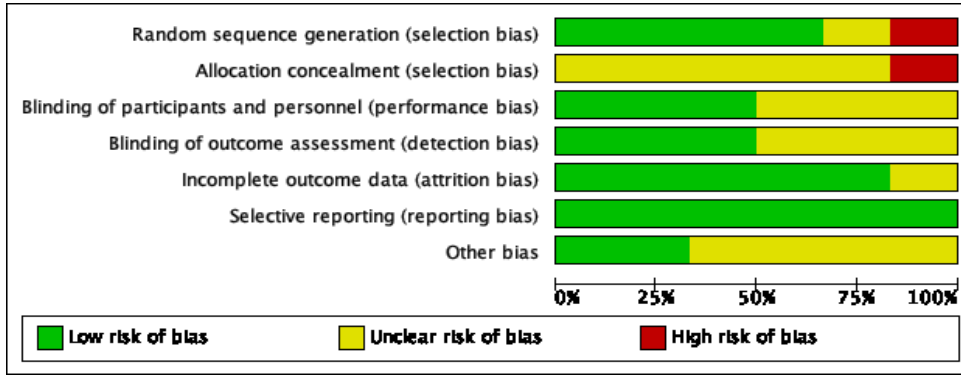


Figure 2.1 Risk of bias graph

Review authors' judgements about each risk of bias item presented as percentages across all included studies.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Buchanan 2010	+	?	+	+	+	+	?
de Buman 1987	?	?	?	?	+	+	+
Malloi 1991	+	?	+	+	+	+	?
Osman 2008	+	?	+	+	+	+	?
Taavoni 2011	+	?	?	?	+	+	+
Wierani 1992	-	-	?	?	?	+	?

Figure 2.2. Risk of bias summary

Review authors' judgements about each risk of bias item for each included study.

2.7.2.1 Allocation (selection bias)

Four of the six included studies (Buchanan 2010; Mallol 1991; Osman 2008; Taavoni 2011) were at low risk of bias in random sequence generation, one was at unclear risk (de Buman 1987) and one was at high risk (Wierrani 1992). de Buman 1987 was at unclear risk due to insufficient information to judge the risk of bias, while Wierrani 1992 was at high risk of bias as alternate day allocation was used to enrol women in the treatment groups. On uneven dates women were included in the treatment group and on even dates women were enrolled in the no treatment group.

Five of the six included studies (Buchanan 2010; de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011) were at unclear risk of bias in allocation concealment and Wierrani 1992 was at high risk of bias. Two of the six studies, with unclear risk of bias for allocation concealment (Buchanan 2010; de Buman 1987), had insufficient information to judge the risk of bias while three of the other four (Mallol 1991; Osman 2008; Taavoni 2011) reported insufficient information on how women were allocated to the study groups. In Wierrani 1992 randomisation was performed according to day of treatment (that is, alternate days).

2.7.2.2 Blinding (performance bias and detection bias)

Three of the six included studies (Buchanan 2010; Mallol 1991; Osman 2008) were at low risk of bias in blinding of participants and personnel and in blinding of outcome assessment. Three of the six included studies were at unclear risk (de Buman 1987; Taavoni 2011; Wierrani 1992) due to insufficient or no information reported to permit judgement of risk of bias for performance or detection bias.

2.7.2.3 Incomplete outcome data (attrition bias)

Five of the six included studies (Buchanan 2010; de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011) were at low risk of bias for incomplete outcome data and one study was at unclear risk (Wierrani 1992). In the study by Wierrani 1992 the number of women randomised was not given, only the number of women included in the analysis. In the Mallol 1991 trial report it was not stated explicitly how many women were randomised, but it was stated that 'The assay was carried out on 100 pregnant women'. They reported total 'valid' cases as 41

for intervention (active cream) and 39 for placebo. Assuming 100 women were randomised, then 20 women were excluded from the analysis overall, giving 20% incomplete outcome data (low risk) (see Characteristics of included studies).

2.7.2.4 Selective reporting (reporting bias)

All of the six included studies (Buchanan 2010; de Buman 1987; Malloy 1991; Osman 2008; Taavoni 2011; Wierrani 1992) were at low risk of bias in selective reporting.

2.7.2.5 Other potential sources of bias

We judged two of the six included studies (de Buman 1987; Taavoni 2011) to be at low risk of other biases, and four studies (Buchanan 2010; Malloy 1991; Osman 2008; Wierrani 1992) at unclear risk of other biases. In the studies by Malloy 1991 and Wierrani 1992, the number of women randomised to each group were not stated explicitly, while in the studies by Buchanan 2010; and Osman 2008 the researchers raised concerns regarding intervention fidelity. Buchanan 2010: 68 stated '...that it was not possible to verify that the patients were using the cream as instructed or whether they were sharing the cream or using other creams', while Osman 2008: 1142 stated that 'Reports of compliance varied greatly for each patient and assessors reported that women may have been telling them what they wanted to hear when they asked about compliance'. They acknowledged that compliance may have been an issue in the study but that use of the study lotion reflected general population use (Osman 2008: 1142). Therefore, we judged Buchanan 2010 and Osman 2008 to be at unclear risk of other biases.

The source of funding was not identified for all but two of the included studies, Osman 2008 where both intervention and placebo lotions were provided by ET Browne Drug Company, Inc and Taavoni 2011 where the authors declared no funding source.

2.7.3 Effects of interventions

This updated review now includes data from six studies involving 800 women.

2.7.3.1 *Topical preparations with active ingredients compared with placebo or no treatment (five trials and 474 women)*

This comparison includes data from the following studies: de Buman 1987; Mallof 1991; Osman 2008; Taavoni 2011; Wierrani 1992.

2.7.3.1.1 Primary outcome (five trials and 474 women)

There was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment (average risk ratio (RR) 0.74; 95% confidence interval (CI) 0.53 to 1.03; five trials, 474 women; random-effects model, $\text{Tau}^2 = 0.09$, $I^2 = 65\%$) (Analysis 1.1, 2.16).

Results were consistent with the main effects when we performed a sensitivity analysis, excluding the Wierrani 1992 study which was at high risk of bias for random sequence generation and allocation concealment (average RR 0.81; 95% CI 0.60 to 1.10; four trials, 424 women; random-effects model, $\text{Tau}^2 = 0.05$, $I^2 = 57\%$).

2.7.3.1.2 Secondary outcome (two trials and 255 women)

There was no statistically significant average mean difference in the severity of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment (standardised mean difference (SMD) -0.31; 95% CI -1.06 to 0.44; two trials, 255 women; random-effects model, $\text{Tau}^2 = 0.26$, $I^2 = 87\%$) (Analysis 1.2, 2.16). The heterogeneity between the two trials was large and therefore the average result may not be meaningful, that is it is unlikely that such an average effect would be found in real life (the effect could be similar to one or other of the trials, but unlikely to be an 'average' of both).

2.7.3.2 *Topical preparations with active ingredients compared with other topical preparations with active ingredients (two trials and 305 women)*

This comparison included two studies with 305 women (Buchanan 2010; de Buman 1987). Buchanan 2010 compared cocoa butter cream, which contained

a variety of constituents for example 25% cocoa butter, glycerin, isopropyl palmitate, hydrolysed collagen, hydrolysed elastin and tocopheryl acetate (vitamin E) with a cream identical to the intervention cream but without the 25% cocoa butter. In the second trial (de Buman 1987), Alphastria cream (containing hyaluronic acid, vitamin A, vitamin E, allantoin, calcium pantothenate) was compared with a cream with vitamins and excipients.

2.7.3.2.1 Primary outcome

There was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients (average RR 0.51; 95% CI 0.16 to 1.60; two trials, 305 women; random-effects model, $\text{Tau}^2 = 0.53$, $I^2 = 74\%$) (Analysis 2.1, 2.16).

2.7.3.2.2 Secondary outcome (one trial and 206 women)

There was no statistically significant mean difference in the severity of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients (mean difference (MD) -0.20; 95% CI -0.53 to 0.13; one trial, 206 women; heterogeneity not applicable) (Analysis 2.2, 2.16).

2.8 Discussion

Stretch marks are a very common connective tissue change that can occur in pregnancy (Lawley 1999), affecting between 50% and 90% (Osman 2007) of women and remaining as silvery scar lines on the skin. They are an unwanted consequence of pregnancy, impacting on women's perception of themselves (Osman 2008) and their quality of life (Salter 2006), and are thus of significant concern to women of child bearing age. There are many products of unproven effectiveness on the market (Burrows 2010), which are tried by many women. This review assessed the effects of topical preparations on the prevention of stretch marks in pregnancy.

The review includes six trials (involving a total of 800 women) conducted mainly in antenatal clinics and medical centres in varied geographical locations. It should be noted that the random-effects model summaries presented are the average effects found for both the development and severity of stretch marks.

The use of the random-effects model is based on the assumption that the treatment effect will be different across the studies due to heterogeneity between the studies. It therefore calculates the average of all the treatment effects across the trials (Riley 2011) and thus may not be the actual effect in any of the included studies.

2.8.1 Summary of main results

2.8.1.1 Topical preparations with active ingredients compared with placebo or no treatment

This review found that there was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment. All studies were relatively small, with four of the five trials including less than 100 women (de Buman 1987; Malloy 1991; Taavoni 2011; Wierrani 1992) and one trial by Osman 2008 including less than 200 women as reflected in the narrower confidence interval.

Trials differed in relation to the timing of commencement of the topical applications. Three of the five studies included women presenting in trimester one (de Buman 1987; Malloy 1991; Osman 2008) while Taavoni 2011 and Wierrani 1992 recruited women at 18 to 20 weeks and 20 weeks' gestation, respectively. All trials recruited women prior to the third trimester when stretch marks usually occur (Atwal 2006; Cunningham 2010).

Parity of the women participating in the included trials also differed. Malloy 1991 included both multigravidae and primigravidae, while Taavoni 2011 and Osman 2008 included primigravidae women only in their studies. The study by de Buman 1987 identifies that one case of stretch marks occurred in a twin pregnancy in the intervention group receiving with active ingredients (Group A). No information on parity was given for the other included study (Wierrani 1992). It is likely, therefore, that some of the women in some trials had stretch marks from an earlier pregnancy, while the inclusion of some women with a multiple pregnancy may have increased the likelihood of those women developing stretch marks. In a multiple pregnancy there may be extra strain and, as

suggested by Watson 1998, extra strain or stretching could be sufficient to tear the elastic fibre network, resulting in the formation of striae.

While topical preparations varied, many of them included some common ingredients. For example, two trials (de Buman 1987; Wierrani 1992) included hyaluronic acid in the active topical preparation (that is Alphastrria cream and Verum ointment, respectively). Hyaluronic acid has been identified as stimulating fibroblastic activity (de Buman 1987), and fibroblasts are key cells in maintaining tissue structure and tone. A number of the preparations also contained vitamin E (de Buman 1987; Mallo1 1991; Osman 2008; Taavoni 2011; Wierrani 1992), which promotes the development of the intracellular substance (Wierrani 1992) and is a known antioxidant used in many skin products. However, it is not evident which, if any, of these ingredients could exert a possible preventative action for the formation of striae.

We found no statistically significant average difference in the severity of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment. Data on the severity of stretch marks were only available in two of the five included studies (Mallo1 1991; Osman 2008). In the study by Osman 2008, severity was assessed by trained assessors using a validated tool, while Mallo1 1991 refers to using 'an arbitrary score 0 = no striae, 1 = few and thin striae, 2 = many thin striae or few thick striae, and 3 = many thick striae'. Neither study refers to inter-rater reliability and therefore it is unclear how errors in measurement were minimised.

From a clinical perspective while none of the topical products in the included trials (Alphastrria cream, Trofolastin, cocoa butter lotion, olive oil, and Verum), with the exception of cocoa butter lotion (Osman 2008) and olive oil (Taavoni 2011), appear to be widely available, some women may indeed be applying cocoa butter lotion or olive oil in the hope of preventing the development of stretch marks. However, this review found no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment. Therefore, based on this review it is not possible to recommend any of the preparations.

2.8.1.2 Topical preparations with active ingredients compared with other topical preparations with active ingredients

This review found no statistically significant average difference in the development of stretch marks or in the severity of stretch marks in women who received topical preparations with active ingredients compared with other topical preparations with active ingredients in trials (Buchanan 2010; de Buman 1987) involving small numbers of participants. In the trial by Buchanan 2010, the topical preparations contained multiple ingredients including isopropyl palmitate (emollient), propylene glycol isostearate (emollient), PPG-15 stearyl ether (1-octadecoxypropan-2-ol) (emollient), hydrolysed collagen, hydrolysed elastin and tocopheryl acetate (vitamin E). Preparations differed only in the addition of cocoa butter (25%). In the study by de Buman 1987, the intervention preparation contained several ingredients (hyaluronic acid, vitamin A, vitamin E, allantoin, calcium pantothenate) while the comparison preparation contained vitamins in addition to the excipient.

Data on the severity of stretch marks were only available in one of the two included studies (Buchanan 2010). In this study, Buchanan 2010 assessed the severity of stretch marks using the '4 quadrant technique of Davey (1972) with a simplification by Fletcher (unpublished)'. The researchers outline the process of ensuring that assessments were reliable and state that checking of researchers' assessments was undertaken with the aid of digital photographs until such time as 'a consensus of the striae scoring system by different observers' was achieved.

2.8.2 Overall completeness and applicability of evidence

Based on the findings of this review, which included six small trials, it is not possible to recommend any of the preparations for the prevention of stretch marks in pregnancy.

2.8.3 Quality of the evidence

We assessed the risk of bias of included trials as 'low risk' for random sequence generation, blinding of participants and personnel, and in blinding of outcome assessment, complete outcome data and selective reporting in only three of the six trials (Buchanan 2010; Malloy 1991; Osman 2008). We assessed one study

(Wierrani 1992) as at high risk of bias for random sequence generation and allocation concealment. Overall findings are not sensitive to exclusion of this study.

The quality of evidence is also impacted on by the possible imprecision of the study results due to the small numbers of participants and events, and their wide confidence intervals. This is particularly evident in some of the trials (Taavoni 2011; Wierrani 1992).

2.8.4 Potential biases in the review process

We have taken every step to ensure that there are no potential biases in the review processes. We undertook a systematic and comprehensive search without language restrictions and adhered to best practice in undertaking the review. Three authors (MB, DD and GY) independently assessed each study and agreed the studies that were for inclusion in the review and those that were for exclusion. Data extraction was also completed independently and checked for accuracy by three authors (MB, DD and GY). We contacted authors from two trials (Horace Fletcher for Buchanan 2010; P Msika for Msika 2002) for further information (see notes in Characteristics of included studies and Characteristics of excluded studies). All data were entered into the Review Manager software (RevMan 2011) and checked for accuracy by three authors (MB, DD and GG). Consequently, biases in the review processes are unlikely.

2.9 Authors' conclusions

2.9.1 Implications for practice

We found no high-quality evidence to support the use of any of the topical preparations in the prevention of stretch marks during pregnancy.

2.9.2 Implications for research

There is a clear need for robust, methodologically rigorous randomised trials involving larger sample sizes to evaluate the effects of topical preparations on the development of stretch marks in pregnancy.

Preparations possibly worth pursuing might include Trofolastin (Mallol 1991), Alphastrin (de Buman 1987), and Verum (Wierrani 1992). The latter two preparations contain hyaluronic acid, which has been identified as stimulating

fibroblastic activity (de Buman 1987) and therefore maintaining tissue structure and tone. In addition, it is important that preparations commonly used by women to prevent and treat stretch marks are evaluated within the context of robust, methodologically rigorous and adequately powered randomised trials.

2.10 Acknowledgements

We would like to acknowledge the assistance of Luciana Figuera, Charlese Allen, Caroline Summers and Gloria Avalos who kindly did some translations of non-English language papers for us.

We thank David Jewell for his contribution to the original version of this review. As part of the pre-publication editorial process, this review has been commented on by four peers (an editor and three referees who are external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

2.11 Declarations of interest

None known.

2.12 Differences between protocol and review

We have separated outcomes into primary and secondary outcomes. The outcome from the previous version of this review (presence of stretch marks) is our primary outcome and we have added a new secondary outcome (severity of stretch marks). The methods have been updated to reflect the latest *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We have also changed the title of the review from 'Creams for preventing stretch marks in pregnancy' to 'Topical preparations for preventing stretch marks in pregnancy'.

For this update we restructured the review comparisons to compare: (1) topical preparations with active ingredients compared with placebo or no treatment, and (2) topical preparations with active ingredients compared with other topical preparations with active ingredients. This is in contrast to comparing active creams with placebo or with no treatment, as presented in Young 1996.

2.13 Published notes

In the next update of this review we will carry out subgroup analysis by parity (nulliparous versus multiparous women), and our criteria for sensitivity analysis will incorporate trials at high risk of bias for blinding. We will also detail how the primary (presence of stretch marks) and secondary (severity of stretch marks) outcomes are measured and by whom. We will include a discussion around if and how included studies have addressed confounding or other risk factors.

2.14 Index terms

2.14.1 Medical subject headings (MeSH)

Cosmetics; Dermatologic Agents [*administration & dosage]; Ointments; Randomised Controlled Trials as Topic; Skin; Striae Distensae [*prevention & control].

2.14.2 MeSH check words

Female; Humans; Pregnancy.

Third-Party Copyright: See Appendix 1 for the Copyright Clearance Agreement permitting inclusion of this paper in this thesis.

2.15 Characteristics of studies

Characteristics of included studies

Table 2.1 Characteristics of included studies: Buchanan 2010

Methods	<p>Study design: randomised controlled trial.</p> <p>Duration of study: not stated.</p>
Participants	<p>Setting: antenatal clinic in the University Hospital, of the West Indies, Mona, Kingston, Jamaica.</p> <p>Inclusion criteria: '...primigravidas and multigravidas with no stretch marks' enrolled before 16 weeks' gestation.</p> <p>Exclusion criteria: 'Women who were taking steroids and women with medical illnesses that caused stretch marks...'; 'Women with a twin pregnancy or polyhydramnios...'</p> <p>Participants randomised: 150 women were randomly assigned to the intervention (cocoa butter group) and 150 women to the comparison group.</p>
Interventions	<p>Experimental: application of 473 ml of cocoa butter cream containing cocoa butter cream (25%), water, glycerin (skin conditioner), distearyltrimonium chloride (skin conditioner), isopropyl palmitate (emollient), cetearyl alcohol (stabilizer), propylene glycol isostearate (emollient), PPG-15 stearyl ether (1-octadecyloxypropan-2-ol) emollient, hydrolysed collagen, hydrolysed elastin, tocopheryl acetate (vitamin E), dimethicone (skin conditioner). Half a cap full of cream was applied to the 4 abdominal quadrants daily (until used up).</p> <p>Control: cream which was identical to the intervention cream with the exception of addition of the 25% cocoa butter.</p> <p>We did not consider this a true placebo as it contains other active ingredients like vitamin E.</p>
Outcomes	<p>Outcomes considered in the review:</p> <ul style="list-style-type: none"> • presence of stretch marks; • severity of stretch marks.
Notes	<p>'...number of stretch marks was assessed using the 4 quadrant technique of Davey (1972) with a simplification by Fletcher (unpublished), which involved using a pictorial chart to aid the providers in using Davey's technique.</p>

	<p>Digital photographs were taken of the abdomen of some women...'. 1 of the study authors Horace Fletcher confirmed that the percentage of women who developed striae was erroneously included in the enrolment data and that none of the woman had striae at enrolment.</p>
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Table 2.2 Risk of bias table: Buchanan 2010

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'The women were assigned cocoa butter cream or placebo using a table of random numbers...'.
Allocation concealment (selection bias)	Unclear risk	Insufficient information on which to judge risk of bias.
Blinding of participants and personnel (performance bias)	Low risk	'The women and the researchers were blinded to the allocation'.
Blinding of outcome assessment (detection bias)	Low risk	'...The researchers were blinded to the allocation'.
Incomplete outcome data (attrition bias)	Low risk	<p>Development of striae In the intervention arm, 30 women were excluded from analysis (lost to follow up n = 28, discontinued intervention due to rash n =2). The 2 women who discontinued treatment were returned to group denominator (n = 122). 18.7% incomplete outcome data.</p> <p>In the control arm 28 women were excluded from analysis (lost to follow up n = 27, discontinued intervention due to skin rash n = 1). The 1 woman who discontinued due to skin rash (n = 1) was restored to the group denominator (n = 123). 18% incomplete outcome data.</p>

		<p>Severity of striae Intervention group: data available for 101 of the 120 women. Missing data = 15.8%. Control group: data available for 105 of the 122 women. Missing data = 13.9%.</p>
Selective reporting (reporting bias)	Low risk	The protocol was not available and following clarification from the authors all the outcomes stated in the methods section were reported adequately in the results.
Other bias	Unclear risk	<p>Intervention integrity Authors state '...that it was not possible to verify that the patients were using the cream as instructed or whether they were sharing the cream or using other creams'.</p> <p>Funding source No funding source identified.</p>

Table 2.3 Characteristics of included studies: de Buman 1987

Methods	<p>Study design: randomised controlled trial.</p> <p>Duration of study: not stated (states women were monitored over 10 months).</p>
Participants	<p>Setting: Obstetrical and Gynecological Clinic in a Hospital in Cantonal, Fribourg.</p> <p>Inclusion criteria: women at the beginning of the third month of pregnancy.</p> <p>Exclusion criteria: not stated.</p> <p>Participants randomised: 90 women randomised: 30 women to each group (group A - Alphastrria cream n = 30; group B - cream with vitamins and excipients n = 30; group C - placebo with just excipient n = 30).</p>
Interventions	<p>Experimental: 'Application of 10cm (3g) Alphastrria cream (contains hyaluronic acid, Vitamin A, Vitamin E, allantoin, calcium pantothenate)...' daily to the thighs, abdomen and chest. 'The cream was massaged gently into each area for a few minutes each'.</p>

	Control: application of 1 of 2 creams: 1 containing vitamins and excipients, and 1 containing excipients only.
Outcomes	Outcomes considered in the review: <ul style="list-style-type: none"> • presence of stretch marks.
Notes	As group B contains vitamins and excipients we compared group A (Alphastrria cream) with group B (vitamins and excipients) and then group A and B with group C (excipients only) [MB].

Table 2.4 Risk of bias table: de Buman 1987

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	States that a randomised 'predetermined code system' was used. Insufficient information on which to judge risk of bias.
Allocation concealment (selection bias)	Unclear risk	Treatments were administered anonymously. Insufficient information on which to judge risk of bias.
Blinding of participants and personnel (performance bias)	Unclear risk	While treatments were administered anonymously and the study is reported as a double blind study no detail is given on who was blinded. Insufficient detail on which to judge risk of bias.
Blinding of outcome assessment (detection bias)	Unclear risk	Insufficient information on which to judge risk of bias.
Incomplete outcome data (attrition bias)	Low risk	In the control arm (group C) (n = 30), 3 women were excluded from the analysis (withdrawals due to intolerance, allergy, and miscarriage). We restored these 3 women to the group denominator (n = 30).
Selective reporting (reporting bias)	Low risk	The protocol was not available but all the outcomes stated in the methods section were reported adequately in the results.
Other bias	Low risk	None identified.

		<p>Funding source No funding source identified.</p>
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Table 2.5 Characteristics of included studies: MalloI 1991

Methods	<p>Study design: randomised controlled trial.</p> <p>Duration of study: 30 months.</p>
Participants	<p>Setting: antenatal clinic in Barcelona.</p> <p>Inclusion criteria: women in the first 12 weeks of pregnancy.</p> <p>Exclusion criteria: none stated.</p> <p>Participants randomised: not stated, study does not state how many were randomised to the intervention and control group. Total valid cases are reported as 41 in the active cream group and 39 in the placebo group.</p>
Interventions	<p>Experimental: application of active cream (Trofolastin) (n = 41) which '...was a marketed product...' containing Centella asiatica extract and alpha- tocopherol and collagen - elastin hydrolysates. Application of active cream (Trofolastin) (n = 41) containing Centella asiatica extract and alpha- tocopherol and collagen - elastin hydrolysates. 'Product applied daily from the end of the 12th week of pregnancy to the day of labour on abdomen, breasts, buttocks and hips'.</p> <p>Control/Comparison intervention: placebo cream containing only the excipient part of the active cream and '...identical in colour, flavour and texture'.</p> <p>'Product applied daily from the end of the 12th week of pregnancy to the day of labour on abdomen, breasts, buttocks and hips'.</p>
Outcomes	<p>Outcomes considered in the review:</p> <ul style="list-style-type: none"> • presence of stretch marks; • severity of stretch marks.

Notes	Striae were evaluated using '...an arbitrary score 0 = no striae, 1 = few and thin striae, 2 = many thin striae or few thick striae, and 3 = many thick striae'.
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Table 2.6 Risk of bias table: Malloy 1991

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Probably adequate as 'randomised code numbers' were used.
Allocation concealment (selection bias)	Unclear risk	No details given as to how women were allocated to the 2 groups.
Blinding of participants and personnel (performance bias)	Low risk	Both intervention and control '...creams were identical in colour, flavour and texture' and were '...marked with a randomised code number'. Codes were not opened until the data collection was complete.
Blinding of outcome assessment (detection bias)	Low risk	Codes were not opened until the data collection was complete.
Incomplete outcome data (attrition bias)	Low risk	States 'The assay was carried out on 100 pregnant women' but does not state explicitly how many women were randomised. Total 'valid' cases are noted as 41 for intervention (active cream) and 39 for placebo. Assuming 100 women randomised, then 20 women were excluded from the analysis overall, due to abortion (n = 1) and 'several address changes' (n = 19). 20% incomplete outcome data.
Selective reporting (reporting bias)	Low risk	The protocol was not available but all the outcomes stated in the methods section were reported in the results.
Other bias	Unclear risk	Number of women randomised into each group is not given. States 'The assay was carried out on 100 pregnant women' but does

		not state explicitly how many women were randomised’.
		Funding source
		No funding source identified.

Table 2.7 Characteristics of included studies: Osman 2008

Methods	<p>Study design: randomised controlled trial.</p> <p>Duration of study: November 2004 to July 2006 (from study protocol).</p>
Participants	<p>Setting: 4 medical centres in Lebanon.</p> <p>Inclusion criteria: nulliparous women with a singleton pregnancy presenting to the clinic in trimester 1, ‘...between November 2004 and December 2005.</p> <p>Exclusion criteria: women with a ‘...known hypersensitivity to cocoa butter...’ or the lotion components.</p> <p>Participants randomised: 105 women were randomised to the intervention group (cocoa butter lotion) and 105 to the placebo lotion group.</p>
Interventions	<p>Experimental: application of a thin layer of a commercially available lotion containing cocoa butter and tocopheryl acetate (vitamin E) to the abdomen, breasts and thighs once daily, from ‘...between 12 and 18 completed weeks of gestation...’ to delivery.</p> <p>Control: placebo lotion with no active ingredients, which ‘...was made to look, smell, and feel the same as the study lotion...’.</p>
Outcomes	<p>Outcomes considered in the review:</p> <ul style="list-style-type: none"> • presence of stretch marks; • severity of stretch marks.
Notes	Trained assessors (n = 5) completed ‘... the data collection tools and...’ assessed ‘...the severity of SG based on a

	<p>scale developed and previously validated by the authors (Osman et al 2007). 'The scale took ...consideration the density and width of striae to estimate the surface area of the body part affected'.</p> <p>'...funding by the Center for Research on Population and Health at the American University of Beirut, Lebanon, with generous support from the Wellcome Trust' '...and the University Research Board (URB) at the American University of Beirut, Beirut, Lebanon'.</p>
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Table 2.8 Risk of bias table: Osman 2008

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'Randomization was conducted using a computer-generated random number table'.
Allocation concealment (selection bias)	Unclear risk	Not stated how participants were allocated to each of the 2 groups.
Blinding of participants and personnel (performance bias)	Low risk	'...researchers, study participants and their physicians were blinded to the lotion assignment'. '...Codes for the study and placebo lotions were opened after the final assessment of the last randomised woman'.
Blinding of outcome assessment (detection bias)	Low risk	'Assessors... were blinded as to the lotion assignment'. '...Codes for the study and placebo lotions were opened after the final assessment of the last randomised woman'.
Incomplete outcome data (attrition bias)	Low risk	<p>In the intervention arm (n = 105), 14 women were excluded from analysis (remaining n = 91) due to abortion n = 3, withdrew n = 2, lost to follow up n = 9. We restored n = 3 (abortion) to the group denominator (n = 94). Equates to 10.5% incomplete outcome data in the intervention group.</p> <p>In the control arm (n = 105), 21 women were excluded from analysis (remaining n = 84) due to abortion n = 5, withdrew n = 6, lost to follow up n = 9, allergic reaction n = 1). We restored</p>

		n = 6 (abortion, and allergic reaction) to the group denominator (n = 90). Equates to 14.3% incomplete outcome data in the control arm.
Selective reporting (reporting bias)	Low risk	Study protocol is available and all outcomes have been reported as planned. However a secondary outcome (severity of striae) is reported in the study which is not identified as such in the protocol. Study protocol reports that women will be asked to give their assessment of the presence or absence of striae and their severity'. Trained assessors assessed the severity of striae in the study.
Other bias	Unclear risk	<p>Intervention integrity</p> <p>Authors state that 'Reports of compliance varied greatly for each patient and assessors reported that women may have been telling them what they wanted to hear when they asked about compliance'.</p> <p>Funding source</p> <p>Both study and placebo lotions were provided by ET Browne Drug Company, Inc.</p>

Table 2.9 Characteristics of included studies: Taavoni 2011

Methods	<p>Study design: randomised controlled trial.</p> <p>Duration of study: not stated.</p>
Participants	<p>Setting: Department of Obstetrics and Gynaecology, Lolagar Hospital and Shahid Akbarabadi Hospital, Iran University of Medical Sciences, Tehran, Iran.</p> <p>Inclusion criteria: '...nulliparous women aged between 20 and 30 years old, in their 18th to 20th week of gestation with body mass indices ranging between BMI 18.5--25'.</p> <p>Exclusion criteria: '...included: [polyhydramnios], occurrence of dermal discuses, administration of corticosteroids, application of other ointments on the abdominal area, lack of compliance with the study protocol'.</p>

	Participants randomised: 35 women were randomised to the intervention group and 35 women to the control group.
Interventions	Experimental: application of '...olive oil topically onto...' the '... abdominal skin ...twice a day...for eight weeks, ...without massaging'. Application continued until week 28. Control: no treatment.
Outcomes	Outcomes considered in this review: <ul style="list-style-type: none"> • presence of stretch marks.
Notes	

Table 2.10 Risk of bias table: Taavoni 2011

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'Subjects were randomised using a computer-generated randomization table to either the control or intervention group'.
Allocation concealment (selection bias)	Unclear risk	No detail given as to how women were allocated to the 2 groups.
Blinding of participants and personnel (performance bias)	Unclear risk	No information given on blinding in the study.
Blinding of outcome assessment (detection bias)	Unclear risk	No information given on blinding of outcome assessment.
Incomplete outcome data (attrition bias)	Low risk	None (percentages in Table 2, p. 168 suggest no losses to follow up).
Selective reporting (reporting bias)	Low risk	The protocol was not available but the outcome stated in the methods section was reported adequately in the results.
Other bias	Low risk	None identified.

		Funding source Authors declared no funding source.
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Table 2.11 Characteristics of included studies: Wierrani 1992

Methods	Study design: quasi-randomised controlled trial. Duration of study: not stated.
Participants	Setting: antenatal clinic in Vienna. Inclusion criteria: pregnant women > 18 and < 35 years. Exclusion criteria: history of metabolic disorders; long term medication use for example corticosteroid use; alcohol abuse; history suggestive of a complicated pregnancy. Participants randomised: not stated. States that '24 participants in the Verum group and 26 in the control group could be included in the final evaluation'.
Interventions	Experimental: application of an ointment (Verum, which contained: vitamin E, essential free fatty acids (vitamin F), panthenol, hyaluronic acid, elastin and menthol. Frequency of application not stated. Control: no treatment.
Outcomes	Outcomes considered in the review: <ul style="list-style-type: none"> • presence of stretch marks.
Notes	

Table 2.12 Risk of bias table: Wierrani 1992

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Alternate day allocation. 'On days with uneven dates the pregnant women were included in the Verum (treatment) group'. Women enrolled on even dates were given no treatment.

Allocation concealment (selection bias)	High risk	Allocation was performed according to day of treatment (see above).
Blinding of participants and personnel (performance bias)	Unclear risk	Insufficient information to judge risk of bias.
Blinding of outcome assessment (detection bias)	Unclear risk	Insufficient information to judge risk of bias.
Incomplete outcome data (attrition bias)	Unclear risk	Number of women randomised not given. States that '24 participants in the Verum group and 26 in the control group could be included in the final evaluation'.
Selective reporting (reporting bias)	Low risk	The protocol was not available but all the outcomes stated in the methods section were reported adequately in the results.
Other bias	Unclear risk	Number of women randomised into each group is not given. States that '24 participants in the Verum group and 26 in the control group could be included in the final evaluation'. Funding source No funding source identified.

Characteristics of excluded studies

Table 2.13 Characteristics of excluded studies: Martius 1973

Reason for exclusion	Not stated whether this study was randomised. Review authors believe it was not and attempts to contact the author have failed.
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Table 2.14 Characteristics of excluded studies: Mendez Velarde 2010

Reason for exclusion	The study does not fit the criteria for inclusion in the review. It compared the application of a topical cream on wet skin versus its application on dry skin. Nor did it have a placebo or a no treatment group.
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Table 2.15 Characteristics of excluded studies: Msika 2002

Reason for exclusion	The study is at unclear risk of bias in five of the seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment and selective reporting. While initial attempts to contact the authors were unsuccessful, eventual contact was made with Expanscience Laboratories. However, it was not possible to get further information on the trial.
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Table 2.16 Characteristics of excluded studies: Puder 1965

Reason for exclusion	Not randomised.
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Characteristics of studies awaiting classification**Table 2.17 Characteristics of studies awaiting classification:
Lachmann 2011**

Methods	Study design: unclear. Duration of study: not stated.
Participants	Setting: not stated. Inclusion criteria: women between '16-19 weeks of amenorrhea...'. 'Primipare were selected according [to] factors which have been associated with the SG occurrence'. Exclusion criteria: not stated. Participants randomised: unclear.
Interventions	Experimental: unclear. Control: unclear. Study involved the application of a cream which 'contains patented ingredients: lupeol, natural biopeptides and arabinogalactane which counteract tissue inflammation and stimulate extracellular matrix (ECM) remodelling'. 'The cream was applied twice daily during 5 months'.

Outcomes	Outcomes considered in the review: <ul style="list-style-type: none"> • presence of stretch marks.
Notes	Funded by Expanscience Laboratories.

**Table 2.18 Characteristics of studies awaiting classification:
Ortega 1985**

Methods	Study design: unclear. Duration of study: not stated.
Participants	Setting: Obstetrics and Gynaecology Department, Mother-Infant Hospital, Palma de Mallorca. Inclusion criteria: women in the second trimester of pregnancy who were 'not obese (more than 10% overweight)'. Exclusion criteria: not stated. Participants randomised: it is unclear if the women were randomised to the different groups. It states that 146 women were 'distributed into groups': Group I (n = 61) was assigned to the cream with excipients only (placebo), group II (n = 55) was assigned the cream with the active ingredients while group III (n = 30) was assigned to the control arm ['neither instructed to massage nor use a cream'].
Interventions	Experimental: application of an 'L. anti-striae cream', containing 'fitelenos (simulating factors of neo-elastogenesis and transcutaneous penetrating factors)' ...'once or twice a day' ...'on the abdomen, legs and breasts, in a down-up direction following the skin's traction lines' from the 'second trimester' until the puerperium. 'They were advised to undergo a massage once or twice a day each lasting from 5 to 10 minutes'. Participation in exercise is also referred to but no details are given. Control: application of a cream containing excipients only 'once or twice a day', 'on the abdomen, legs and breasts, in a down-up direction following the skin's traction lines' from the 'second trimester' until the puerperium. 'They were advised to undergo a massage once or twice a day

	each lasting from 5 to 10 minutes'. Participation in exercise is also referred to but no details are given. Or no treatment [no massage or cream].
Outcomes	Outcomes considered in the review: <ul style="list-style-type: none">• presence of stretch marks;• severity of stretch marks.
Notes	

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2.16 Data and analyses

Comparison 1: Topical preparations with active ingredients compared with placebo or no treatment

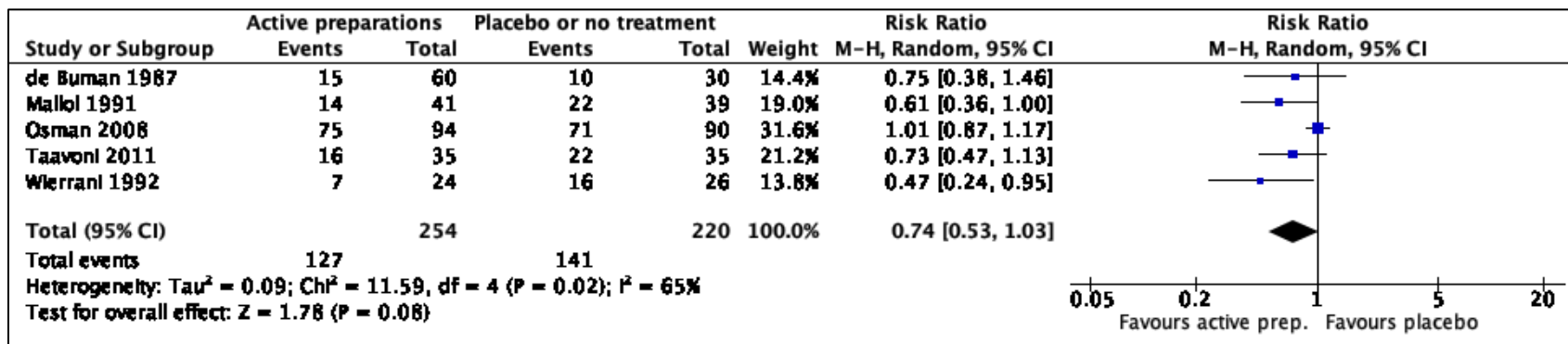
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Presence of stretch marks	5	474	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.53, 1.03]
1.2 Severity of stretch marks	2	255	Std. Mean Difference (IV, Random, 95% CI)	-0.31 [-1.06, 0.44]

Comparison 2: Topical preparations with active ingredients compared with other topical preparations with active ingredient

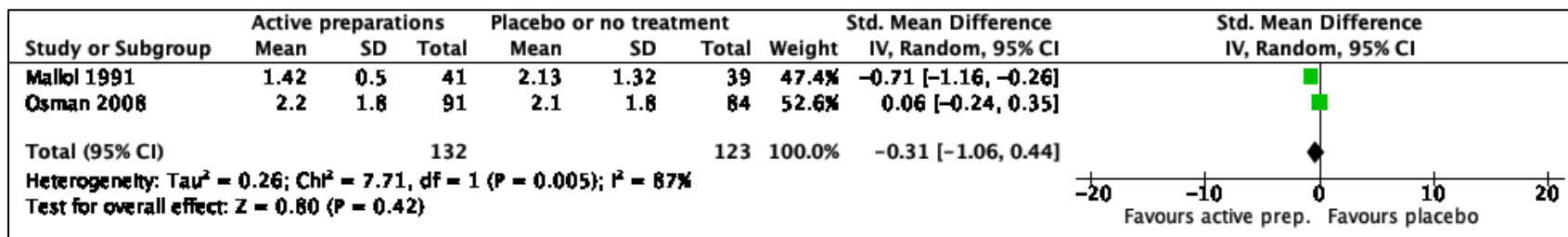
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Presence of stretch marks	2	305	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.16, 1.60]
2.2 Severity of stretch marks	1	206	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.53, 0.13]

Comparison 1: Topical preparations with active ingredients compared with placebo or no treatment

Outcome 1.1: Presence of stretch marks



Outcome 1.2: Severity of stretch marks



2.17 Sources of support

Internal sources

- No sources of support provided.

External sources

- No sources of support provided.

2.18 Feedback

2.19 Appendices

1 Methods used to assess trials included in previous versions of this review

The following methods were used to assess Mallof 1991, Wierrani 1992 in previous versions of this review (Young 1996).

We evaluated trials under consideration for methodological quality and appropriateness for inclusion, without consideration of their results. We processed trial data as described in Clarke 2000.

2.20 Summary of key points

The aim of this chapter was to address question one and determine the current evidence in support of the use of topical preparations for the prevention of striae gravidarum. This was undertaken by means of a Cochrane systematic review and meta-analysis and involved updating substantially the original review 'Creams for preventing stretch marks in pregnancy' (Young & Jewell, 1996). The main findings of the review were that there was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment and that there was no statistically significant average mean difference in the severity of stretch marks. Similarly, there was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients and there was no statistically significant difference in the severity of stretch marks. The review concluded that we found no high-quality evidence to support the use of any of the topical preparations in the prevention of stretch marks during pregnancy and there is a clear need for robust, methodologically rigorous randomised trials involving larger sample sizes to evaluate the effects of topical preparations on the development of stretch marks in pregnancy. Furthermore, that preparations commonly used by women to prevent and treat stretch marks are evaluated within the context of robust, methodologically rigorous and adequately powered randomised trials.

In light of these findings and in particular towards the evaluation of preparations used commonly by women to prevent and treat striae gravidarum, we felt it important to identify what products or preparations are used by women. We did this through a cross-sectional survey, which we report in Chapter 3.

Chapter 3: Paper 2

3.1 Introduction

This chapter presents paper 2; the descriptive cross-sectional survey of women on their use of skin products to prevent or reduce the development of striae gravidarum. It addresses question 2 i.e. What are the topical products used commonly by women during pregnancy to prevent or reduce the development of striae gravidarum? The survey also explored issues around application of the product, cost incurred and influences on women's decisions to use and choice of product.

3.2 Paper 2

The use of anti stretch marks' products by women in pregnancy: a descriptive cross-sectional survey

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3.3 Abstract

Background

Stretch marks (Striae gravidarum) are a cutaneous change occurring commonly during pregnancy. A variety of products are available and promoted as ways to prevent or reduce their development, but it is not clear what products are used most commonly. The objectives of this study was to identify topical products used during pregnancy to prevent or reduce the development of striae gravidarum. We also explored issues around application of the product, cost incurred and influences on women's decisions to use a product.

Methods

In this cross sectional, descriptive survey we collected data from 773 women, via a paper (n=707) or online (n=66) questionnaire. Due to missing data in the online survey, 753 women at 36 weeks gestation or more were included in the analyses. Descriptive and inferential statistical analyses were undertaken.

Results

Most respondents (n=589, 78.2%) indicated that they used a product to prevent or reduce the development of stretch marks during their current pregnancy. A large range of products were used and more than one third of women (36.5%, n=210) had used two or more products. Bio-oil was the most frequently used product (n=351, 60.9%) and it was also the most frequently used product among women who used only one product (n=189, 32.8%).

Conclusions

Many women apply one of the many products available to prevent or reduce the development of striae gravidarum. Bio-oil was the most commonly used product identified in this study. There is a need for high-quality evidence on the effectiveness of Bio-oil and other products.

Keywords: Pregnancy, Striae gravidarum, Topical products.

3.4 Background

Striae gravidarum, or stretch marks of pregnancy, are a common cutaneous physiological change occurring during pregnancy [1]. They are considered the most common connective tissue change of pregnancy [2] and affect both primiparae and multiparae women. Women of all racial groups are at risk [3]. Rates of occurrence vary, [4] with reported rates ranging between 50% and 90% [5]. Striae gravidarum usually first appear around the sixth and seventh month of pregnancy [6] but have been reported prior to 24 weeks gestation [7]. They occur most commonly during a first pregnancy but have been known to occur for the first time in a second pregnancy [4]. Striae vary in quantity and severity, frequently affecting the abdomen, [8] breasts and thighs where there is greatest stretching of the skin [9].

Striae begin as 'reddish slightly depressed streaks', [10] which lighten in colour over time, [11] fading [12] to leave glistening, [10] or pale wrinkled lines [13] on the skin by about six months after birth [14]. The exact aetiology of striae remains unclear [2, 5, 7, 8, 15-19]. Possible explanations centre on stress on the tissue or stretching of the skin and hormonal factors [2, 9]. At a micro level, it is suggested that changes occurring in the collagen elastin and fibrillin, which contribute to the tensile strength and elasticity of the skin, [13, 20] are significant factors in their development.

While the cause of striae remains unclear, certain predisposing factors have been identified, albeit inconsistently. They include an inherent susceptibility to developing striae [13] or family history of striae, [7, 16, 21, 22] higher maternal weight gain, [5, 17, 22-24] younger aged mothers, [5, 17, 21, 24-26] high pre-pregnancy body mass index [17, 22, 26] and a high infant birth weight [16, 17, 24]. Younger mothers are more likely to develop striae and to develop severe striae [17, 21]. More recently, geographic location and environmental factors [27] were found to influence the development of striae, while age was not found to be a predisposing factor [28].

Although striae are not considered a significant health issue, they can affect women in different ways and may cause distress to some women [4]. They may

also cause pruritus [1, 7, 29] or discomfort [7] while some refer to them as 'disfiguring' [3, 7, 13] or as an aesthetic [17] or cosmetic concern [5, 22, 30, 31]. Some authors suggest that striae impact on women's perception of themselves and on their quality of life [4]. However, a cross sectional study on quality of life in Japanese pregnant women with striae [32] found that general quality of life scores did not differ between those with or without striae but that women with severe striae had significant higher emotion scores on the dermatology specific health related quality of life instrument (HRQoL) Skindex -29 [32].

Interventions for stretch marks include those that focus on prevention and those that focus on treatment [33]. During pregnancy, the focus is on prevention of striae or on reducing their severity and a wide range of products are available purporting to prevent or minimize the development of stretch marks. Consequently, women may use these products during pregnancy, many of which are considered cosmetic products [34] incurring significant expense [4]. However, the effectiveness of many products is unclear [35] due to the limited amount of research undertaken to date. A recent Cochrane Review [36] which included six trials involving a total of 800 women, found no high-quality evidence to support the use of any of the topical preparations identified in the review for the prevention of stretch marks during pregnancy. The authors recommended that preparations commonly used by women to prevent and treat stretch marks should be evaluated in large trials.

This cross sectional, descriptive survey, which is part of a planned investigation of topical products to prevent or reduce stretch marks in pregnancy, sought to identify the topical products used during pregnancy to prevent or reduce the development of striae gravidarum. We also explored issues around application of product, costs incurred and factors that influenced women's decision to use a product.

3.5 Methods

We used a cross sectional, descriptive survey because of its suitability for ascertaining viewpoints [37] at one point in time [38]. Data were collected via a purposefully developed questionnaire (Appendix 2) in both paper (main study)

and online format. The questionnaire contained 21 items chosen after an extensive search of the literature on stretch marks in pregnancy and discussions with researchers and clinical staff [38, 39]. The final instrument had both open and closed ended items, included 'skip logic', and mainly addressed behaviours [40] in relation to product application. Closed items required participants to tick one or more options from a choice of options [41]. The item seeking information on which product, if any, participants used asked participants to identify the product or products used by selecting 'all that apply' from a list of commonly used products generated from the literature and discussion with clinical staff. Response options included an option to select 'other' and add narrative to identify a product respondent may have used but which was not captured in listed response options. A similar item stem and response options were used for the item asking about information sources to help women decide which product to use (Questionnaire is available from MB).

Content validity testing, informed by the work of Lynn [42] and Polit et al, [43] was undertaken with the assistance of a panel of 12 experts (Appendices 3 & 4). Criteria used for panel selection were mainly methodological and clinical expertise plus consumer representation. When tested, the instrument was found to have good content validity with each item having a content validity index value (I-CVI) ≥ 0.83 while the entire instrument had a content validity index of 0.94 (Appendix 5).

Data collection occurred over 16 months between July 2013 and April 2014¹. Data for the paper version were collected by one author (MB) and two research assistants, with support from staff in the antenatal clinic. Only one data collector was present at any time. Women were approached as they checked in or were waiting for their routine antenatal appointment at 36 weeks or more gestation. Almost all eligible women who were approached to participate agreed to do so. Women attending parentcraft sessions were recruited with the help of the parentcraft team. Completed questionnaires were deposited by women in a box on the clinic reception desk.

¹ April 2015 in publication

Potential participants were given information on the study including its purpose and what participation involved (Appendices 6 & 7). Completion of the questionnaire was taken as an explicit indication of consent to participate in the study and this was outlined with the tenets of informed consent in the first section of the questionnaire. The online version of the questionnaire was supported by the online provider SurveyMonkey™. This study was approved by the Clinical Research Ethics Committee for the Galway University Hospitals Group (Appendix 8) and by the Research Ethics Committee of the National University of Ireland Galway (Appendix 9).

Participants were women who were at least 36 weeks pregnant attending the antenatal clinic and parentcraft education in a large regional hospital in the West of Ireland. Only English speaking women were eligible to participate, due to insufficient resources for translation of study material. The sample size for distribution of the main survey (paper questionnaire) was 692 women. This was calculated based on a total population size of 3500 (average births per annum in the study site) and 95% confidence level, 5% margin of error, which estimated a required sample size of 346. This was doubled, based on an assumption that the response rate would be 50%. As the likely population size for the online survey was unknown, it was not possible to predetermine the sample size for this mode of data collection because women were notified through the maternity care advocacy groups and the number of women in these groups is unknown.

As data quality is contingent on respondents being able to understand what is being asked, [39] pre testing and piloting of the questionnaire was essential. Colleagues assisted with this, specifically focusing on the interpretation and clarity of questions [39]. A pilot study was also undertaken to evaluate the questionnaire and the entire survey process [38, 44]. Respondents (n=33) similar to the intended main sample completed the questionnaire and commented on the flow, length, ease of completion and acceptability [45]. No significant changes were required to the questionnaire in relation to layout or instructions following this preliminary testing.

Collected data were entered into SPSS version 21 manually [46] and checked and cleaned. Statistical analysis involved both descriptive and inferential statistics. Descriptive statistics included frequencies and measures of central tendency and variation while inferential statistics included Pearson Chi-square and Two proportion z test to explore relationships and differences in relation to product use between primigravida and multigravida women. Data are reported for completed items i.e. we did not impute missing values.

3.6 Results

Of the 730 women asked to participate in the main survey, 707 agreed to do so, giving a response rate of 96.8%. Of the 66 women who completed the online version 20 were ineligible because the woman's gestation was not provided or she was under 36 weeks' gestation. This left 46 completed online questionnaires and an overall total of 753 eligible participants (707 paper version, and 46 online).

The mean gestational age of respondents was 38 weeks (SD 1.5). First time mothers accounted for 40.2% (n=302) of respondents while the majority of respondents (n=449, 59.8%) were expecting their second or subsequent baby and the mean number of previous babies women had was 0.93. Most participants were Irish (n=589, 78.3%), followed by Polish (n=58, 7.7%), and 35 other nationalities were represented in the sample.

The majority of respondents (n=589, 78.2%) indicated that they had used a product to prevent or reduce the development of stretch marks during their current pregnancy. Of the women who used a product and completed the question on the use of specific skin products (576, 98%), 60.9% (n=351) used Bio-oil, followed by 'other' products (n=202, 35.1%), while the next most popular product was cocoa butter cream, which was used by 174 (30.2%) women and cocoa butter lotion used by 50 (8.7%) women (Table 3.1). A large range of products were included by women in the 'other' category with examples including baby oil (n=31, 5.4%), coconut oil (n=16, 2.8%) and almond oil products (n=11, 1.9%). Respondents also included some cocoa butter products (n=4, 0.7%) and many commercially available anti striae products in the 'other' category. Cocoa

butter products (cream, lotion and other) were the second most popular product used (n=228, 39.6%). More than one-third of women (36.5%, n=210) used two or more products. When comparing primigravida and multigravida women, we found that significantly more primigravida women reported using a product compared to multigravida women (87.4% versus 72.2%, $\chi^2(1, n=751) = 24.7, p = 0.000$) (Fig. 3.1). However, there was no significant difference in the average number of products used between primigravida and multigravida (mean difference (MD) = 0.11, $t(573) = 1.809, p = 0.071$).

Table 3.1 Stretch mark products used

Product Name	Responses	Percent of overall respondents (<i>n</i> = 576)	Numbers (%) using specific product only	Numbers (%) using specific product plus one or more products
	<i>n</i>			
Bio-oil	351	60.9 %	189 (32.8 %)	162 (28.1 %)
Other product	202	35.1 %	97 (16.8 %)	105 (18.2 %)
-Baby oil	31	5.4 %		
-Coconut oil	16	2.8 %		
-Almond oil products	11	1.9 %		
-other	144	25 %		
Cocoa butter Cream	174	30.2 %	49 (8.5 %)	125 (21.7 %)
Cocoa butter lotion	50	8.7 %	10 (1.7 %)	40 (6.9 %)
Mama Mio tummy rub stretch mark oil	28	4.9 %	12 (2.1 %)	16 (2.8 %)
Olive oil	13	2.3 %	4 (0.7 %)	9 (1.6 %)
Revitol stretch mark cream	6	1.0 %	2 (0.3 %)	4 (0.7 %)
Germ oil	4	0.7 %	3 (0.5 %)	1 (0.2 %)

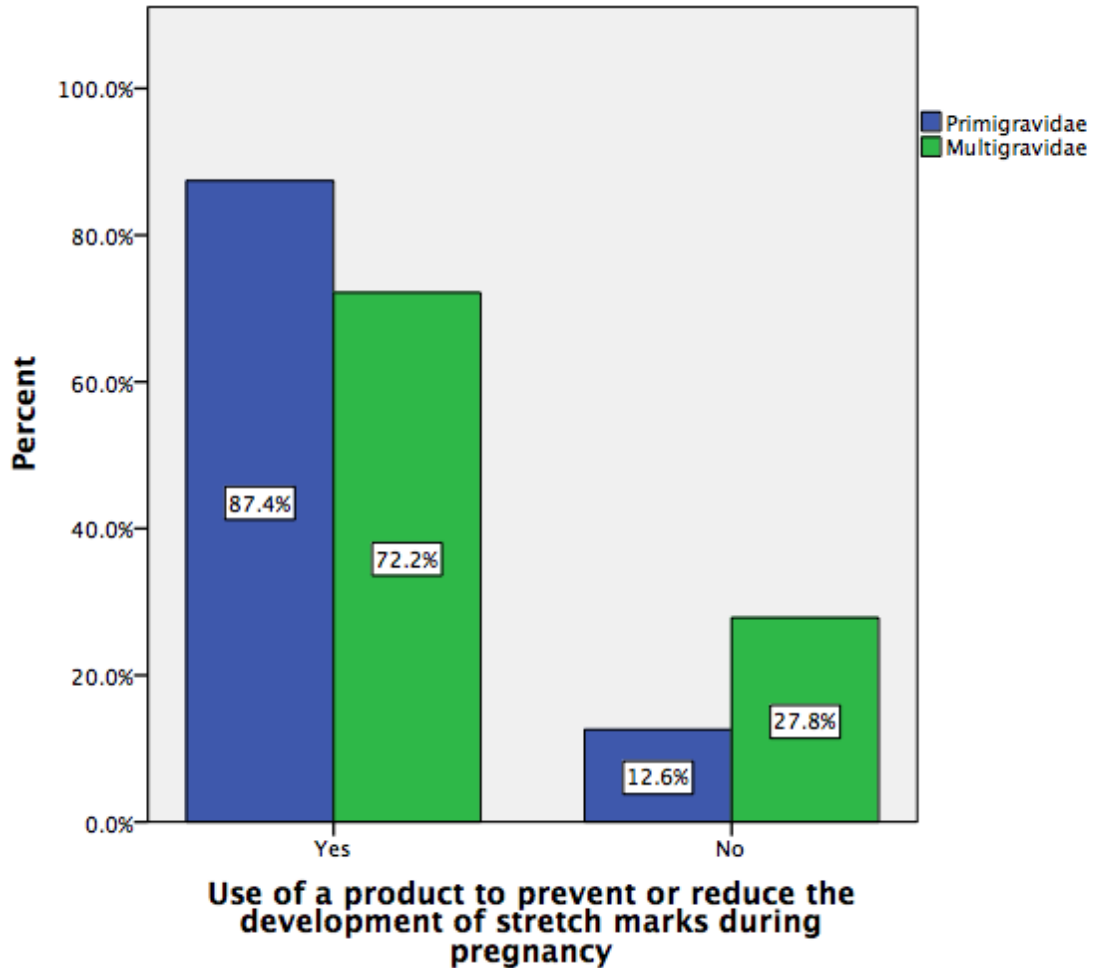


Figure 3.1 Use of a product to prevent or reduce the development of stretch marks by gravida

In relation to information sources that helped women to choose a product, 49.3% (n=278) of women based their decision on advice from friends, 23% (n=130) on product advertisement, 18.8% (n=106) on advice from a family member and 14.7% (n=83) on advice from the internet. In relation to health care professionals the pharmacist was the most frequently identified information source (n=41, 7.3%) followed by the general practitioner (GP) (3.4%, n=19) while midwives and obstetricians were consulted by 1.2% (n=7) and 0.2% (n=1) (0.2%) of women, respectively. Some women identified that they had used the product in a previous pregnancy or had got the product as a gift and therefore did not choose the product deliberately or incur any cost. Excluding the five (0.8%) women who got the product as a gift, the average amount spent by women on products to prevent or reduce the development of stretch marks was €16-20 per

woman. We found an association between the amount of money spent on skin products to prevent or reduce the development of stretch marks between primigravida and multigravida women. Significantly more multigravida women spent <€5 on skin products than primigravida (8.6% versus 3.8% respectively, $p=0.015$). However, at the upper spending range, significantly more primigravida women spent €51 or more when compared with multigravida woman (15.2% versus 9.2% respectively, $p=0.029$) (Table 3.2).

Table 3.2 Amount of money spent on skin products by gravida

Table 2 Amount of money spent on skin products by gravida

Amount of money	Number (%) of Primigravidae (n = 263)	Number (%) of Multigravidae (n = 315)	P-value
< €5	10 (3.8 %)	27 (8.6 %)	*0.015
€5–10	38 (14.4 %)	62 (19.7 %)	0.122
€11–15	35 (13.3 %)	37 (11.7 %)	0.614
€16–20	45 (17.1 %)	57 (18.1 %)	0.827
€21–30	42 (16.0 %)	46 (14.6 %)	0.727
€31–40	27 (10.3 %)	36 (11.4 %)	0.689
€41–50	26 (9.9 %)	21 (6.7 %)	0.171
€ ≥ 51	40 (15.2 %)	29 (9.2 %)	*0.029

* $p < 0.05$

In this survey, 46.3% (n=342) of women had developed stretch marks before their current pregnancy and 46.7% (n=344) developed them during the current pregnancy. Of all respondents, 209 (28.6%) developed stretch marks both before and during this current pregnancy (Fig. 3.2). On comparing primigravida and multigravida women, 48.1% (n=142) of primigravida and 45.9% (n=202) of multigravida women developed stretch marks during the current pregnancy. The majority of women (67.1%, n=232) classified the amount they got during this pregnancy as 'a few'. A Chi-square test for independence indicated no significant association between application of a skin product to prevent the development of stretch marks and the development of stretch marks during this pregnancy ($X^2 (1, n=737) = 2.174, p=0.140$), or with having developed stretch marks prior to the pregnancy, $X^2 (1, n=739) = 3.179, p=0.075$. When comparing

women who developed stretch marks prior to and during the current pregnancy versus those who did not develop stretch marks prior to pregnancy but developed them during the current pregnancy, we found that women who developed stretch marks both prior to pregnancy and during the current pregnancy were significantly more likely to use cocoa butter lotion than those who did not develop stretch marks prior to pregnancy but developed them during the current pregnancy (11.0% versus 3.7% respectively, $p=0.016$) (Fig. 3.3). In relation to Bio-oil, we found those women without stretch marks prior to pregnancy and who developed them during the current pregnancy were significantly more likely to use Bio-oil than women with stretch marks prior to and during the current pregnancy (73.4% versus 58.5% respectively, $p=0.009$) (Fig. 3.4). There was no difference in relation to the other products like cocoa butter cream or olive oil.

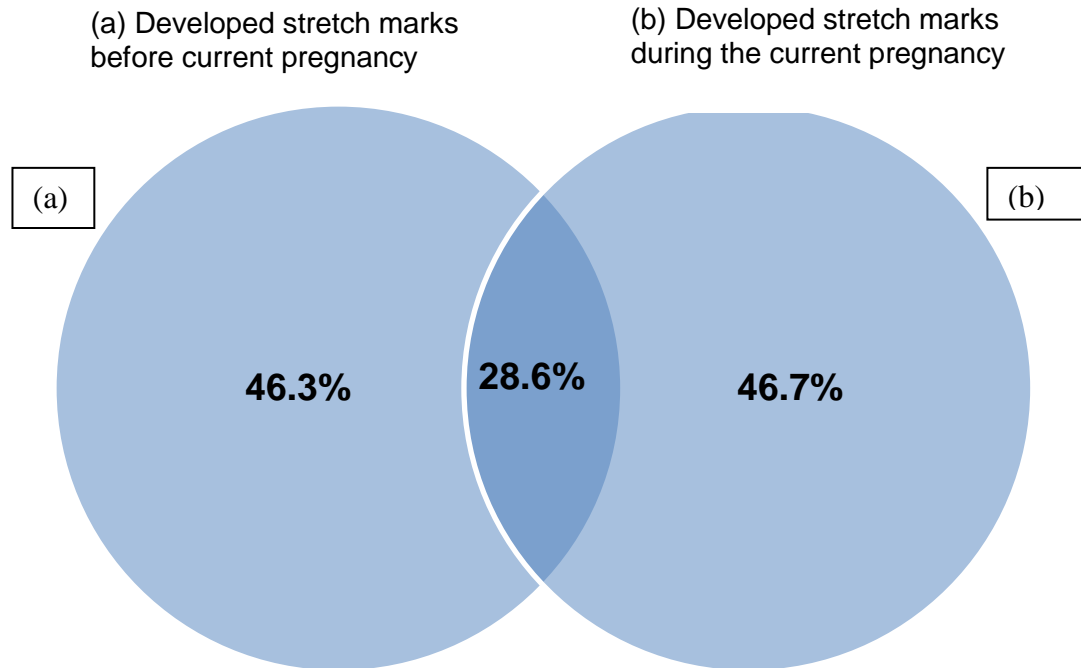


Figure 3.2 Venn diagram depicts (a) % of women who developed stretch marks prior to current pregnancy (46.3%) and (b) % of women who developed stretch marks during the current pregnancy (46.7%). Intersection represents the % of women who developed stretch marks both before and during the current pregnancy (28.6%).

Figure 3.2 Percentage of women developing stretch marks both before and during current pregnancy

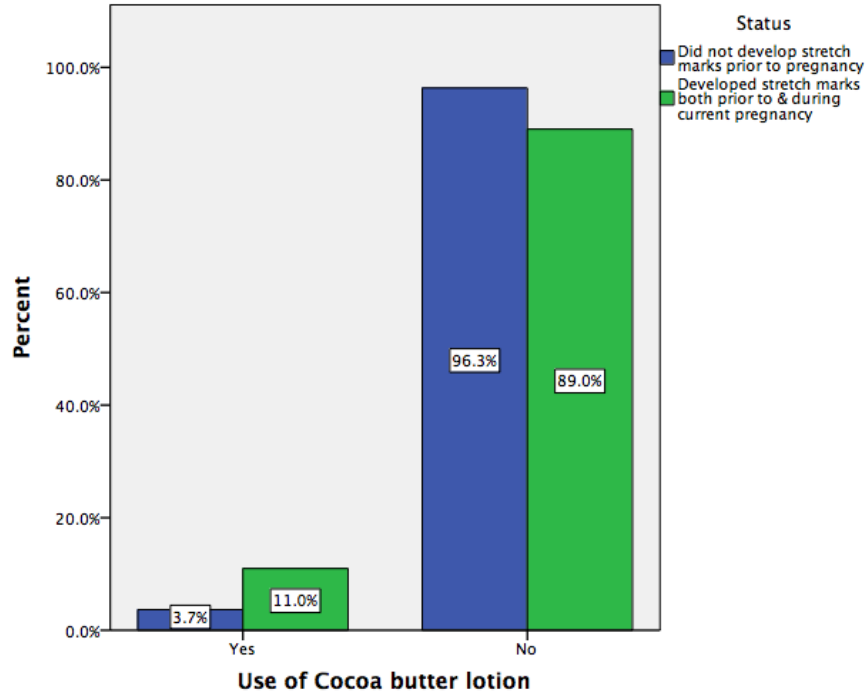


Figure 3.3 Use of cocoa butter lotion and timing of development of stretch marks

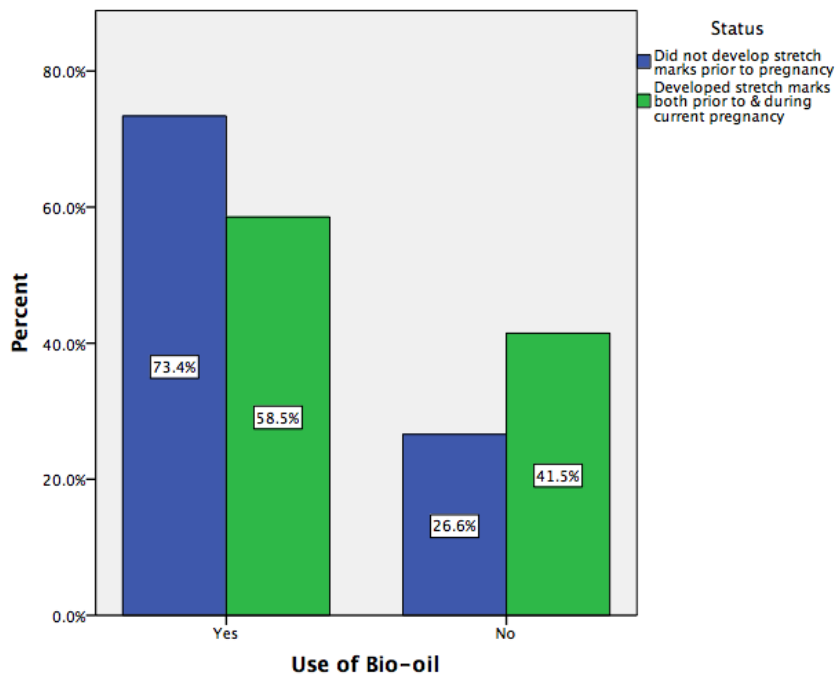


Figure 3.4 Use of bio-oil and timing of development of stretch marks

Women were asked about the amount of time they spent applying the product and how often they applied it. Almost half of respondents (n=262, 46.2%) who used a product and completed this question (n=567) had started to apply it in the first trimester and 266 (46.6%) were applying it seven days a week. The majority of women (n=398, 71.6%) applied the product once a day (women selected from a list of time options) and the mean time spent applying it was 3.8 minutes (range: 29.9, 0.1 minute to 30 minutes; median: 2.5 minutes). There was no significant association between the stage of pregnancy women were at (≤ 20 weeks or > 20 weeks) when they started to apply the product and being a primigravida or a multigravida woman ($X^2(1, n=566) = 0.944, p=0.331$) nor was there a significant difference between the average length of time spent per day applying the product and being a primigravida or a multigravida woman (MD=0.459, $t(558) = 1.52, p=0.129$).

However, there was a statistically significant difference between the number of times per day the product was applied and being a multigravida or a primigravida woman ($p < 0.05$). The majority of mothers (primigravida and multigravida) used the product once or twice a day. However, more multigravida women used a product once a day in comparison with primigravida women (75.7% versus 66.5% respectively, $p = 0.018$) and more primigravida used a product twice a day in comparison with multigravida (29.5% versus 20.4% respectively, $p = 0.014$) indicating that primigravida women were applying the product more frequently during the day (Fig. 3.5).

The majority of respondents (75.5%, n=542) indicated that their decision to use a product to prevent stretch marks in pregnancy would be influenced by the findings of a research study and 68.3% (n=514) indicated that they would consider participating in a future trial of a product to prevent or reduce stretch marks in pregnancy. Further, significantly more primigravida women would consider participating in a future trial when compared with multigravida women (78.1% versus 67.0% respectively, $p=0.001$) (Fig. 3.6).

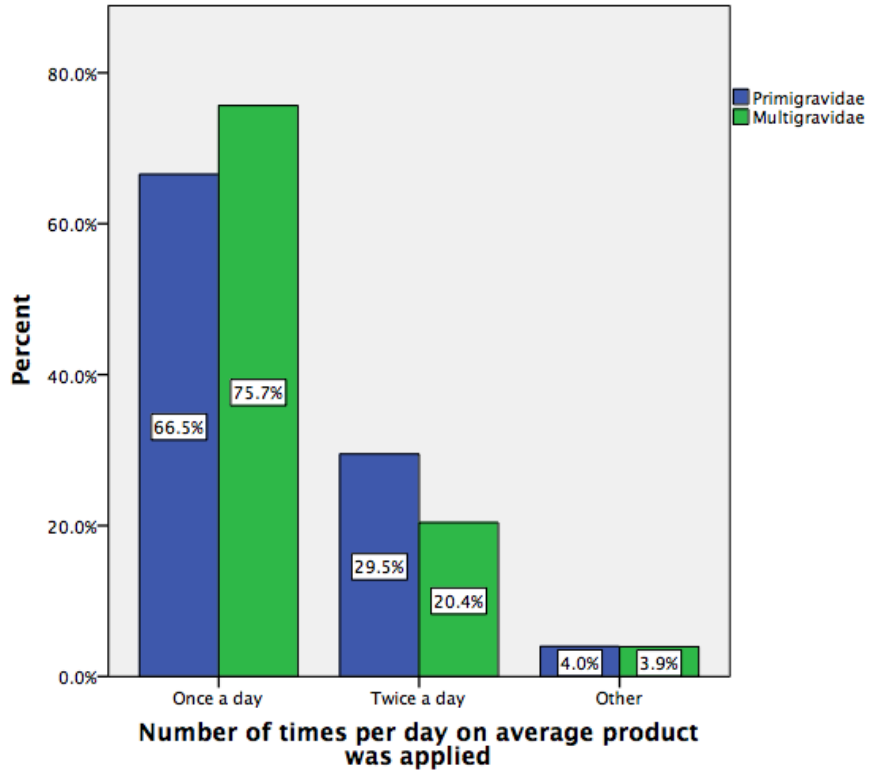


Figure 3.5 Number of times per day on average product was applied by gravida

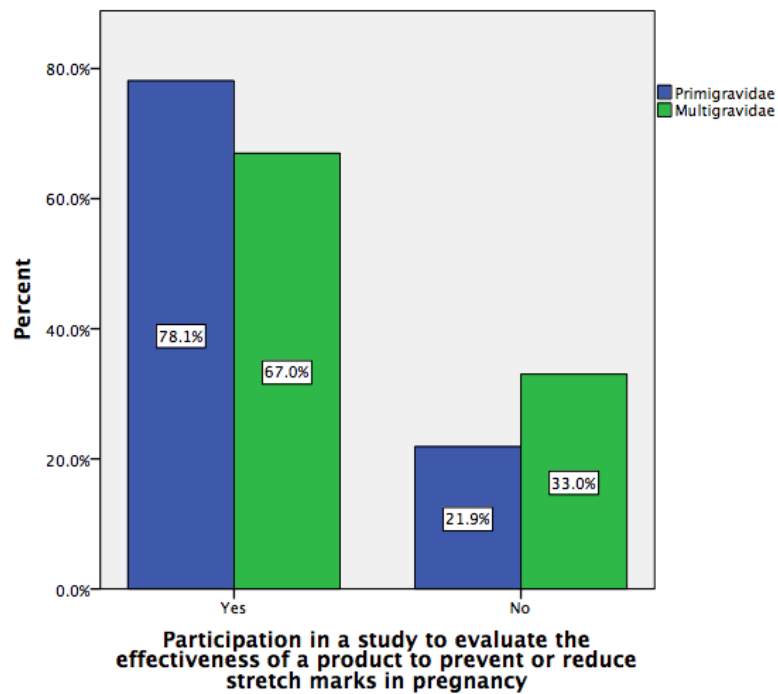


Figure 3.6 Consideration to participate in a future trial by gravida

3.7 Discussion

A large proportion of women in this survey used anti striae products, with 78.2% of women indicating that they used one or more product to prevent or reduce the development of stretch marks during pregnancy. This is similar to a recent Japanese study [47] but higher than that reported by others [5, 26, 48]. Similar to the aforementioned Japanese study [47], we also found that significantly more primigravida women than multigravida women reported using a product to prevent stretch marks in pregnancy. Furthermore, primigravida were also more likely to spend more money and to apply the product more frequently compared to multigravida women. This suggests that primigravida women may be more motivated to attempt prevention or reduction in severity of striae. This is supported by our finding that primigravida women would be more likely to consider participating in a future trial compared to multigravida women.

A large range of products were used, as reported by others [4, 48]. Similarly, the use of more than one product has been identified by other researchers [5, 22, 48]. The most common product used by women in this study was Bio-oil, which consists of a plant and vitamin extract suspended in an oil base with fragrances and colouring added. We do not know how representative this is of other populations and occurs in the absence of high-quality evidence of the effectiveness of Bio-oil for the prevention of stretch marks in pregnancy, although it has been found to significantly improve stretch mark appearance in an exploratory study of non pregnant women [34]. Bio-oil is marketed widely in the print and electronic media and in recent years is more readily available in diverse high street locations, which may contribute to its popularity. One participant added how you 'hear lots about Bio-oil everywhere'

Cocoa butter products were also used by a large proportion of women, as has been found by others [5] despite the lack of evidence to demonstrate their effectiveness in preventing striae gravidarum. One trial [3] that compared cocoa butter cream to a placebo found no significant difference between the control and intervention group. Similar results were found for cocoa butter lotion [49]. Cocoa butter is also present in some of the other products used by women in this study and the effectiveness of these and the many other commercially

available products used by women remains uncertain [35]. Some women may also have used cocoa butter lotion to prevent worsening of pre existing striae based on our finding of its use by women who developed stretch marks both prior to pregnancy and during the current pregnancy. In relation to olive oil, studies have yielded conflicting results. One early observational study [50] found that it did not prevent striae in primigravidae, but Davey [23] found in his non experimental study that olive oil massaged into the skin was associated with a lower incidence of stretch marks. More recently, olive oil was evaluated in two trials [51, 52] and neither supported its use for the prevention of striae gravidarum. In contrast to olive oil, bitter almond oil, has been found to be effective in a quasi-experimental study, [53] which found that bitter almond oil and massage was effective, not the almond oil on its own. The use of baby oil has also been reported in other studies [5].

Women use various sources of information to help them to make pregnancy related decisions [54] and this is also true for anti striae products. Although other studies have found that women often seek advice from midwives and doctors on how to prevent striae [5, 22] this was not the case here. Advice from friends was the most commonly identified source of information. The role of friends, family and the internet has being identified by others [54]. Product advertisement was also influential in this study [48]. There is increasing awareness of the role of the internet to assist women in making decisions [55] and women are using the internet to inform pregnancy related choices, [56, 57] especially in the early part of pregnancy [57]. While midwives have been identified as very important sources of information in pregnancy [54] this was not so in relation to anti stretch mark products but this is not surprising as many women had decided on which product to use in early pregnancy, before they had come into contact with a midwife or obstetrician.

It is also possible that the lack of consultation with health care professionals reflects the view that striae are a cosmetic or aesthetic concern [5, 17, 22, 30, 31] and therefore, unlike other physiological changes that arise in pregnancy, women might decide that they do not merit discussion with the maternity care provider. The majority of women using a product were applying it once a day,

which concurs with advice to women participating in some studies [3, 49, 51, 58]. However, some advocate application at least twice a day [35].

Many of the products that women reported using have not been evaluated or, where they have been, have not been shown to prevent stretch marks. The majority of women in this survey indicated that they would be influenced by research evidence on the effectiveness of products for prevention or reduction of stretch marks in pregnancy and would be willing to participate in a trial of a product to prevent or reduce stretch marks in pregnancy. This is promising given the need for such evaluation and the recruitment problems for research studies generally and trials in particular [59].

The sample size and high response rate are key strengths of this study. Although the majority of the women were Irish, other ethnic groups were represented. Furthermore the sample closely represents the accessible [60] and national population [61] for 2014 in terms of women having their second or subsequent babies. They accounted for 59.8% of all women in this study, which is very close to the accessible population (60.3%) and the national picture (62%).

More women developed stretch marks during the current pregnancy (46.7%) than found in the Japanese cross sectional study [32] which included both primiparae and multiparae (39.1%) but this was fewer than the 71.2% of women who developed stretch marks found in a Polish study [28].

This survey also has some limitations including a non probability convenience sample that may not be truly representative of all pregnant women and how information provided by survey participants may be subject to recall bias [62]. While many women were still using the products, there may have been some bias with information recall, for example in relation to amount of money spent on products. Another possible consideration is that we could have asked women to identify specifically where they applied the anti striae product rather than asking a generic question on the application of a product to their skin to prevent stretch marks in pregnancy. Therefore, some caution is necessary when interpreting the findings.

3.8 Conclusion

In conclusion, this is a large survey of women's use of products to prevent or reduce the development of striae in pregnancy and highlights further the importance of preventing or minimising stretch marks to many women. However, there is a lack of high-quality evidence on the effectiveness of the products being used. This study, which is part of a planned investigation of topical products to prevent or reduce the development of stretch marks in pregnancy, follows on from the Cochrane Systematic Review exploring the effects of topical preparations on the prevention of stretch marks in pregnancy and provides the platform for a future trial to investigate the effectiveness of such products. It also provided us with an insight into the feasibility of recruiting women to a future trial. Future trials evaluating the effects of topical products on the prevention and reduction of stretch marks in pregnancy are necessary and can help to resolve the uncertainty around product efficacy and provide women with the information they need to make well-informed choices and to help health care professionals who are asked for advice by women.

3.9 Abbreviations

HRQoL, Health related quality of life.

3.10 Acknowledgements

We wish to thank the staff at the antenatal clinic (including parentcraft education team) at Galway University Hospital for permission to access the site and collect data and the Maternity care advocacy groups (AIMS Ireland, Cuidiu and Rollercoaster team) for access to participants. Also Aoife Ward and Eve O Meara, two midwifery students who helped with data collection. Finally, we would like to thank Davood Roshan for assistance with the inferential statistical testing.

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3.12 Availability of data and material

Data are available from the corresponding author upon request.

3.13 Authors' contributions

MB, MC and DD conceived the study. MB developed the questionnaire with the support of DD. MB was responsible for the data collection and did the data entry into SPSS and did the descriptive analysis. MB prepared the initial manuscript draft. MC and DD reviewed the manuscript at each stage and edited sections accordingly. All the authors saw and approved the final version of this article.

3.14 Authors' information

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3.15 Competing interests

The authors declare that they have no competing interests.

3.16 Consent for publication

Not applicable.

3.17 Ethics approval and consent to participate

This study involved the use of an anonymous questionnaire. Completion of the questionnaire was taken as an explicit indication of consent to participate in the study and this was outlined with the tenets of informed consent in the first section of the questionnaire (Appendix 2). This study was approved by the Clinical Research Ethics Committee for the Galway University Hospitals Group and by the Research Ethics Committee of the National University of Ireland Galway (Appendices 8 & 9).

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3.18 Summary of key points

This cross-sectional, descriptive survey sought to identify topical products used during pregnancy to prevent or reduce the development of striae gravidarum. It also explored issues around application of the product, cost incurred and influences on women's decisions to use a product. Data were collected by means of a questionnaire via a paper (n=707) or online (n=66) version. Due to missing data in the online survey, 753 women at 36 weeks' gestation or more were included in the analyses. The survey found that most respondents (n=589, 78.2%) indicated that they used a product to prevent or reduce the development of stretch marks during their current pregnancy. A large range of products were used and more than one third of women (36.5%, n=210) had used two or more products. Bio-oil was the most frequently used product (n=351, 60.9%) and it was also the most frequently used product among women who used only one product (n=189, 32.8%). We concluded that many women apply one of the many products available to prevent or reduce the development of striae gravidarum.

Chapter 4: Paper 3

4.1 Introduction

This chapter presents paper 3; the protocol for the pilot trial on the prevention of striae gravidarum. It addresses question 3 i.e. Is it feasible to undertake a large trial on the effectiveness of a moisturising oil (commercially available) compared to no treatment for the prevention and reduction in severity of striae gravidarum?

4.2 Paper 3

Prevention of striae gravidarum: study protocol for a pilot randomised controlled trial

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4.3 Abstract

Background

Striae gravidarum (stretch marks) are considered the most common connective tissue/skin change in pregnancy. Though not a health issue they can affect women in different ways, for example, cause stress or be an aesthetic or cosmetic concern. Many women use one or more of the commercially available products to try and prevent their development during pregnancy despite the fact that there is a lack of high quality evidence to support their use. There is a dearth of studies on the prevention of striae gravidarum and large, robust trials are lacking. Until such time as more products are investigated, much of the knowledge remains anecdotal. This pilot study will evaluate the feasibility of conducting a study to evaluate the effectiveness of a commercially available moisturising oil compared to no treatment for the prevention and reduction in severity of striae gravidarum.

Methods

The definitive study will be a randomised controlled trial to evaluate the effectiveness of a moisturising oil (commercially available moisturising oil) compared to no treatment for the prevention and reduction in severity of striae gravidarum. This protocol is for a pilot randomised trial to evaluate the feasibility of conducting such a study. The pilot study will be a two arm, unblinded, pragmatic parallel randomised trial with a 1:1 randomisation ratio between control and intervention groups. Women in the intervention group will be asked to apply a moisturising oil to their abdomen during pregnancy, while women in the control group will not use any treatment. It is proposed to recruit 20 primigravida who are 12-16 weeks pregnant from an Irish Maternity Hospital, in each arm to assess the feasibility of running such a trial.

Discussion

This pilot trial will evaluate the feasibility of conducting the main study to evaluate the effectiveness of a moisturising oil (commercially available moisturising oil) compared to no treatment for the prevention and reduction in severity of striae

gravidarum. It will potentially initiate the generation of high quality evidence to guide women in their choice of anti stretch mark product.

Trial Registration:

ISRCTN trial registration number: 76992326

<https://doi.org/10.1186/ISRCTN76992326>. Registered on 14th July 2017.

Keywords: Striae gravidarum, Stretch marks, Protocol, Pilot trial, Randomised controlled trial.

Protocol version: 2: 25th January 2018.

4.4 Background

Striae gravidarum or stretch marks occurring in pregnancy, are considered the most common connective tissue change in pregnancy [1]. They affect all racial groups [2] with reported rates of occurrence usually between 52% and 90% in women of different ethnicities [3-7]. Striae gravidarum are common during the first pregnancy [8] and usually present during the third trimester [9]. Striae start as 'reddish slightly depressed streaks' [9] [p. 111], and fade gradually [8] to leave pale wrinkled lines [10], which are permanent skin changes [11, 12]. These benign skin changes [4] occur commonly on the abdomen but are also seen on the breasts and thighs [8, 9, 13] and the hips and buttocks [14].

The exact cause of striae gravidarum remains unclear [5] but is considered to be related to the effects of stress on the tissue, or stretching of the skin and hormonal effects [1, 15].

Risk factors associated with the development of striae gravidarum have been identified [4, 6] albeit inconsistently [16]. While some risk factors are modifiable, others are not [16]. Two of the commonly identified risk factors are higher weight gains in pregnancy [4, 5, 7] and higher birth weight babies [2, 4, 6, 13, 17]. Other risk factors include a family history [6, 7, 16, 18-20], a personal history of striae [18] and young maternal age [5, 13, 17, 19-21].

Though not a health issue [8, 14, 17], striae gravidarum have concerned women since early times [8] and continue to do so. They have caused anxiety or psychological/ emotional distress to some women [8, 20, 22], while for others they are an aesthetic or cosmetic concern [4-6, 14, 18-20] and can impact negatively on a woman's self esteem and body image [14]. Consequently many women during pregnancy have tried to prevent or treat striae gravidarum over the years and often at great expense [8] and indeed continue to do so [23].

4.4.1 Prevention and treatment of striae gravidarum

There are many products available for women to choose during pregnancy purporting to prevent [24] or treat [14] striae gravidarum [5, 17, 21, 23, 25]. In one recent large survey involving 753 pregnant women [23], most respondents

(78.2%, n=589) indicated that they used a product to prevent or reduce the development of stretch marks during the current pregnancy and over one third (36.5%, n=210) had used two or more products.

The highest quality evidence available to date on the prevention of striae gravidarum is from a recent Cochrane Review [26] which evaluated the effects of topical preparations on the prevention of stretch marks in pregnancy. Six trials with 800 women were included in the review which found that there was no statistically significant average difference in the development of striae gravidarum in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment (average risk ratio (RR) 0.74; 95% confidence interval (CI) 0.53 to 1.03; five trials, 474 women; random-effects model, $\text{Tau}^2 = 0.09$, $I^2 = 65\%$). There was also no statistically significant average mean difference in the severity of striae gravidarum (standardised mean difference (SMD) -0.31; 95% CI -1.06 to 0.44; two trials, 255 women; $\text{Tau}^2 = 0.26$, $I^2 = 87\%$).

Similarly there was no statistically significant difference between women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients in the development of striae gravidarum in (average RR 0.51; 95% CI 0.16 to 1.60; two trials, 305 women; $\text{Tau}^2 = 0.53$, $I^2 = 74\%$) or in the severity of striae gravidarum (mean difference (MD) -0.20; 95% CI -0.53 to 0.13; one trial, 206 women; heterogeneity not applicable). The authors concluded that they found no high-quality evidence to support the use of any of the topical preparations evaluated in the review [26].

4.4.2 Why a trial is needed?

The prevention of striae is important to women [27], and women often ask how they can be prevented during pregnancy [5, 16]. There is a dearth of studies on their prevention and large, robust trials are lacking [26, 28]. This protocol is for a pilot randomised trial to evaluate the feasibility of conducting a larger trial and will compare a moisturising oil versus no treatment for the prevention and reduction in the severity of striae gravidarum. The null hypothesis for the future definitive trial is that there will be no difference in the proportion of participants

who develop striae gravidarum or in the severity of the striae between the group who apply the moisturising oil and the group who do not apply any product.

All aspects of the pilot protocol presented here are informed by the 2013 SPIRIT statement [29], which seeks to ensure high quality trial protocols.

4.5 Methods

The definitive study will be a randomised controlled trial to evaluate the effectiveness of a moisturising oil (commercially available moisturising oil) compared to no treatment for the prevention and reduction in severity of striae gravidarum. This protocol is for a pilot randomised trial to evaluate the feasibility of conducting such a study. The study will follow the Standard Protocol Items as per Recommendations for Interventional Trials (SPIRIT) guidelines for the design and conduct of a trial (Fig. 4.1; Additional file 1). The pilot study will be a two arm, unblinded, pragmatic parallel randomised trial with a 1:1 randomisation ratio between control and intervention groups, comparing the effectiveness of a moisturising oil (commercially available moisturising oil) compared to no treatment for the prevention and reduction in severity of striae gravidarum.

While a randomised trial design is the most effective design for testing the effects of a healthcare intervention [30] a pilot trial enables the testing of the feasibility and acceptability of undertaking a larger trial [31]. It will also contribute to modification of the trial protocol for a larger study [31].

	STUDY PERIOD						
	Enrolment	Post-allocation					Close-out
	0	12-37 weeks					38-41 weeks
ENROLMENT:							
Eligibility screen	X						
Informed consent	X						
Demographic	X						
Allocation	X						
INTERVENTIONS:							
Application of oil		←————→					
No product applied		←————→					
ASSESSMENTS:							
[Base line variables --Ethnicity, gestation, weight before pregnancy, weight at recruitment, BMI, Mid abdominal circumference, medication/drug use, personal or family hx of striae, skin type.	X						
[Outcome variables: Number & proportion of women recruited, enrolled, complete the study & adhere to the guidelines, % of potentially eligible women who are recruited/enrolled, challenges with randomisation process, Number and proportion of women who withdraw, drop out or deviate from the protocol guideline, Reasons for non-recruitment, non adherence, or attrition, Women's rating of the tolerability/acceptability and effectiveness of the intervention, Completeness of data collection for outcomes, Challenges with data analysis, Number and proportion of women developing striae gravidarum in the intervention and control group, Number and proportion of women developing mild, moderate or severe striae gravidarum, Women's perception of the severity of striae gravidarum							X
Post birth -Birth gestation & infant weight							X
Diary completion		X	X	X	X	X	
Adverse event		X	X	X	X	X	X

Figure 4.1 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) schedule of enrolment, interventions and assessments for the duration of the study.

4.5.1 Objectives of the pilot trial

- Measure recruitment, enrolment, completion, adherence and attrition (withdrawal, drop outs) rates;
- Evaluate recruitment and randomisation processes;
- Evaluate the data collection instruments;
- Collect qualitative data on reasons for refusal to participate; reasons for non adherence with the intervention and control guidelines and reasons for attrition;
- Ascertain women's rating of the tolerability/acceptability and effectiveness of the intervention;
- Measure the completeness of data collection for outcomes;
- Evaluate the data analysis methods.

As this is a feasibility study, formal hypothesis testing will not be performed. Suitable descriptive statistics and graphical summaries will be used to summarise participant characteristics. Means and standard deviations will be used for continuous variables; counts and percentages will be used for categorical variables with accompanying 95% CI estimates.

4.5.2 Participants

4.5.2.1 Eligibility criteria for participants

4.5.2.1.1 Inclusion criteria

- Primigravid women;
- Singleton pregnancy;
- 12-16 weeks' gestation at time of recruitment;
- Absence of abdominal striae;
- Aged ≥ 18 years at recruitment;
- English speaking women.

4.5.2.1.2 Exclusion criteria

- Multigravid women (due to risk of having striae from an earlier pregnancy);
- Women taking corticosteroids for any reason (due to their association with skin striae);

- Multiple pregnancy (due to increased maternal weight gain and skin stretching);
- Women with a known hypersensitivity to agents in baby oil (due to risk of allergic reaction);
- Women with known disorders or illnesses that may be associated with striae, e.g., Marfan syndrome, Cushing syndrome;
- Women who decline to discontinue other creams or lotions;
- Women who are unable to give informed consent.

4.5.3 Interventions

4.5.3.1 Experimental intervention

The intervention product for this pilot trial is a moisturising oil (commercially available moisturising oil) marketed to increase skin moisture. It contains an oil base: Paraffinum liquidum and Isopropyl Palmitate and parfum (Johnson's baby oil).

Each woman randomised to the experimental intervention group will receive 2 plastic bottles of the moisturising oil with 200 ml in each. This is based on each woman applying ~2 ml per day, (14 ml per week). Based on each woman applying the oil over 26 weeks, i.e. up until approx. 38 weeks gestation (Fig. 4.1), each woman will require approximately 400 ml of oil in total. Each woman will be asked to apply ~2 ml to their abdominal skin daily after showering and before drying their skin. This will equate with two pumps of oil to ensure consistency in amount applied.

Instructions for applying the oil will be printed on a label on the bottles as will the appropriate safety advice (see safety and undesirable effects below). Women will be advised to apply the oil into their abdominal skin once daily from 12-weeks gestation. They will be advised to apply the oil to their damp abdominal skin after showering and to 'pad dry' the area. The researcher will instruct them in the application of the oil. Women will be asked not to use any other skin product on their abdomen to maintain treatment fidelity and to complete a diary record (Appendix 10) of their daily application of the intervention oil and of any other product applied to their abdomen during the trial period (Fig. 1). They will also

be asked to keep the empty oil bottles and bring them to the outcome assessment interview at 38-41 weeks.

4.5.3.2 Control intervention

Women allocated to the control group will not use any treatment and will be asked not to use any other skin product on their abdomen to maintain treatment fidelity. They will also be asked to keep a diary record (Fig. 4.1) (Appendix 11), and to document any product applied to their abdominal skin so that this can be assessed as part of the pilot trial.

All women will receive a two weekly text to remind them about their participation in the trial and to complete the diary. A text message reminder will also be sent to women at 37 weeks to bring their empty oil bottles to the outcome assessment interview as appropriate.

4.5.4 Outcome measures

In order to evaluate the feasibility of conducting a definitive randomised controlled trial to evaluate the effectiveness of a moisturising oil (commercially available moisturising oil) compared to no treatment for the prevention and reduction in severity of striae gravidarum the outcomes for this pilot study are:

1. Number and proportion of women who are recruited, enrolled, complete the study and adhere to the intervention and control guidelines;
2. Percentage of potentially eligible women who are recruited/enrolled to the study;
3. Challenges with the randomisation process;
4. Number and proportion of women who withdraw, drop out or deviate from the protocol guidelines;
5. Reasons for non-recruitment, non adherence, or attrition;
6. Women's rating of the tolerability/acceptability and effectiveness of the intervention;
7. Completeness of data collection for outcomes;
8. Challenges with data analysis;
9. Number and proportion of women developing striae gravidarum in the intervention and control group;

10. Number and proportion of women developing mild, moderate or severe striae gravidarum;
11. Women's perception of the severity of striae gravidarum (Fig. 4.1).

In addition to the above outcomes, birth data will also be collected following each birth from the labour ward register on birth gestation and infant weight (Fig. 4.1) and recorded on the outcomes assessment form (Appendix 12).

4.5.4.1 Assessment of the development and severity of striae gravidarum

The development and severity of striae will be assessed using the Davey instrument [32] and the classification system of mild, moderate or severe as used by Soltanipour et al. [33]. It will entail dividing the abdomen into 4 quadrants and using an ordinal scoring scale to score each quadrant based on the number of striae present as above. However, the numbers in each quadrant will be interpreted as follows: 0= no striae in a quadrant, 1= striae do not affect a quadrant completely, and 2 = striae affect a quadrant completely [33]. Scores for each quadrant will be combined and graded as follows: women with a total of '0' will be graded as having 'none', '1-3 mild striae, 4-6 as moderate striae, and 7-8 as severe striae' [33]. The assessment will take place in a well-light room with adequate natural day or artificial lighting and will be undertaken by the researcher or a research assistant (Appendix 12).

4.5.5 Sample size and feasibility of sample size

A sample size of 228 women (114 per arm) is needed in the definitive trial to have 80% power to detect an absolute difference in the proportion of participants developing stretch marks of 0.20 [14] that is 0.47 [23] to 0.27 at the 5% significance level based on a two-sample test for a binomial proportion. This sample allows for 20% attrition. However, for the pilot trial it is proposed to recruit 20 women in each arm to assess the feasibility of running such a trial and to inform variable parameters. This sample size equates to 17.5% of the sample size needed for the main trial. The pilot data will be incorporated into the definitive trial if feasible, as a seamless trial with an indicator variable used to distinguish pilot from non-pilot data. Furthermore, the attrition rate in the pilot

trial will inform the final sample size for the main trial. This sample size is considered acceptable for a pilot study [34].

The pilot trial will involve one large maternity hospital with approximately 3000 births annually, which includes approximately 1100 first time mothers. It is anticipated that circa 80 mothers will be booked per month and it will be feasible to recruit 40 first time mothers over a three-four month period. This takes in to consideration women who will refuse to participate and women who will not be eligible.

4.5.6 Randomisation

4.5.6.1 Random sequence generation

The random allocation sequence will be generated using the random number generator (the Mersenne Twister) available in StatsDirect [35] by an independent person. Women will be allocated to the intervention and control group using a 1:1 randomisation ratio using random block sizes to ensure that the group to which each woman will be allocated will be determined by a chance process and cannot be predicted.

4.5.6.2 Allocation concealment mechanism

Allocation concealment will be ensured using sequentially numbered opaque envelopes prepared previously by a person independent from recruitment or allocation of participants to groups. Integrity of the process will be ensured by the researcher recording the woman's name and the number of the next unopened envelope in the woman's trial register form (Appendix 13) in the presence of another colleague, and by both persons signing the unopened envelope. Following this the envelope will be opened and the group allocation and study ID revealed [36]. Group allocation and study ID number which corresponds to the envelope number for that woman will be recorded on the trial register form.

4.5.6.3 Blinding

4.5.6.3.1 Blinding of participants and personnel (performance bias)

Due to the technical design of the intervention, the women, the healthcare professionals caring for them and the researcher will not be blinded to which group the participant is randomised to.

4.5.6.3.2 Blinding of outcomes assessment (detection bias)

As above, the outcome assessor will not be blinded to the group to which the participant is randomised.

4.5.7 Recruitment to the trial

Given that most first time mothers will be eligible for inclusion in the study, an ethics committee approved study information pack will accompany the booking appointment notification sent to each first-time mother by the clinic administrator. The study pack will include a letter inviting the woman to participate in the study (Appendices 14 & 15) and an information leaflet (Appendix 16) describing the background, purpose and study details. The information leaflet will provide contact details should potential participants have questions about any aspect of the study. This process ensures participants have time to decide if they wish to participate or not and complies with best practice in obtaining consent [37].

The researcher will approach women as they wait for their booking appointment in the clinic while the support of midwives and obstetricians will be sought in identifying potentially eligible women. Thus, at each antenatal booking clinic during the recruitment phase, all primigravid women will be approached by the researcher or a research assistant and given the opportunity to discuss the study details before inviting them to participate in the study. A trial register form (Appendix 13) will be completed for each woman and each woman screened will be assigned a unique study ID number.

4.5.7.1 Enrolment to the trial

Women who are attending for their antenatal booking appointment and who are screened and deemed eligible and agree to join the study will be asked by the researcher or a research assistant to give written consent (Appendix 17) prior to

randomisation (Fig. 4.2), including consent to receiving two weekly reminder texts, which reminds participants to complete the daily study diary.

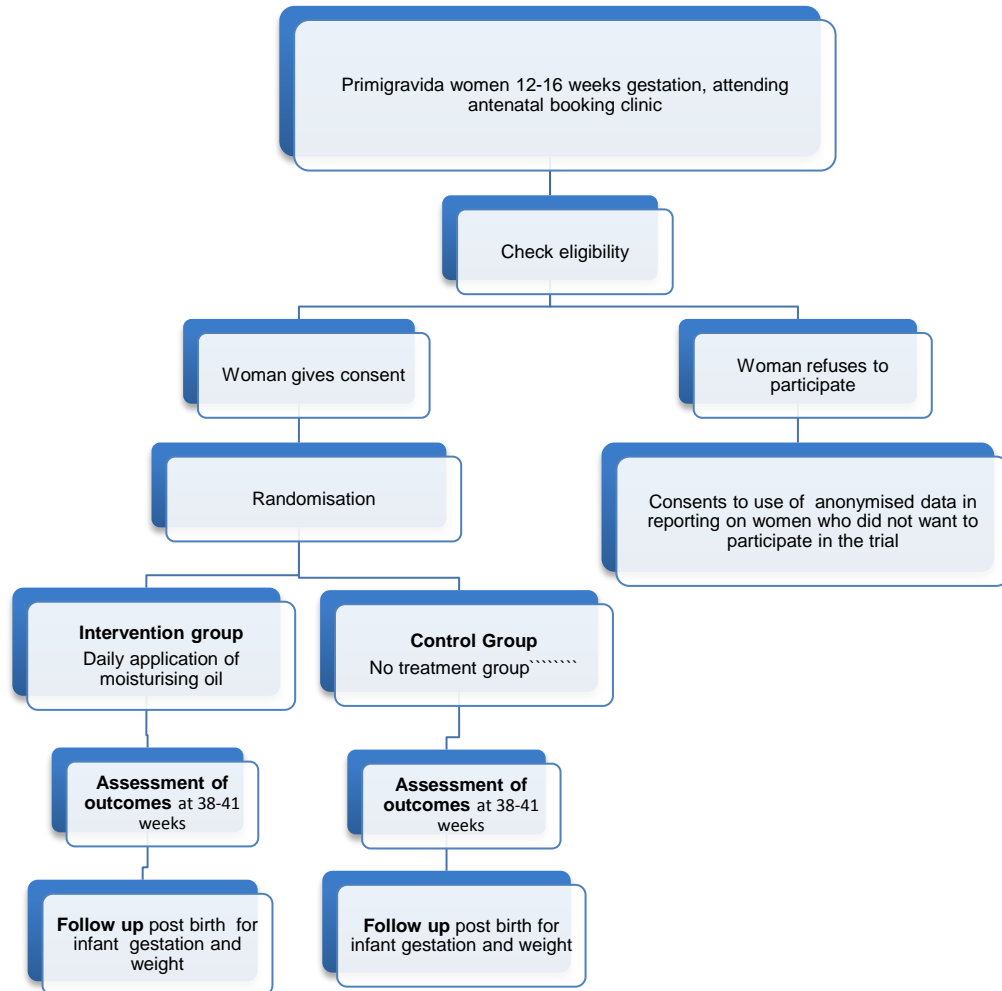


Figure 4.2 Flow of participants through the trial

Women who agree to participate will be asked to sign three copies of the consent form and these will also be signed by the researcher. One copy will be returned to the woman, one will be put in the woman's hospital records and the third will be kept for the research records. Women who are eligible and who decline to participate will be asked for their consent to disclose their reasons for non-participation. Further, women who subsequently decide to withdraw from the study will be asked to contact the researcher as outlined on the participant information leaflet (Appendix 16). Women will then be asked by the researcher

over the phone to give their consent to 1) retention of data collected prior to their withdrawal from the study, or 2) retention of data collected prior to their withdrawal from the study and the inclusion of data collected routinely, or 3) that they wish to withdraw completely (Appendix 18).

When written consent is obtained as outlined, the researcher will select the next sequentially numbered opaque envelope with the woman's allocation. The researcher will then record the woman's name and the envelope number in the woman's trial register form (Appendix 13) in the presence of another colleague, and then both persons will sign the unopened envelope. Following this the researcher will open the envelope revealing the group allocation and study ID, both of which will be recorded in the trial register form as above.

Women will complete a demographic and baseline characteristics' data form (Appendix 19) as part of the case report form (CRF), which seeks information on name, date of birth, medical history, drug use, smoking status, maternal body mass index (BMI) at enrolment (BMI will also be assessed at 38-41weeks gestation at time of outcome assessment) and family history of first degree relative developing striae in pregnancy.

4.5.8 Participant follow up

Women will be followed up over an approximately 26 period during which two-weekly reminder texts to complete the study diary (Appendices 10 & 11) will be sent. Outcome data will be collected at the antenatal clinic appointment at 38-41 weeks gestation (Fig. 4.1).

Based on the clinic attendance lists the researcher will arrange to meet each woman at one of their antenatal appointments between 38-41 weeks gestation as above to undertake the outcome assessment. Women will be assessed for the development of striae and the severity of striae using the assessment instruments outlined above (Appendix 12). In addition, the following data will be collected:

- Gestation at assessment;

- Current weight (to determine Weight gain (% and absolute gain) during pregnancy);
- BMI;
- Mid abdominal circumference;
- Development of polyhydramnios;
- Gestation at onset of striae as applicable;
- Development of striae in other body areas;
- Adherence to the intervention or control guidelines or not and reasons for same;
- Adverse event/undesirable effect (see below);
- Women's evaluation of the tolerability and the effectiveness of the intervention;
- Women's perceptions of the severity of striae gravidarum.

In addition, following the birth the researcher will collect data on the following, from the labour ward register:

- Gestational week at birth;
- Weight of infant (Fig. 4.1).

4.5.9 Safety and undesirable effects

In keeping with the safety advice for the moisturising oil, women will be advised at recruitment that the oil is for external use only, and should be kept out of the reach of children. They will be advised that in the event of a rash occurring or breathing problems or any other undesirable effect associated with the oil, that they discontinue the application of the oil and contact their general practitioner. They will also be asked to contact the researcher who will complete an undesirable effect form (Appendix 20) and the undesirable effect record log (Appendix 21). The researcher will also complete a Cosmetic Product Undesirable Effect Report (Appendix 22) for the Health Products Regulatory Authority (HPRA) [38].

Adverse events for this study are classified as undesirable effects and serious undesirable effects [38] as follows:

- **Undesirable effect** – ‘...an adverse reaction to a cosmetic product under normal or foreseeable conditions of use’, (e.g. ‘...irritant and allergic effects, sensitivity to light and itching’);
- **Serious undesirable effect** – ‘...an undesirable effect which results in temporary or permanent functional incapacity, disability, hospitalization, congenital anomalies, an immediate vital risk or death’.

4.5.10 Criteria for proceeding to the main trial

The decision to proceed to the main trial will be made by the Trial Steering Committee based on the following criteria:

- ≥40% of eligible women can be recruited;
- ≥70% of women adhere to the intervention and control guidelines;
- <20% of women lost to follow up.

4.5.11 Data management

All data will be recorded carefully on the appropriate case report forms, which will be stored in a locked cabinet in the researcher's work office. Quality of case report form completion will be monitored on an ongoing basis by the researcher. Only the researcher and a research assistant will have access to the paper data, while the researcher, her supervisor, a research assistant, and a statistician will have access to the electronic data, which will be anonymised based on individual participant trial numbers and stored in a password protected file on a password protected, encrypted laptop. All data will be kept secure by the researcher for a period of five years and then shredded.

4.5.12 Statistical analysis

Data will be entered into a secure database using the Statistical Packages for the Social Sciences (SPSS) version 21 [39] as collected. Data will be coded and cleaned. As this is a feasibility study, formal hypothesis testing will not be performed. Suitable descriptive statistics and graphical summaries will be used

to summarise participant characteristics. Means and standard deviations will be used for continuous variables; counts and percentages will be used for categorical variables with accompanying 95% CI estimates.

In addition, numbers and percentages of women recruited, eligible, randomised, enrolled, and who completed the trial will be outlined in a Consort Flow Chart.

4.5.13 Intervention fidelity

Complete intervention adherence will be defined as the woman applying the allocated oil daily over approximately 26 weeks. Anything less than this, will be considered incomplete adherence, with < 10 applications in total over the approximately 26 weeks being regarded as non-adherence.

4.5.14 Trial monitoring

4.5.14.1 Data monitoring

The researcher will monitor recruitment and reasons for non-recruitment of potentially eligible women as the trial proceeds. The researcher will ensure that sufficient time is given for individual discussion about the trial to potential participants. Due to the aim, objectives and size of this pilot study, it was not considered necessary to have a data monitoring committee.

4.5.14.2 Trial management

The day to day management of the trial is the researcher's responsibility under the supervision of her supervisors, while a Steering Group will also be established to supervise the trial as below.

4.5.14.3 Trial Steering Committee (TSC)

A TSC will be established to provide overall supervision of the trial and to ensure that the trial is conducted rigorously. It will include a midwifery manager and a research expert. The TSC will discuss protocol once a month and at the end of the trial. Further, they will offer guidance on continuation, modification or cessation of the trial as appropriate and will review any cases of reported trial-related undesirable effects.

4.6 Ethics

The trial will be conducted in accordance with the WMA Declaration of Helsinki ethical principles for research [40]. Ethical approval was granted by the local Clinical Research Ethics committee (Appendix 23).

In the event of the protocol requiring any amendments the researcher will inform the ethics committee, the participants and any other party as appropriate (Appendix 23). Consent will be obtained by the researcher as outlined above. All study data will be kept confidential as above before, during and following the study. Access to the dataset will be restricted to the persons named above.

4.7 Discussion

Many women use the commercially available anti striae products to try and prevent the development of striae gravidarum. This pilot trial will evaluate the feasibility of conducting the main study to evaluate the effectiveness of a moisturising oil (commercially available moisturising oil) compared to no treatment for the prevention and reduction in severity of striae gravidarum. It will potentially initiate the generation of high quality evidence to guide women in their choice of anti stretch mark product which heretofore is unavailable.

4.8 Trial status

Protocol version: 2 - 25th January 2018.

Date recruitment began: 18th July 2017 for two weeks, recommenced February 2018, however no participant has been enrolled to date.

Approximate date recruitment will be completed: May 2018.

4.9 Abbreviations

IBM Corp: International Business Machines Corporation;

WMA: World Medical Association.

4.10 Acknowledgements

We would like to thank the staff at the antenatal clinic for supporting this study and to the women who will participate in the study.

4.11 Funding

We would like to thank the School of Nursing & Midwifery, National University of Ireland Galway, Ireland for the funding received for this study.

4.12 Dissemination

Study results will be published and contribute to MB's PhD by publication.

4.13 Availability of data and materials

The consent form, data collection forms and datasets generated and/or analysed during the current study will be available from the corresponding author on reasonable request.

4.14 Authors' contributions

MB conceptualized and designed the study and drafted the manuscript. MB revised the manuscript following feedback from DD, MC and JN.

MC participated in the conceptualisation, design of the study, and in the review and revision of the manuscript.

DD participated in the conceptualisation, design of the study, and in the review and revision of drafts of the manuscript. DD oversaw the manuscript writing and recommended revisions as appropriate.

JN advised and supported the writing of the statistical analysis section.

All authors approved the final manuscript.

4.15 Ethics approval and consent to participate

The Clinical Research Ethics Committee for the Galway University Hospitals, Galway, Ireland approved this study (C.A. 1770).

All participants who are eligible to participate in the study will sign a consent form as per ethical approval.

Ethical approval for all protocol modifications will be sought from the ethics committee accordingly.

4.15.1 Consent for publication

Not applicable.

4.15.2 *Competing interests*

The authors declare that they have no competing interests.

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4.16 Summary of key points

This paper comprised the protocol for the pilot trial on the prevention of striae gravidarum, which sought to determine the feasibility of undertaking a large trial on the effectiveness of a moisturising oil (commercially available) compared to no treatment for the prevention and reduction in severity of striae gravidarum. The background and the rationale for the proposed pilot study were outlined and informed by the findings from a Cochrane systematic review (Brennan *et al.*, 2012), which concluded, that the reviewers found no high-quality evidence to support the use of any of the topical preparations evaluated in the review and that there was a clear need for larger and more rigorous trials to evaluate the effectiveness of anti-striae products. This protocol was also informed by the findings from the survey (Brennan *et al.*, 2016) undertaken to determine the use of anti-striae products by women during pregnancy.

The proposed pilot trial was a two arm, unblinded, pragmatic parallel randomised trial with a 1:1 randomisation ratio between control and intervention groups (n=40). It was planned to recruit primigravid women who are 12-16 weeks' gestation and who are attending for their booking appointment at the antenatal clinic of a large maternity hospital. Women in the intervention group were asked to apply the oil daily up until approximately 38 weeks' gestation. Women in the control group did not apply any product to their abdomen during pregnancy. Both groups were asked to keep a diary during the study to record their application of oil or not, as appropriate and would receive two weekly texts to remind them to do so.

Outcome assessment interviews for both groups were planned for 38-41 weeks and included development of striae and severity of striae, adherence to the study guidelines or not and reasons for same. As this was a feasibility study no formal hypothesis was planned and statistical analysis will consist of suitable descriptive statistical tests.

This pilot trial will potentially initiate the generation of high quality evidence to guide women in their choice of anti-stretch mark product.

Chapter 5: Paper 4

5.1 Introduction

This chapter presents paper 4; the qualitative study of the factors influencing recruitment to a pilot trial on the prevention of striae gravidarum. It addresses question 4 i.e. What are the factors influencing recruitment of women to the pilot trial on the prevention of striae gravidarum? The need for the study emanated from the challenges in recruitment to a pilot randomised trial designed to evaluate the feasibility of a definitive trial to compare a moisturising oil to no treatment in the prevention and reduction in severity of striae gravidarum.

5.2 Paper 4

A qualitative study of the factors influencing recruitment to a pilot trial on the prevention of striae gravidarum

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Under review

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5.3 Abstract

Background

Striae gravidarum are a common occurrence in pregnancy and many women use a topical product to prevent their development or lessen their appearance if they do develop. There is a lack of evidence on the effectiveness of many of the products used by women. This study arose from challenges in recruitment to a pilot randomised trial (ISRCTN trial registration number:76992326) designed to evaluate the feasibility of a definitive trial to compare a moisturising oil to no treatment in the prevention and reduction in severity of striae gravidarum. The study reported here explored the factors influencing recruitment to that pilot trial.

Methods

A qualitative descriptive study was undertaken involving primigravid women attending an Irish maternity hospital. Data were collected by semi-structured telephone interviews and analysed using the framework method of analysis. Fifteen interview transcripts were included in the analysis.

Results

Four main themes consisting of twelve categories were identified from the interview data. The themes focused on women's prevention of stretch marks and their choice of anti-stretch mark product, who and what influenced that choice and influences on trial participation. In relation to influences on trial participation, the possibility of being randomised to the non-intervention or control group was a deterrent for many women.

Conclusions

The prevention of stretch marks is important to pregnant women, as is their choice of product to prevent them. Offering women the opportunity to be part of a trial that would be of low burden and would test a well-known product may optimise recruitment. However, reluctance to be randomised because of the possibility of being allocated to the non-intervention control group suggests that further work is needed in this field on how best to communicate uncertainty to potential participants.

Key Words

Pregnancy, Striae gravidarum, Stretch marks in pregnancy, Trial participation, Qualitative research.

5.4 Background

Striae gravidarum or stretch marks are common in pregnancy, usually during the third trimester. They have been shown to affect 50% to 90% of pregnant women [1] and commonly occur during their first pregnancy [2]. Striae gravidarum frequently occur on the abdomen but are also seen on the breasts and thighs [3]. They appear as reddish or purple streaks and remain as glistening lines on the skin [3] and have been more recently described as '...scar like, hypopigmented linear bands displaying a crinkled shiny surface...' [4] (p.750).

The cause of striae remains unclear but they may be related to the effects of stretching or tension on the dermal extracellular matrix involving the elastin and collagen elements. According to Shuster [5] (p.161) they are always associated with stretching and occur in skin where '...the connective tissue is partially mature with a critical titre of rigid cross linked collagen and 'elastic' unlinked collagen...'. Others report that there may also be some changes in the elastin fibre network important in skin elasticity, as a result of persistent strain on the dermal tissue, which may be related to a deficiency in cutaneous fibrillin [6]. Even moderate strain may be enough to damage the elastic fibre network [6]. More recent research suggests that there may be '...ineffective repair of collagen disrupted by intense skin stretching' [4] (p.749).

Several risk factors are associated with striae but not consistently so [7]. Risk factors can be classified as maternal factors in place before pregnancy, for example, family history of striae or young age, maternal factors during pregnancy, for example, increased weight gain and increased body mass index at birth of baby and neonatal factors, which include increased gestational age at birth of baby and increased birth weight [7]. Pregnant women with one or more of the 'attributes' may be at increased risk for striae gravidarum [7] (p.607). In a recent study addressing risk factors for striae in primigravid women, Kocaöz et al [8] found increased risk in those without social security, who sleep nine or more hours per day, have a body mass index (BMI) of 30 kg/m² or more and have a family history of striae.

Striae can have both physical and psychological implications for women. They can be seen as disfiguring [9, 10] and are regarded as a significant cosmetic issue [11]. They can impact on a woman's perception of herself [12], and cause 'psychological distress' [13] (p.595). Furthermore, although not impacting on general quality of life, striae have been found to impact women's dermatology specific quality of life based on scores obtained on the emotion scale of Skindex-29 used by Yamaguchi et al., [14]. More recently, Kocaöz et al., [8] report how women's body image declined in the presence of striae and their increasing severity.

That striae are of significant concern to women of child bearing age is reflected in the use of products for their prevention or to reduce their severity. In our large survey of 753 pregnant women in Ireland [15], most respondents (78.2%, n=589) indicated that they used a product to prevent or reduce the development of stretch marks during their current pregnancy and more than one third (36.5%, n=210) had used two or more products. This was similar to a Japanese study [13] but higher than other earlier studies [1]. Most recently, 40.9% (n=172) of participants in a Turkish study reported using a product [8].

However, studies addressing product effectiveness are few in number [7]. A Cochrane Review [16] found no high-quality evidence to support the use of any of the topical preparations identified in the review for the prevention of stretch marks during pregnancy. Furthermore, the review recommended that preparations commonly used by women to prevent and treat stretch marks should be evaluated in large trials [16]. To address this, we developed a protocol for a pilot randomised trial (ISRCTN: 76992326) to evaluate the feasibility of conducting a definitive trial to evaluate the effectiveness of a moisturising oil (Baby oil) compared to no treatment in the prevention and reduction in severity of striae gravidarum. Following ethical approval, the pilot study sought to recruit women between 12-14 weeks' gestation attending for booking at the antenatal clinic of the maternity unit in an Irish hospital. However, recruitment was challenging and following further ethical approval, it was decided to adjust the gestation inclusion criterion from 12-14 weeks to 12-16 weeks to maximise the chances of recruitment. Nevertheless, despite this adjustment and a concerted

effort to recruit women during four weeks in February 2018, it was evident that recruitment to the trial was difficult. This is not unique to this study. Challenges with recruitment to trials in maternity care is reported by others [17-20]. In light of this, and following a review of the literature on maternal trials and discussion with maternity staff, we decided that an exploration of the factors influencing recruitment to the trial was necessary to elucidate factors influencing recruitment and to guide future research on this topic. Efforts to recruit to the trial continued following ethical approval and women who declined to participate in the pilot trial were invited to participate in a qualitative study to explore the factors influencing recruitment.

5.5 Methods

5.5.1 Study aim

To explore factors influencing recruitment of women to a pilot trial on the prevention of striae gravidarum.

5.5.2 Study design, setting and participants

The design adopted was qualitative descriptive [21, 22]. Qualitative research is a type of '...social inquiry that focuses on the way people make sense of their experiences...' and their world [23] (p.3). Therefore, this approach enabled a close interaction with purposively chosen participants to understand in more depth the factors influencing recruitment to the pilot trial on the prevention of stretch marks in pregnancy. Furthermore, while there is a growing body of qualitative evidence in relation to influences on trial participation by pregnant women, we are not aware of any study which focused specifically on stretch mark prevention in pregnancy.

In relation to sample size, the research was guided by the work of Sandelowski [21] who advises that the research team must make a judgment on what is an adequate sample size. Morse [24] also highlights how many factors influence the sample size required for data saturation in qualitative studies, including the study scope, 'nature of the topic' and the quality of the data. In light of these factors, it was proposed to interview 10-15 participants depending on the point

at which data saturation is reached, i.e. no new data is being obtained and data is being repeated by participants [25].

Eligible study participants were English speaking primigravid women with a singleton pregnancy, aged 18 or over, attending their first visit (booking appointment) in the antenatal clinic of the maternity unit in an Irish hospital who had previously declined to participate in the pilot trial outlined above. On their first visit (booking visit), all eligible participants were approached by one author (MB) who informed them of this qualitative study and offered the information pack, which included a cover letter (Appendix 24), participant information sheet (Appendix 25), consent form (Appendix 26), the interview guide (Appendix 27) and a stamped addressed envelope.

Participants who took the information pack were asked if they were agreeable for MB to contact them by telephone after 24 hours to address any questions they may have and to ascertain if they were willing to participate in a short semi-structured telephone interview, lasting 20-30 minutes at a mutually acceptable time. Thirty-five women agreed to the follow up call.

Sixteen of these primigravid women who were 12-16 weeks' gestation agreed to take part in semi-structured telephone interviews exploring the factors influencing recruitment to the pilot trial on the prevention of striae gravidarum. Interviews were audio recorded, took place over four weeks in June and July 2018 and lasted between eight and nineteen minutes each. Two women provided written consent before their telephone interviews. The remainder returned the consent form following their interview. However, one participant did not return the completed consent form despite a follow up reminder and therefore her interview data were not used in the analysis.

While telephone interviews can be challenging in establishing a rapport, MB had met all the study participants in the antenatal clinic at recruitment and also spoke to them during the follow up telephone call to arrange the interviews, so a rapport had already been developed before the interviews.

5.5.3 Data collection and analysis

An interview guide (Appendix 27) developed by all authors was used and only minor changes were made following the initial interviews. Each interview began with an open question on the reasons for not participating in the pilot trial. Thereafter, the interview followed a semi-structured format using the topic guide [26], which included questions around product choice, influences on product choice, confidence in effectiveness of chosen product, and influences of randomisation and specific trial requirements (such as diary keeping) on the decision to not participate in the pilot trial. The topic guide was applied flexibly in response to the participants' responses, as noted by Kenyon et al [27]. This method offered flexibility for the participants and facilitated them in sharing their perspective in their own words. Data saturation was evident by the tenth interview.

Framework analysis [28] guided the analysis process. This approach '...sits within a broad family of analysis methods often termed thematic analysis or qualitative content analysis' [29] (p.2). The Framework Method of analysis was considered a suitable method for the thematic analysis of semi-structured interview transcripts which were used in this study and which were consistent with the study aim [29]. Moreover, due to the homogeneity of the interview data, they were suitable for classification which is a requirement of the Framework method [29]. Management of the data involved the following five steps:

5.5.3.1 Step 1 Familiarisation

Firstly, transcript auditing [30] was undertaken by MB to check for accuracy as interviews were transcribed professionally. All the transcribed interviews were read several times to get an overview of the content and to become more familiar with it. During this stage, recurrent topics or themes relevant to the study aim were identified and compiled into a comprehensive 'inventory' [31]. Following this, each item on the inventory was checked for relevancy against the study aim and interview guide, resulting in a list of topics or themes present in the data.

5.5.3.2 *Step 2 Construction of the initial thematic framework*

This second stage involved grouping and sorting the themes to form a hierarchical structure of themes and sub themes [31, 32], which were labelled with descriptive terms staying '...close to the language and terms used in the data set' [32] (p.222). This stage resulted in ten themes with varying numbers of sub themes (total-39), including an 'other' category in some themes which were reclassified subsequently. Further revision resulted in eight themes and 25 sub themes (See eight themes in table 5.1).

5.5.3.3 *Step 3 Use of the framework for indexing and sorting the data*

MB then cross checked each transcript with the framework, identifying where each topic appeared and labelling it with the framework or thematic reference, which Spencer et al [31] refer to as 'indexing'. Following indexing, a table was devised for each theme and sub theme, which also brought together data of similar content and indexed it accordingly for each participant or case.

5.5.3.4 *Step 4 Reviewing data extracts*

Further refinement of the framework involved reviewing the indexed data and looking back over the transcripts again to detect any omissions in indexing or from the framework. This resulted in some changes to titles of themes and sub themes, and some sub themes were merged to reduce fragmentation of the data. This necessitated some re-labelling and changes to indexed numbers. Memos were kept of all changes made at each stage. The framework at this stage consisted of six themes and 23 categories.

5.5.3.5 *Step 5 Data summary and display*

This stage involved the development of framework matrices for each individual theme, which is specific to framework analysis. Matrices are constructed in such a way that comparisons can be seen between different parts of the framework at the individual level and '...across cases within a single thematic matrix' [31] (p.305). MD reviewed the matrices in conjunction with reading all 15 transcripts and following discussions with MB, further refinement of the framework occurred with minor changes being made to some wording and moving and collapsing of

some sub themes (Four themes and 15 sub themes) (See four themes in Table 5.1).

5.5.4 Abstraction and interpretation

These five steps were followed by further discussions between MB and MD and identification of constituent elements and underlying dimensions, identifying possible categories and finally group classification or themes [31] to reflect the data. This entailed trying to move from 'surface features of the data to more analytic properties' [31] (p.285). It also involved some refinement and movement of sub themes (now referred to as categories) within the framework (See final themes in Table 5.1).

Table 5.1 Framework with themes from the end of step 2, step 5, and with final themes

End of step 2	Step 5	Final
1. Anti-stretch mark product chosen	1. Prevention of stretch marks and anti-stretch mark product choice	1. Preventing stretch marks and choice of anti-stretch mark product
2. Influences on decision or choice of product	2. Influences on product choice	2. Who knows best?
3. Confidence in chosen/planned product	3. Influences on trial participation or not	3. Influencers: Current trial participation
4. Influences on trial participation	4. Influences on future trial participation	4. Influencers: Future trial participation
5. Influences on future trial participation		
6. Influences on future anti-stretch mark product purchases		
7. Stretch marks in pregnancy		
8. Other		

In terms of rigour, notes were kept at all stages of the framework analysis method, providing an audit trail which contributes towards dependability of the data. Furthermore, all stages of the analysis were validated by MD in support of confirmability of findings. Finally, the framework method with its systematic and comprehensive data analysis, facilitates both within and between case examination and transparency [31].

5.6 Results

After analysis, four main themes and 12 categories were identified from the interview data (Table 5.2) on factors influencing recruitment to the pilot trial on the prevention of striae gravidarum.

Table 5.2 Final themes and categories identified

Preventing stretch marks and choice of anti-stretch mark product	<ul style="list-style-type: none"> • Better to try prevent than do nothing • Knowing or not knowing what product I will use • Prior knowledge • Keep it natural • Will it work? • Cost
Who knows best?	<ul style="list-style-type: none"> • Friends and Family • Retail and Advertising
Influencers: Current trial participation	<ul style="list-style-type: none"> • I want a choice • Trial requirements should fit with my routine
Influencers: Future trial participation	<ul style="list-style-type: none"> • I want a good quality product with a good name • Incentives may be helpful

5.6.1 Preventing stretch marks and choice of anti-stretch mark product

Stretch marks and their prevention during pregnancy was important to many of the participants and they had already thought about and planned to use a topical product to try to prevent the development of stretch marks during their pregnancy. Many had actually purchased their chosen product and, in some cases, had started to use it.

For many of the women, there was an innate belief that they were better to apply a product to the skin during pregnancy to try to prevent stretch marks rather than not applying anything. For some, it was the moisturising or hydration aspect,

while for others they were ‘taking no chances’ and viewed any product as potentially beneficial. Some products were more popular than others; specifically, many women wanted a ‘natural’ product and emphasised the organic nature of the product.

Cost was a factor in product choice for many participants. For others, cost was not an important factor but they felt it may have become one if they were actually getting stretch marks. Where cost was important in the choice of product for some participants, it was related to unknown effectiveness in that they did not wish to spend a lot of money on anti-stretch mark products particularly as they did not know if they would work. Others always went for a cheaper product. Many of the participants had a cut-off point or a price that they would not go above. Other participants were going to buy their product of choice whatever the cost and would pay what was required (Table 5.3).

Table 5.3 Themes and categories illustrating women’s views in response to questions relating to preventing stretch marks and choice of anti-stretch mark product

Theme	Categories	Sample quote
Preventing stretch marks and choice of anti-stretch mark product	Better to try prevent than do nothing	<p><i>I'm hopeful it will [work] but I suppose I'm thinking I'm probably in a better position by using it than not doing anything. [...] I'd rather be trying to prevent them than just doing nothing. (Participant 1)</i></p> <p><i>I just know it's important to moisturize. (Participant 3)</i></p> <p><i>...so I think it would be great to just hydrate it and keep the skin a little bit more hydrated. (Participant 4)</i></p> <p><i>I am probably seventy per cent confident that it will help me but I don't know if anything can prevent them you know. (Participant 6)</i></p> <p><i>...I think that if you are going to get stretch marks you are probably just going to get them anyway but I think that maybe it just might help to decrease them. (Participant 8)</i></p> <p><i>...definitely I would feel like you are better off using a rich moisturising cream than using anything at all [...] I would prefer to definitely do something on myself because I feel like a little bit of technique and creams or whatever it may be you know even</i></p>

		<p><i>if it is actually [product name] that would be better than nothing. (Participant 10)</i></p> <p><i>...I frankly don't want stretch marks...(Participant 12)</i></p> <p><i>...I suffer from stretch marks through puberty [...] I will try and prevent it now if possible and so I gave I mean I would give it a go by applying cream. (Participant 13)</i></p> <p><i>...I had picked a product it was like reasonably cheap and I suppose I have stretch marks already on my legs and stuff so I would be prone to them anyway but it was kind of one of my reasons just like if I don't want to get them [...] if you can prevent them I suppose if you don't want something for like even though they have fade down they are still you are still scared like do you know. (Participant 14)</i></p> <p><i>...I am just not a risk taker so I would want to use a product no matter what. (Participant 16)</i></p>
	<p>Knowing or not knowing what product I will use</p>	<p><i>I had already started using a cream by the time I met you [researcher] in the hospital. [...] it's a spur of the moment [...] so I threw it in the basket, there was no, you know, intention beforehand or anything [...] it was literally only that day that I saw the cream and just thought oh sure I'll throw this in the basket. (Participant 1)</i></p> <p><i>I had planned on using a product myself [...] I had my own kind of idea of what I wanted to do already at that stage [...] what I'm using at the moment is just the [product name] on myself but I'm going to use [product name]...(Participant 2)</i></p> <p><i>...I actually haven't even thought about it until you [researcher] spoke to me that day... (Participant 5)</i></p> <p><i>I am about the fourteen weeks and I haven't any stretch marks yet I thought it is too soon but I am already beginning to apply cream just in case. (Participant 6)</i></p> <p><i>...I have kind of had it in my head to use that [product name]. (Participant 8)</i></p> <p><i>Right now it's not a priority for me I am not even thinking about stretch marks and I don't think it would be I probably won't use anything. I am certainly not planning using anything from or at this stage...(Participant 9)</i></p>

		<p><i>...I have chosen to use [product name] [...] I didn't have to go out and buy it, it was something that I had before I became pregnant so it was easy access in that I already had the product. (Participant 11)</i></p> <p><i>...I am currently applying [product name] to try and prevent stretch marks. (Participant 13)</i></p> <p><i>...I would use [product name] for moisturizer [...] Well I had extremely dry skin there for a while and I just thought that that would be good for dry skin so it wasn't really for the stretch marks but means I have the bottle now I may as well use it. (Participant 14)</i></p> <p><i>...I actually decided I came to the conclusion that I will be going for [product name]...(Participant 15)</i></p>
	<p>Prior knowledge</p>	<p><i>...I've used the same face cream probably for the last fifteen years I'd probably look to that range first as well to see do they have a product available for body moisturising especially for stretch marks [...] if I had heard it had good reviews about it I certainly would try it. (Participant 3)</i></p> <p><i>...like clinical trials and attempts that were done in this university. They wrote articles and I followed that for a good while you see that is 2015, 2016 really I wasn't pregnant but I was doing an awful lot of reading about it. (Participant 10).</i></p> <p><i>...I would have looked at ingredients in each of the products... (Participant 13)</i></p> <p><i>...none of them are proven they don't state that they are going to eliminate it forever you know so I would always go for a cheaper option. But I still like a brand name like I like the branding and I like the good quality [product name]. (Participant 14)</i></p> <p><i>...I did a bit of research myself but at the same time my main priority was to use a natural product as natural as possible. (Participant 15)</i></p>
	<p>Keep it natural</p>	<p><i>...I'd like something a little bit more organic, rather than, I got the [product name] [...] But I found it very kind of chemical smell off it. I wasn't that into it. So my other sister was saying about some sort of cream from the health shop that was more organic. (Participant 4)</i></p> <p><i>...I love anything that is natural I am a vegetarian I am very much against any animal testing or animal cruelty. So those factors would be hugely important to me. (Participant 6)</i></p>

		<p>...it's [product name] a nice smelling kind of oil and also just that it actually says on the [product] that it does prevent stretch marks or minimises the appearance of them. (Participant 8)</p> <p>...I can't remember the exact name of it but it's basically the option that you had for stretch marks that natural skin care company[...] Basically they are all natural because I don't use anything that has got preservatives in it so I also have sensitive skin. (Participant 10)</p> <p>...I would use [product name] for moisturiser [...] I find it very nice and a nice smell and it's kind of leaves the skin very soft. (Participant 14)</p> <p>...it's a pure essence basically an orange oil that actually helps with stretch marks. And it is anti-oxidant as well so it's good for everything...(Participant 15)</p>
	<p>Will it work?</p>	<p>...I'm hopeful it will [work]...(Participant 1)</p> <p>...I honestly don't know how it's going to work...(Participant 2)</p> <p>I'm not too sure if it's (pauses) a particular product or a particular (pauses) oil versus cream, I just know you should moisturize. (Participant 3)</p> <p>...not 100%, (laughing) hmm (pauses) I don't know, I won't know. [...]</p> <p>...I do think it is hereditary as well. Both of them [sisters] no one in my family seems to, touch wood, to get stretch marks. (Participant 4)</p> <p>...I suppose my belief I don't have any proven findings of fact. I mean a lot of these are research and you know it may work for some women it may not but I would hope that it would work for me. (Participant 10).</p> <p>...I don't know how confident I am that it will work... (Participant 11)</p> <p>...I am probably not very confident I am probably aware of the fact that I am predisposed to getting them anyway it might it might help [pauses] I suppose maybe heal them faster by going from you know from the red you know the initial ones that they are red or purple and move to silver. I suppose maybe that is what I am trying to do to get give me make my skin as prepared as possible. (Participant 13)</p>

		<p><i>...I suppose I wouldn't be that confident because I suppose I just think that you are going to get them you will probably get the stretch marks I don't know can you fully prevent them. (Participant 14)</i></p> <p><i>But I am not obviously a hundred per cent sure that it will work just it was just recommended this one from this people that helped me to make my choice and to trust that product. (Participant 15)</i></p> <p><i>...maybe you are going to get stretch marks no matter what you use [...] other people saying it doesn't matter what products you use you know stretch marks are genetic so you are going to get them if you are going to get them you are going to get them no matter what. (Participant 16)</i></p>
	<p>Cost</p>	<p><i>I think it was about five or six euro like to me that didn't seem that expensive it's a big enough bottle. (Participant 1)</i></p> <p><i>...if I was getting the stretch marks I don't think it [cost] would be huge, a huge factor in it [choice of product]. (Participant 2)</i></p> <p><i>I mean it [cost] would certainly play a part...(Participant 3)</i></p> <p><i>But I wouldn't go spending like 50 euro on one bottle of cream now. But hmm (pauses) yeah, it wouldn't influence me too, I wouldn't go too high a price bracket but yeah, there's no point in getting something really cheap just for the sake of it either. (Participant 4)</i></p> <p><i>...I wouldn't be spending a huge amount of money on anything like that. (Participant 5)</i></p> <p><i>I would be a middle of the range price person [...] I wouldn't buy anything maybe fifty euro or more. (Participant 6)</i></p> <p><i>...like I think if you feel something is going to work it doesn't really matter how expensive it is I mean I well actually [product name] isn't that expensive hmm you know I don't know I suppose you wouldn't want to be spending too much either. I mean yes it has to be kind of a reasonable price...(Participant 8)</i></p> <p><i>...I would be within a reasonable price point I am not going to go up to eighteen or even sixteen euro on something that may or may not work you know something that is going to be a natural product is not going to cost the earth anyway because it</i></p>

		<p><i>wouldn't be made by a huge big brand. (Participant 10)</i></p> <p><i>...cost wouldn't have influenced my decision in picking a product over the other. (Participant 11)</i></p> <p><i>...it was very expensive for a small bottle I think it was twenty something euro but like I just like I suppose it will probably last a good while and if it stops the stretch marks I don't really mind how much it's going to cost. (Participant 12)</i></p> <p><i>...yes I wouldn't want to be spending a fortune on something that I am not a hundred per cent will work anyway. (Participant 13)</i></p> <p><i>...I would always go for a cheaper version...(Participant 14)</i></p> <p><i>So I actually didn't even look into the prices just about the recommendations and then the price [...] I would not look into [price] I would pay what I would need to pay for it. (Participant 15)</i></p> <p><i>...the price is important. Like I mean if this bottle of [product name] is two euro at Ever Green that is nice but I would spend more than that on a product that I think is going to be high quality but not too much. (Participant 16)</i></p>
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5.6.2 Who knows best?

This theme captures who or what resource was accessed most frequently by participants. Friends and family were a key influence on choice of anti-stretch mark product. Friends and particularly those who had been pregnant previously were often reported by participants as a source of influence. Participants often added that their friends had recommended the product and or had found it effective and participants seemed to value the advice and recommendations they received in most cases. Other sources also influenced women's choice. Some noticed products when shopping, while others were more targeted with some women referring to a local health food store and how they talked to the assistants there (Table 5.4).

Table 5.4 Themes and categories illustrating women's views in response to questions relating to resources accessed in choosing an anti-stretch mark product

Theme	Categories	Sample quote
Who knows best?	Friends and Family	<p><i>...recommendations from friends who have been pregnant before... (Participant 2)</i></p> <p><i>...one of my sisters used the [product name] and she found it great. (Participant 4)</i></p> <p><i>...I have a couple of friends that are nurses and I would probably ask them as well if they used anything or they found anything good.(Participant 5)</i></p> <p><i>...I purchased it [product name] as a gift from my good friend who became pregnant last year and she swore by it. She said it was fantastic so based on her recommendation... (Participant 6)</i></p> <p><i>I have a family member who have used it before and she didn't get any stretch marks and she felt that it worked really well. (Participant 8)</i></p> <p><i>...I had heard friends say that they used it [...] and they found it effective. (Participant 11)</i></p> <p><i>...I am only going with what people told me so [...] family and friends telling me to apply the [product name] to the stomach. (Participant 12)</i></p> <p><i>...my friends one of my friends recommended the [product name] [pause] stretch mark cream and I think that is kind of one just one girl recommended that but I didn't get it because I had the other one already. I have the other ones already got...(Participant 14)</i></p>
	Retail and Advertising	<p><i>...just from generally from shopping and seeing what's on the shelves. (Participant 3)</i></p> <p><i>I was going to go into Ever Green [Health food store] and ask them what they thought. (Participant 4)</i></p> <p><i>...I would kind of do a bit of research just through the internet just to see on the maybe on the forums and that what people use and use that sound good. (Participant 5)</i></p> <p><i>...I have seen ads on television for the oil as well. (Participant 8)</i></p>

		<p><i>...advertisement of [product name] that it advertises that it helps like in prevention of stretch marks and maybe why I picked it as well. (Participant 11)</i></p> <p><i>...it's the pharmacist advised that I do it for no stretch marks... (Participant 12)</i></p> <p><i>...I am [...] big into natural products and I kind of I went to the Evergreen shop [Health food store] and I discussed that with the health care professionals there. (Participant 15)</i></p> <p><i>...I have just started researching just at online reviews...(Participant 16)</i></p>
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5.6.3 Influencers: current trial participation

This third theme addresses the factors influencing participants' decisions not to participate in the pilot trial. Central to this theme is the trial design or methodology that involved participants being randomised to a group that applied an oil to their abdomen or to a group that did not apply any product (control group). Women were unhappy that they might be allocated to a group that would not apply any product. Many participants related how they had a clear preference for the intervention group if they were to participate. Such favouring of the trial's intervention suggested that despite the absence of evidence of effectiveness, the intervention was perceived to be better and this belief moved potential participants from a position of individual equipoise or uncertainty. One participant said she was already concerned about stretch marks and would be put off by being in the group that was not applying a product (participant 1). Others wanted to use an anti-stretch mark product and did not want to be in the non-intervention group (Participant 2 & 16), while another participant indicated that she always moisturised her skin and would not be prepared to stop.

Trials often have certain requirements from participants and this category captures participants' willingness or not to comply with the pilot trial requirements, such as daily showering before application of the oil and the keeping of a paper diary during the study to record the use of the oil application on a daily basis. For some, these requirements were not a problem and would fit with their daily routine (Participant 1, 3 & 11) while for others they did not fit

(Participant 8 & 9). Fitting in with participants' daily routine was important and emphasised by many participants.

Some participants' responses related to not being able to commit to doing either the showering, completing the diary or both and they often identified implications of this for the overall study. Where this occurred, participants acknowledged openly the importance of adherence to the requirements for the overall study integrity. Examples include participant 2 who did not like the commitment to the trial requirements and mentioned about recording inaccurate detail in the diary. Similarly, participants 5 and 16 mentioned not having the dedication to comply and were aware of the impacts of this on the study results. Not being able to commit was also raised by participant 13, while for others, it was important that the requirements did not take up too much time (participant 14).

Some participants identified a preference for an on-line tool or other method of maintaining the diary on their telephone to fit their lifestyle (Participant 6). While others raised practical issues such as forgetting the diary if they were away at the weekend and suggested that a smart phone based system would work better for them (Participant 10) (Table 5.5).

Table 5.5 Themes and categories illustrating women's views in response to questions relating to participating in the prevention of striae gravidarum trial

Theme	Categories	Sample quote
Influencers: Current trial participation	I want a choice	<p><i>...if I was participating in it I think I'd prefer to be in the group that would be doing it as opposed to the group that's doing nothing [...] like if I was told I was in the group to do nothing well maybe I'd already been you know a bit concerned about stretch marks and so I'd be a bit more concerned you know maybe it would put me off. (Participant 1)</i></p> <p><i>...if it was randomised and then you were in the group that wasn't that would kind of, that would have been one of the reasons as well for saying not to on it [...] because I had it in my head I had planned on starting it I didn't want to be randomised into the group that was not. (Participant 2)</i></p> <p><i>... if I was put in the group that wasn't to use any moisturiser that straight away you know I'd only be lying (laughing) I'm not going to stop the habit of a lifetime. (Participant 3)</i></p> <p><i>...I think when the choices are taken out of your hand that is harder for me. It was just picked at random I don't know how you would pick it but I know I would struggle with random selection of how the people would be chosen. (Participant 5)</i></p> <p><i>If it was something that I hadn't considered I wouldn't mind being in either or of the groups obviously if it was no harm to myself or the baby there was no risk of harm. (Participant 6)</i></p> <p><i>...I think that if I did feel strongly one way or the other about whether I wanted to use the cream or not I wouldn't mind taking part if I got to choose what options I would have to go with. (Participant 9)</i></p> <p><i>...I probably wouldn't have been happy because I wouldn't have had the choice you know. (Participant 11)</i></p> <p><i>...I would not want to be in the group without using any kind of product just because I feel like I would want to use one either way. Just to be as a precaution so if I was in one of the group without the oil and then I would (laughs) disappointed as I want to use something anyway. (Participant 16)</i></p>

	<p>Trial requirements should fit with my routine</p>	<p><i>...I shower twice a day and I've no problem I keep a diary anyway. So there would be no bother with either of those [trial requirements]. (Participant 1)</i></p> <p><i>...I wouldn't like to commit to it and then forget to do it and then not, and put an inaccurate detail on it. But that would be a little thing actually for me when I think about it day to day. (Participant 2)</i></p> <p><i>...the cream would be my morning routine anyway [...] I wouldn't have a problem with that [diary], you are not noting down, it wouldn't take a massive amount of time. (Participant 3)</i></p> <p><i>...when you [researcher] gave me details of how the trial would be run and the amount of times you would have to apply it during the day. And that you would have to shower in the morning I just feel that I wouldn't have the dedication to it to you know give you satisfactory results. (Participant 5)</i></p> <p><i>I would have no problem with that [trial requirements] if you use the online tool that I can keep track on my phone or something that would make it even handier for me. (Participant 6)</i></p> <p><i>...yes again that could be like people might just feel like it might get in the way of their routine kind of like maybe they don't want to have a shower in the morning or they usually have their shower before they go to bed or something like that you know. That might be a problem or a nuisance or something. (Participant 8)</i></p> <p><i>...I can see how you need everybody to have the same conditions when they are applying the oil I can see why you set that kind of a standard. To be honest it's just an extra piece of work I know like everybody showers of course but some people might be showering before bed and others might be showering in the morning. And if I need to do it every day and if they are leaving it a day and they can't do that it's another pressure. (Participant 9).</i></p> <p><i>I suppose if you keep it in a reminder on your phone except for diaries because I know I am difficult to forget or to bring it with me or if I went away for the weekend you can forget your diary and where would you write it. [...] If you had a little quick even a word like email google doc like you know you can get into on your phone all the time. (Participant 10)</i></p> <p><i>...that is a fairly easy because I suppose I leave the oil on my bedside locker so I could leave the pen and paper there as well and just jot it when I did it. (Participant 11)</i></p>
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		<p><i>I don't know if I would commit to that [trial requirements]...(Participant 13)</i></p> <p><i>...I suppose it would be fine if it was just like a tick like diary you know something like very quick. [...] You don't want things that take up too much [time]...(Participant 14)</i></p> <p><i>...I do know some people that don't shower that often you know maybe once every three days or something so then I would think maybe it's not if you weren't showering as frequently then you are not applying the lotion every day. So and that would be the only issue I could see...(Participant 16)</i></p>
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5.6.4 Influencers: future trial participation

Participants also identified factors that would influence their participation in a future trial on stretch mark prevention in pregnancy. Although they were not keen on being randomised, they would be more inclined to join a study that involved the testing of a known anti-stretch mark product and often added that they would like to see some data or research to support the effectiveness of the proposed product. For others, the type of product was important with many women expressing a preference for use of an organic product or a natural product.

Participants also had views on the use of incentives in a future stretch mark prevention trial. Most participants would not be influenced to join the study unless they were already interested in participating in it. Incentives may be helpful but were not a major factor determining participation (Table 5.6).

Finally, participants were asked if they had been offered participation in other research studies after becoming pregnant (to determine if they might have been overburdened by research), but none of them reported any such offers and, therefore, it was not a factor in their decision to not participate in the pilot trial.

Table 5.6 Themes and categories illustrating women's views in response to questions relating to participating in future trials on anti-stretch mark products

Theme	Categories	Sample quote
Influencers: Future trial participation	I want a good quality product with a good name	<p><i>I suppose it would be dependent on maybe reputation of it. Because I've heard [product name] is very good. Or I suppose if there was some study that showed that using that certain oil was seen to reduce the stretch marks by a certain percentage I suppose that would swing me towards using it. (Participant 1)</i></p> <p><i>I don't actually really know if there was any, a moisturiser or that, that was effective [...] I suppose research behind it. (Participant 2)</i></p> <p><i>...knowing the product and it being a product I would have heard of would probably gain my interest a little bit more. (Participant 3)</i></p> <p><i>Just something a little bit more organic and something that, yeah as I said absorbs into the skin, not a big film sitting on your skin. Yeah, just something kind of not too heavy...(Participant 4)</i></p> <p><i>...I would do research based on recommendations. That you know to find out if it's actually as good as the price... (Participant 6)</i></p> <p><i>...I suppose if you have got trials if you had trials done already and you had a little bit of evidence that could support it...(Participant 10)</i></p> <p><i>...I suppose I would be more I would be swayed more by I suppose results or you know previous sort of you know if there was any if there was previous tests done. (Participant 13)</i></p>
	Incentives may be helpful	<p><i>Incentives like that [money] wouldn't, no. (Participant 2)</i></p> <p><i>...I suppose a discount on the product. (Participant 3)</i></p> <p><i>...I suppose if I was a little bit more interested in it, it might persuade me if you got some little gift at the end of it. (Participant 5)</i></p> <p><i>...if there is a voucher at the end of it I wouldn't turn it down either. (Participant 6)</i></p> <p><i>Yes I think an incentive like that be put in a draw or that you could win something that would</i></p>

		<i>definitely encourage people to be part of it.</i> (Participant 8)
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5.7 Discussion

This qualitative descriptive study explored factors influencing recruitment to a pilot trial on the prevention of striae gravidarum, using semi-structured telephone interviews with 15 primigravid women. In keeping with a qualitative descriptive design and its 'low-inference' description [21], the findings have remained close to the original data and are relayed 'in everyday language' [21] (p.336) through the themes and categories generated via the framework analysis method [31].

Our findings emphasise the importance of striae prevention for women during pregnancy. Many participants had already thought about stretch mark prevention at an early stage of pregnancy and had already planned to use a topical product to try to prevent them. This echoes previous research, where most respondents in a large survey in Ireland reported using a product to prevent or reduce stretch marks in pregnancy [15]. Many believed that they were better to apply a product to the skin during pregnancy (even it was not known to be effective) rather than not applying anything. They were not prepared to negotiate on anything that could increase their chance of getting stretch marks. This supports the views in the literature that many women are concerned by stretch marks [12], particularly because they do not completely disappear [33]. Moreover, although not a medical issue, these marks are a significant cosmetic issue for women [11, 34], commonly referred to as 'disfiguring' [7, 9, 10, 34]. Furthermore, they can cause distress to some women [2, 14]. Thus, women want to try to prevent them.

A range of anti-stretch mark products were chosen or in use by the participants, which concurs with other studies [1, 15]. Some products were more popular than others, which has also been identified previously [15]. Under the category 'prior knowledge', in the narratives we could see some of the influences on participants' choice of product, for example, brand familiarity and perceived product quality. Natural or organic products were clearly important to some women. No evidence of these influences were uncovered in the literature.

Women's uncertainty on the relative effectiveness of their chosen product reflects the current status of knowledge on the effects of these products [7, 16, 34]. Finally, in relation to cost, some participants were prepared to spend more than others to get their product of choice. Although the amount of money spent by women is not widely reported in the literature, our earlier research showed that primigravid women are more likely to spend more money on anti-stretch mark products than multigravid women [15].

The influence of family and of advertising on participants' choice of anti-stretch mark product is in keeping with our previous research, where 49.3% (n=278) of respondents identified advice from friends in helping them choose a product, followed by 23% (n=130) for product advertisement, 18.8% (n=106) for advice from a family member and 14.7% (n=83) from the internet [15].

The possibility of being randomised to the non-intervention or control group in the pilot trial was a significant barrier to participation and is reflected in the category 'I want a choice'. Participants did not want to be allocated to the control group and not be able to use a product. Furthermore, some wanted to choose their own anti-stretch mark product. This suggests that some participants did not seem to understand trial design fully and this has been noted by others [20, 27]. Kenyon et al., [27] interviewed women about their experiences of being recruited to a trial on antibiotics in pre-term labour (ORACLE) and reported that some women seemed to have poor understanding of trial processes [27]. Similar points have also been made in non-maternity studies [35].

The issue that randomisation is a barrier to recruitment to research is reported by others. Ballantyne et al., [36] (p.480) report how some pregnant women when interviewed about their involvement in a randomised trial comparing a probiotic supplement versus a placebo (PiP study) in New Zealand, saw possible randomisation to a control group involving a placebo 'as a burden or disadvantage', although it was not the main barrier. However, they add how anecdotal evidence from staff revealed that one main reason for women not agreeing to participate in the trial was their wish to take a probiotic during pregnancy, which they would not have been able to do if randomised to the

placebo group. While participants in our qualitative study were discouraged by the use of a non-intervention group, others have reported how women during pregnancy have said that they were less inclined to agree to placebo-controlled trials because of the uncertainty of receiving or not receiving an intervention considered advantageous [37]. Uncertainty around placebo use and randomised trials has also been identified by others [20, 38], and Rodger et al., [39] found that pregnant women identified fear of being randomised to the placebo group as a reason for non-participation. In addition, some participants in our study referred to lack of choice, which may be related to lack of control which was identified by Baker et al., [40].

These issues are central to the concept of equipoise. Baker et al., [40] highlight how women must believe equipoise exists before considering to participate in research. It was evident in our study that some women did not believe equipoise existed. Most felt products worked. Distrust of equipoise has also been highlighted by Oude Rengerink et al., [20] in their qualitative case control study on barriers and motivators for pregnant women participating in Dutch trials. In addition, participants in our study thought that using any product was better than not doing anything and some also thought that the intervention product in the pilot trial was not as good as some of their known products despite not having evidence to support this view. Perhaps these participants needed clearer information on the study, as highlighted by Baker et al., [40]. However, it is unclear if this would have changed their decision not to participate.

Both randomisation and equipoise or uncertainty are integral to randomised trials. Randomisation is the foundation for '...testing the statistical significance of differences...' between the intervention and control groups in relation to the trial outcomes [41] (p.155) while uncertainty, equipoise or 'clinical equipoise' in the context of the 'community' refers to the principle that there is no agreement as to which treatment is best [42]. Furthermore, randomisation is considered to be the most ethical means of assigning participants to study groups in the presence of clinical equipoise [43]. Notwithstanding this, these concepts have proven to be problematic for participants [44]. Research has shown that participants might either not understand or remember the information given to them on both

concepts [44]. While acknowledging the complexity of the task of explaining randomisation, Robinson et al., [44] suggest focusing on its scientific advantages through a clear understandable explanation, while also helping potential participants to consider how the trial will advance knowledge on the topic. More recently, and related to the clear explanation suggested by Robinson et al., [44], is the need for some communications skills' training for clinicians recruiting to clinical trials [42]. This recommendation arose from a study on how clinicians communicated equipoise to potential participants during recruitment and included both interviews with the clinicians and audio recording of the recruitment meeting. These findings may be beneficial in the context of future trials on the prevention of striae gravidarum.

Support for the second category identified under this theme: 'trial requirements should fit with my routine' is also evident in the trial by Ballantyne et al., [36] (p.480). In that study, the participants identified the main burdens to participating in research as being associated with the 'inconvenience and time commitment' involved. They wanted to know how the 'time commitments ... would fit into their schedule'. This was consistent with our data. Furthermore, Ballantyne et al., [36] report how some women had said they had declined to participate in other studies during pregnancy where greater time commitment was involved. Similarly, time was a barrier in the qualitative study by Ayoub et al., [45] on recruitment and participation of pregnant women in research. They highlighted how having a balance between participation and other life demands was central in the decision to participate in research. Some of our participants said they were unable 'to commit' to the trial requirements, which resonates with Baker et al., [40] (p.65) who said '...issues, such as self-commitment..' are central to deciding to participate in a study. The linkage between non or partial compliance with trial requirements and study results can be seen in other studies. For example, Ballantyne et al., [36] (p.479), report how the participants cared about the study outcome, which included being interested in the results and hoping that the '...study would show meaningful results'.

In relation to diary related issues and how smart phone based diaries were suggested by some participants to ensure compliance, caution is advised by

Laughland & Kvavilashvili [46] (p.552) from their recent studies in the UK. They compared participant owned smart phone based diaries and paper diaries in three studies designed to determine if smart phones were associated with greater compliance and a higher number of entries compared to the paper diary. They found that those using their smart phone were compliant because they had diaries with them continually and completed their diary entry sooner; however, in all three studies 'significantly fewer memory events were recorded in smart phones than paper diaries...'. They offer some suggestions for overcoming this challenge around sending reminder to participants using their smart phone and conclude how 'participant-owned smartphone diaries will become the standard tool' [46] (p.561).

In our study, some participants wished to see a better known product being investigated while some had a preference for organic products. We were using a common baby oil considered to be a hypoallergenic Paraben-free product. Baby oil tends to be chosen by a smaller proportion of women to prevent stretch marks in pregnancy but nevertheless continues to be some women's choice [1, 8, 15] and, as with other products used by women, there is a lack of strong evidence of effectiveness from high quality trials [7] to support its use. Our participants also mentioned a product that has research to support its effectiveness, which may relate to some misunderstanding of randomised trials and the concept of equipoise as highlighted above or indeed the influence of product marketing. The suggestion for use of more organic or natural products is not surprising due to their attraction for pregnant women who increasingly request '...advice on natural ways to deal with the discomforts [they experience] during pregnancy' [47] (p.274).

Finally, we interpreted from the data that incentives may be useful but not a major determining factor in participation in a future study. Women's decision to participate in research is often related to their belief in contributing to scientific inquiry [20, 36, 40], wanting to help others or the chance of a better outcome for their own pregnancy [27, 40]. For example, participants in the ORACLE study were influenced by the possibility of delaying pre-term labour [27]. While participants in the MAGPIE trial of prophylactic anti-convulsants for severe pre-

eclampsia reported that participation was a means to getting the 'active treatment...a drug they would not otherwise receive...' and which they had been advised would prevent a seizure [48] (p.e543). Some studies also refer to the concept of altruism [40, 45], which is often related to contributing to scientific inquiry and benefitting society and themselves [45].

Participants in our study were not over burdened by requests to participate in other research studies since becoming pregnant. We are not aware of any evidence on research demands on women during pregnancy but Close et al., [18] report how participation in another study was an exclusion criteria in their study due to the extra time and travel expense burden. Not being asked to join other studies was most likely related to the early stage of their pregnancy for participants in our study. Timing and how participants are approached are also important [19, 40]. Timing in particular has been identified as a factor for non-participation, as has being given 'an overwhelming amount of information' [20] (p.8). Information overload has relevance for our study due to recruitment to the pilot trial being at the booking visit when much other information is given to women, but this did not seem to be an issue in our study overall perhaps because the waiting times at the clinic allowed women adequate time to discuss the trial. Nevertheless, in other studies women have reported how a 'conducive environment' is important during study recruitment [40] (p.63) and antenatal clinics can be busy areas.

Our study has some limitations. The participants were from one geographical area and only included English speaking women. In addition, all participants had been invited to participate in a single trial investigating the effectiveness of a moisturising oil (Baby oil) compared to no treatment for the prevention and reduction in severity of striae gravidarum. However, a strength is that factors identified relate to actual decisions not to participate in a real trial rather than a hypothetical trial or trial scenario, and, as such, our findings may inform recruitment strategies in other similar trials. This focus on a real, rather than a hypothetical trial is in keeping with the plans for the Cochrane review of recruitment strategies for randomised trials which will be limited to real trials only in future updates [49].

5.8 Conclusion

This qualitative descriptive study contributes to the existing body of evidence on striae gravidarum and offers insight into the factors influencing recruitment to the pilot trial on their prevention. It highlights how stretch mark prevention in pregnancy is important to most women and most take preventative action. Product choice is important and while there is a lack of strong evidence in relation to the effects of most of the products women are using, women do not seem to be influenced by that. In addition, participants in our study thought that using any product was better than not doing anything and some also thought that the intervention product proposed for the pilot trial was not as good as some of their known products, despite not having evidence to support this opinion.

Key points arising from this study for future striae gravidarum prevention trials is that a trial involving a well-known intervention product may be more likely to be accepted by women and may promote recruitment, while trial requirements need not be too burdensome on women. Finally, our study suggests that further work is required to overcome the non-acceptability of randomisation and to convey equipoise or uncertainty during trial recruitment, although our discussion section includes some suggestions for future trials on the prevention of striae gravidarum.

5.9 List of abbreviations

Not applicable.

5.10 Declarations

5.10.1 Ethical approval and consent to participate

This study was approved by the Clinical Research Ethics Committee for the Galway University Hospitals (C.A. 1989) (Appendix 28).

5.10.2 Consent for publication

Not applicable.

5.10.3 Availability of data and materials

The data analysed during the current study are available from the corresponding

author on reasonable request.

5.10.4 Competing interests

The authors declare that they have no competing interests.

5.10.5 Funding

Funding was received in support of the study from the School of Nursing & Midwifery, National University of Ireland Galway, Galway, H91 TK33, Ireland.

5.10.6 Authors' contributions

MB, MC and DD conceived the study. All authors contributed to the development of the interview guide. MB was responsible for the data collection and did the data analysis under the supervision of MD. MB prepared the initial manuscript draft and MD, DD and MC reviewed and contributed to subsequent drafts. All the authors saw and approved the final version of this article.

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5.12 Summary of key points

This qualitative descriptive study explored the factors influencing recruitment to a pilot trial that experienced challenges to recruitment. The pilot trial was designed to evaluate the feasibility of a definitive trial to compare a moisturising oil to no treatment in the prevention and reduction in severity of striae gravidarum. Sixteen primigravid women, attending an Irish maternity hospital participated in a semi-structured telephone telephone interview. Data from 15 women were included in the analysis which was guided by the framework method.

On analysis four main themes consisting of 12 categories were identified from the interview data. The themes focused on women's prevention of stretch marks and their choice of anti-stretch mark product, who and what influenced that choice and influences on trial participation. In relation to influences on trial participation, the possibility of being randomised to the non-intervention or control group was a deterrent for many women.

This study supported the view that striae prevention is important to pregnant women, as is their choice of product to prevent them. Offering women the opportunity to be part of a trial that would be of low burden and would test a well-known product may optimise recruitment. However, reluctance to be randomised because of the possibility of being allocated to the non- intervention control group suggests that further work is needed in this field on how best to communicate uncertainty to potential participants.

Chapter 6: Discussion

This chapter presents the overall discussion of the thesis, providing a review and critical discussion of the findings of the studies undertaken. It begins with an outline of the thesis followed by the key findings from the four papers, and then discussion of the findings in the context of the literature on the prevention of striae gravidarum, and the contribution of the thesis in the context of knowledge generation on the prevention of striae gravidarum. Strengths and limitations of the thesis are identified and, finally, implications for practice and further research are discussed.

6.1 Outline of the thesis

This thesis focuses on the prevention of striae gravidarum in primigravid women and comprises four papers. First, I undertook a Cochrane systematic review and meta-analysis to review the evidence of the effectiveness of topical preparations for the prevention and treatment of striae gravidarum (Chapter 2). The review findings informed the next two papers (survey and pilot trial). The descriptive cross-sectional survey on the use of anti-stretch-mark products by women in pregnancy identified the topical products used by women during pregnancy to prevent or reduce the development of striae gravidarum (Chapter 3). This paper was followed by the protocol for the pilot trial of the feasibility of conducting a randomised controlled trial to evaluate the effectiveness of a commercially available moisturising oil compared to no treatment (Chapter 4). Finally, the last paper arose from recruitment difficulties in the pilot trial and addressed the factors influencing recruitment of women to trials of interventions for the prevention of striae gravidarum (Chapter 5).

6.2 Key findings

6.2.1 Topical preparations for preventing stretch marks in pregnancy

The Cochrane systematic review and meta-analysis found that there was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment, and that there was no statistically significant average mean difference in the severity of stretch marks. Similarly, there was no statistically significant average difference in the

development of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients and there was no statistically significant difference in the severity of stretch marks. The review found an absence of high-quality evidence to support the use of any of the topical preparations tested in the prevention of stretch marks during pregnancy, and identified a clear need for robust, methodologically rigorous randomised trials involving larger sample sizes to evaluate the effects of topical preparations on the development and treatment of stretch marks in pregnancy.

6.2.2 *The use of anti-stretch-marks' products by women in pregnancy: a descriptive, cross-sectional survey*

In the survey, it was found that most respondents (n = 589, 78.2%) used a product to prevent or reduce the development of stretch marks during their current pregnancy. A large range of products were used and more than one-third of women (n = 210, 36.5%) had used two or more products. *Bio-oil* was the most frequently used product (n = 351, 60.9%) and it was also the most frequently used product among women who used only one product (n = 189, 32.8%). We concluded that many women apply one of the many products available to prevent or reduce the development of striae gravidarum, that *Bio-oil* was the most commonly used product identified in this study, and that there is a need for high-quality evidence on the effectiveness of *Bio-oil* and other products in the prevention or reduction in the development of striae gravidarum. In addition, the majority of respondents (n=514; 75.5%) indicated that they would consider participating in a future trial to evaluate a product to prevent or reduce striae gravidarum.

6.2.3 *Study protocol for a pilot randomised controlled trial*

Recruitment to this pilot trial was challenging from the offset (Summer 2017). Following review and consultation, the gestational weeks inclusion criterion was changed from 12-14 weeks to 12-16 weeks to maximise the recruitment opportunity. However, it became apparent after a month of trying to recruit women to the study that an alternative strategy was necessary. We decided that an exploration of the factors influencing recruitment to the trial was necessary to

elucidate factors influencing recruitment and to guide future research on this topic. Efforts to recruit to the trial continued following ethical approval, and women who declined to participate in the pilot trial were invited to participate in a qualitative study to explore the factors influencing recruitment.

6.2.4 A qualitative study of the factors influencing recruitment to a pilot trial

This study of 15 women identified four main themes, consisting of 12 categories. The themes focused on women's prevention of stretch marks and their choice of anti-stretch-mark product, who and what influenced that choice, and influences on trial participation. In relation to influences on trial participation, the possibility of being randomised to the control group was a deterrent for many women. The study concluded that the prevention of stretch marks is important to pregnant women, as is their choice of product to prevent them. Offering women the opportunity to be part of a trial that would be of low burden and would test a well-known product may optimise recruitment. However, reluctance to be randomised because of the possibility of being allocated to the control group suggests that further work is needed in this field on how best to communicate randomisation to potential participants.

6.3 Discussion

As outlined above, the Cochrane systematic review and meta-analysis (six trials involving 800 women) substantially updated the original review, 'Creams for preventing stretch marks in pregnancy' (two trials involving 130 women) (Young & Jewell, 1996) and included a meta-analysis, which had not been included in the previous version. Updating of reviews is seen as '*more efficient than starting afresh*' (Garner *et al.*, 2016:1) and was embarked on in light of the review meeting a number of the criteria for updating (Garner *et al.*, 2016); for example, a current objective or question, and the availability of new studies. Our updated review included both primary and secondary outcomes, i.e. presence of stretch marks and severity of stretch marks respectively compared to the presence of stretch marks. We also restructured the review comparisons. In addition, the review reflected updated review methods as included in the updated Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green, 2011).

6.3.1 Agreements and disagreements with other studies or reviews

As can occur with an updated review, with the addition of new studies (Garner *et al.*, 2016), our findings differed to the earlier version of the review (Young & Jewell, 1996), which suggested that one or both of the interventions may be helpful in preventing striae gravidarum. Young & Jewell (1996) suggested that one of the products, Trofolastin cream, when compared to a placebo (Mallol *et al.*, 1991), seemed to help prevent the development of striae gravidarum in some women, while the second product, Verum ointment (Wierrani *et al.*, 1992), may also be helpful compared to no treatment. However, they cautioned that the effect of Verum may be due to massage alone. Our findings differed from findings in the previous version of the review due largely to us having used updated review methods (Higgins & Green, 2011).

- (i) We assessed risk of bias using the seven items advised by Higgins & Green (2011). This contrasts with the previous version where the focus was on randomisation and blinding only. Risk of bias was addressed by Young & Jewell (1996) according to the guidance in an earlier version of the Cochrane handbook (Clarke & Oxman, 2000, cited in Young & Jewell, 1996). This closer examination of the risks of bias of included studies informed the overall conclusion of an absence of high-quality evidence to support the use of any of the topical preparations studied. None of the studies was '*at low risk of bias across all seven domains*' (Brennan *et al.*, 2012:9). Furthermore, '*all of the included studies were at unclear risk of bias for allocation concealment except for Wierrani (1992), which was at high risk of bias*' (Brennan *et al.*, 2012:9).

- (ii) We included a meta-analysis using a random-effects model due to the clinical diversity of interventions (different topical preparation with different active ingredients) '*to produce an overall summary of the average treatment effect across the six included trials*' (Brennan *et al.*, 2012:8).

Our assessment of the implications for research concurred with that of Young & Jewell (1996) with respect to the need for larger studies to examine the effectiveness of anti-striae products. However, we diverged somewhat in relation

to the nature of the intervention; i.e. we recommended that preparations used commonly by women to prevent and treat striae be evaluated within the context of robust, methodologically rigorous and adequately powered randomised trials, in contrast to examining individual ingredients as suggested by Young & Jewell (1996) which pose many challenges. Our recommendation reflects our awareness of the many products available for women to choose and that many of the products used commonly by women had not been evaluated in the context of high-quality randomised trials.

Systematic reviews should be up to date to maintain their influence in informing practice and policymaking (Garritty *et al.*, 2010). Updating is important to ensure that they retain their validity (Garner *et al.*, 2016) and do not misguide consumers (Garner *et al.*, 2016). Findings from new studies are included, resulting in speedier dissemination of effective findings (Mulrow, 1994, citing Chalmers *et al.*, 1986). Our review and the original one (Young & Jewell, 1996) present 'a snapshot' of the available knowledge on the prevention of striae gravidarum at that point in time, i.e. from the date of the literature search (Garner *et al.*, 2016). Such reviews are valuable and often lead to changes in clinical practice (Greener, 2011). Our review provided the best evidence for the prevention of striae for clinicians. An example of how a review can reach and inform practitioners is evident from the reporting of the review in the *British Journal of General Practice* in 2013 by McAvoy, serving to update general practitioners on the review findings. This is important particularly as we found that many women start to use topical products for the prevention of striae gravidarum prior to their first antenatal clinic visit in the maternity unit (Brennan *et al.*, 2019 under review) and will have visited their general practitioner in advance of this. While it may be a topic addressed during this visit by some women, our research would suggest that women are not influenced by their general practitioner when choosing an anti-striae product (Brennan *et al.*, 2016; Brennan *et al.*, 2019 under review). In our survey, we found that only 3.4% (n=19) of our sample got information on anti-striae products from general practitioners, while general practitioners did not feature in the interview data from our qualitative study (Brennan *et al.*, 2019 under review).

Our review has been noted and cited in the literature by other researchers and reviewers on both striae in general (Al-Himdani *et al.*, 2014; Ud-Din *et al.*, 2016; Wehner *et al.*, 2017) and striae gravidarum specifically (Antoszewski *et al.*, 2015; Kocaöz *et al.*, 2019; Korgavkar & Wang, 2015; Lee *et al.*, 2016; Tang-Lin *et al.*, 2017). Interestingly, some studies – eg, Soltanipour *et al.* (2014) and Ersoy *et al.* (2016) – cite the previous version of the review (Young & Jewell, 1996), thereby not benefiting from the latest evidence.

Since 2012, two other reviews on striae gravidarum have been published. Both are in dermatology-related journals (Farahnik *et al.*, 2017; Korgavkar & Wang, 2015) and add to the current state of knowledge. Furthermore, a number of reviews have looked at striae distensae or striae in general; for example, Al-Himdani *et al.* (2014) and Ud-Din *et al.* (2016) but, as they also include striae gravidarum, they will be considered here. No Cochrane systematic review was identified that addressed topical products for the prevention of striae distensae; there was a protocol for 'interventions for established stretch marks' (Wehner, *et al.*, 2014) but this was withdrawn subsequently (Wehner *et al.*, 2017) for unknown reasons. Here, I describe and compare the four reviews that focus on or include striae gravidarum with our review (Brennan *et al.*, 2012).

The earlier of the two reviews on striae gravidarum (Korgavkar & Wang, 2015) reviewed topical prevention and risk factors for striae gravidarum. Prevention was examined in relation to 'the de novo development of' striae gravidarum and 'reducing the severity' of lately developed ones (Korgavkar & Wang, 2015:606). Korgavkar & Wang (2015) performed a systematic search in PubMed and Google Scholar, using an array of appropriate keywords. A broad search strategy is evident; it included '*review articles, observational studies, case series and cohort studies published from 1950 to 2014*' (Korgavkar & Wang, 2015:607). Although not mentioned under the methods, randomised trials were included in the review. Where translation was possible, non-English publications were also included, reflecting the comprehensiveness of the review. Excluded publications are explicit; for example, conference proceedings. Seventeen studies are included in the review on topical prevention of striae gravidarum, but some of these (n=5) include non-pregnant women, postnatal women and in some cases

those with striae due to any cause. Elson (1990) included 19 females and one male with striae in their study. While they had developed striae related to puberty, pregnancy and obesity, 60% (n=12) developed them during pregnancy. Studies are described and findings and limitations reported both in the narrative and in a supporting table. Overall, the Korgavkar & Wang review is not a systematic review and meta-analysis that follows a clear protocol and guidelines for the methods (Higgins & Green, 2011). Further, there is no clear and transparent detail on the assessment of risk of bias, which is integral to a robust, systematic review.

Korgavkar & Wang (2015) structured their review narrative of topical prevention under broad '*modalities*' or categories such as Centella ('a medicinal herb' found in some products and thought to be the active ingredient), almond oil, Hyaluronic acid (also thought to be the active ingredient and found in some products), Tretinoin and cocoa butter-related studies. They included five studies involving non-pregnant women under the evaluation of Tretinoin (contra-indicated in pregnancy) for the treatment of striae gravidarum, but highlight that three of the five studies included women with pregnancy-related striae, and in one study the women had newly developed striae. The authors found that there was insufficient evidence to support the use of Centella and probably bitter almond oil massage to prevent or reduce the severity of striae gravidarum. Further, the evidence in support of hyaluronic acid is tenuous. Korgavkar & Wang (2015) state in their discussion that the effects of massage compared to the hyaluronic acid need clarification. Though not appropriate in the context of our review, they report that the study results for tretinoin for reducing the severity of newly developed striae gravidarum seem encouraging (Korgavkar & Wang, 2015), but not in pregnancy. In relation to cocoa butter and olive oil, neither was found to be effective for prevention or reducing the severity of striae gravidarum (Korgavkar & Wang, 2015). Korgavkar & Wang (2015:606) concluded that '*reliable methods for preventing SG are scarce*' and that strong evidence is lacking from rigorous well-thought-out randomised controlled trials involving large samples in support of the available topical '*modalities*' generally. They also direct the focus of further research towards clarifying the pathogenesis of striae in the hope of identifying '*prevention modalities*' (Korgavkar & Wang, 2015:606).

They do not recommend further trials but instead highlight that there are significant barriers to doing rigorous trials on striae gravidarum, referring to the aversion of doctors and the '*scientific community*' to allocating significant resources to such research in light of how striae gravidarum are not physically harmful. This contradicts the view held commonly that striae can affect women both physically and psychologically, in particular when they are severe (Chang *et al.*, 2004). One is reminded here of how Liberati (2011:1777) highlighted a '*need to realign patient-oriented and commercial and academic research*' in his *Lancet* correspondence as recently as 2011. He reports how patients usually do not get to influence the focus of research and there is often a discrepancy between what is researched and patients' need.

Korgavkar & Wang (2015) included trials and observational designs, whereas we included only randomised and quasi-randomised trials in our review. The six studies included in our review (five randomised trials and one quasi-randomised trial) were all included by Korgavkar & Wang (2015). While highlighting poor randomisation in the limitations of the Wierrani *et al.* (1992) study, Korgavkar & Wang do not classify it as quasi-randomised *per se*. Korgavkar & Wang (2015) included three randomised trials completed since our review (García Hernández *et al.*, 2013, n=183; Soltanipoor *et al.*, 2012, n=100; Soltanipoor *et al.*, 2014, n=150), 'a posttest-only quasi-experimental design with a control group' (Timur Taşhan & Kafkasli, 2012:1570, n=141) and two observational studies (Davey, 1972, n=74; Poidevin, 1959, n=116).

The more recent review by Farahnik *et al.* (2017) considered risk factors, prevention and management of striae gravidarum, including modalities of treatment beyond topical preparations eg, light therapy. They searched the literature systematically, including PubMed and MEDLINE databases, textbooks and the reference list of retrieved studies. The review identified 28 studies from 1959 to 2016 focused on striae gravidarum. Twelve studies on prevention of striae gravidarum and five on treatment of striae gravidarum were included. Interestingly, studies on treatment included non-pregnant women and possible non-pregnancy-related striae (though this is unclear). Their rationale for including these relates to how the treatments may be helpful in the treatment of

striae gravidarum in future. Study designs included '*cross-sectional, prospective, randomised controlled, and quasi-randomised controlled studies*' (Farahnik *et al.*, 2017:78). Though Farahnik *et al.* (2017) exclude non-English language studies, they include two articles translated from German.

While acknowledging the shortage of studies supporting prevention of striae gravidarum, Farahnik *et al.* (2017) found that Centella, hyaluronic acid, and daily massage offer some hope. They suggest that Centella has the most evidence and that, while hyaluronic acid has been found to reduce significantly the incidence of striae gravidarum, they suggest that its effectiveness is unclear and may indeed be attributed to massage. They acknowledge that there have been improvements in the treatment of general striae recently, referring to improvements with Tretinoin $\geq 0.05\%$ and non-ablative fractional lasers in treating striae distensae. They conclude that there has been a revival in striae gravidarum research, with some promising findings and new options for treating '*these disfiguring marks of pregnancy*' (Farahnik *et al.*, 2017:77).

The findings from both these reviews highlight the lack of clarity on the effectiveness of the different products reviewed and also the lack of high-quality evidence in support of their use. Centella may offer some benefit, but currently there is insufficient evidence to advocate strongly in its favour. While hyaluronic acid and bitter almond oil with massage or indeed massage alone might also be helpful, more research is needed. Both authors differ in their recommendations for this research; Farahnik *et al.* (2017) support our position while Korgavkar & Wang (2015) emphasise learning more about how striae develop as a means of identifying preventative strategies for striae gravidarum. This is challenging, as evident from a more recent study by Wang *et al.* (2018), who investigated the molecular changes in collagen fibrils in early striae as a means of determining the cause of fading or 'atrophy' of striae gravidarum. In their study, which compared skin samples from 28 women from three sites (centre of striae gravidarum, normal abdominal but stretched skin near striae gravidarum, and normal non-stretched skin from the hip area [control]), they found that early striae gravidarum are characterised by significant separation and disorganisation of the collagen bundles. They suggest that treatments such as topical retinoids

may be helpful in treating early striae but add that it is unclear if they can prevent new striae and that they are not usually given in pregnancy.

Comparing our review with Farahnik *et al.* (2017) and Korgavkar & Wang (2015), first, we adopted a systematic approach to searching, screening, risk of bias assessment and synthesis – in both of the above studies, the reviews are less systematic in approach. Secondly, they included the more recent trials on prevention of striae gravidarum, while Korgavkar & Wang (2015) also included the quasi-randomised and observational studies, which contrasts with our inclusion of randomised and quasi-randomised trials only (Brennan *et al.*, 2012). Thirdly, we conducted a robust risk of bias assessment of included studies which was not performed by Farahnik *et al.* (2017) and Korgavkar & Wang (2015), and, fourthly, unlike both studies, we undertook a meta-analytical synthesis.

Compared with our review findings, both Korgavkar & Wang (2015) and Farahnik *et al.* (2017) specify certain ingredients and/or products which may or may not be of some help, though they differ as to which ones. According to Korgavkar & Wang (2015), there is not enough evidence in support of Centella while, according to Farahnik *et al.* (2017), it offers hope. With hyaluronic acid, both seem to be saying the same thing, as Korgavkar & Wang (2015) say that the evidence is weak but add that the effects of the product compared to massage need to be unravelled, while Farahnik *et al.* (2017) sees it as hopeful but note in the discussion that its effectiveness may be due to massage. Secondly, unlike Korgavkar & Wang (2015), and Farahnik *et al.* (2017) our meta-analysis and synthesis yielded clear results and conclusions.

Both Farahnik *et al.* (2017) and Korgavkar & Wang (2015) mention the quality of available randomised controlled trials, while Farahnik *et al.* (2017) note the dearth of well-conducted randomised controlled trials. Korgavkar & Wang (2015) cite our review in support of an absence of high-quality evidence to support the use of any of the topical preparations tested in the prevention of striae gravidarum (Brennan *et al.*, 2012). Our highlighting of the need for well-designed randomised trials with large samples to evaluate the effects of topical

preparations, in particular those used commonly by women, is echoed by Farahnik *et al.* (2017).

Both reviews on striae distensae (Al-Himdani *et al.*, 2014; Ud-Din *et al.*, 2016) included striae gravidarum in addition to striae due to other risk factors (eg, adolescence and Cushing's syndrome). Al-Himdani *et al.* (2014) focus on prevention and treatment of striae distensae. Unlike the previous two reviews (Korgavkar & Wang 2015; Farahnik *et al.*, 2017), Al-Himdani *et al.* (2014) assessed and graded the evidence level according to the study design and methodology, which they adapted from the Oxford Centre for Evidence-Based Medicine (Ball *et al.*, 2001, cited in Al-Himdani *et al.*, 2014). The review findings from 16 studies are presented in both narrative and in table form. In the narrative, prevention of striae gravidarum is included under the broad heading of treatment and topical agents, and includes the six studies included in our review in addition to one non-randomised trial (Timur Taşhan & Kafkasli, 2012) not included in our review due to being published in 2012. However, they also include a study (Méndez Velarde *et al.*, 2010), which we excluded from our review because it compared cream application on wet skin compared to dry skin and did not include a placebo or control group (Brennan *et al.*, 2012). The finding by Al-Himdani *et al.* (2014:527) that topical agents appear to lack efficacy is tentative in the absence of an appropriate meta-analysis, in contrast to our meta-analyses findings (Brennan *et al.*, 2012). Their conclusion that there is a lack of high-quality evidence from large randomised controlled trials supporting the use of creams and lotions in the prevention of striae gravidarum concurs with our review conclusion (Brennan *et al.*, 2012).

Similar studies on prevention of striae gravidarum were included by Al-Himdani *et al.* (2014) (including our six) as in the other two reviews (Korgavkar & Wang 2015; Farahnik *et al.*, 2017). However, unlike Korgavkar & Wang (2015) and Farahnik *et al.* (2017), they do not include the trial by García Hernández *et al.* (2013, n=183), which was also not included in our review due to being published in 2013. This trial found that the incidence of striae for women without pre-existing striae was significantly lower for the treated group compared with the control group (5.6% vs. 35%, P = 0.031, OR: 9.2 [95% CI: 1.0–83.3]) while the

severity of striae was greater in the control group than in the treatment group (García Hernández *et al.*, 2013). Finally, Al-Himdani *et al.* (2014) highlight the scarcity in rigorous trials evaluating topical treatments for striae distensae, which includes both prevention and striae gravidarum, while Korgavkar & Wang (2015) say there is a lack of strong evidence in support of the topical modalities for preventing striae gravidarum. Both points concur with our conclusions (Brennan *et al.*, 2012).

In the second review on striae distensae, Ud-Din *et al.* (2016) focus on prevention and treatment but refer to striae rubra and alba specifically. They sought to assess the evidence in support of topical agents in striae distensae, and offer a structured approach to their management (i.e. of signs and symptoms of striae with the appropriate agent). They ascribed a level of evidence to the 11 studies according to their design involving five levels ranging from randomised controlled trials to expert opinion or case report. In relation to striae gravidarum prevention, they included five of our studies (Brennan *et al.*, 2012), but excluded Wierrani *et al.* (1992) for unknown reasons. However, like Al-Himdani *et al.* (2014), they also include the study by Timur Taşhan, & Kafkasli (2012).

Ud-Din *et al.* (2016) note that most of the data in relation to the commercial products included are unpublished and that most of the topical products have no peer-reviewed evidence to support their use, while some – for example, Clarins® Stretch Marks Cream – have no clinical trials supporting them (Ud-Din *et al.*, 2016), which reinforces our conclusion (Brennan *et al.*, 2012) on the need for these products to be evaluated in the context of randomised controlled trials.

The reviews by Al-Himdani *et al.* (2014) and Ud-Din *et al.* (2016) differed from our review (Brennan *et al.*, 2012) in that they (i) focused on striae distensae but also included striae gravidarum, (ii) focused on prevention and treatment of both, (iii) adopted a less systematic approach to searching, screening, risk of bias assessment and synthesis, (iv) considered prevention and treatment under treatment, (v) included a non-randomised controlled trial published in 2012 not included in our review, (vi) in the case of Ud-Din *et al.* (2016), did not include

Wierrani *et al.* (1992), and (vii) in the case of Al-Himdani *et al.* (2014), included Méndez Velarde *et al.* (2010). However, both recommended the need for randomised controlled trials to evaluate topical products for both prevention and treatment of striae distensae, similarly to Brennan *et al.* (2012).

When we last updated our review, there were two studies awaiting classification (Lachmann *et al.*, 2011; Ortega, 1985) and since then further studies have been published, as noted above (Timur Taşhan & Kafkasli, 2012; Soltanipoor *et al.*, 2012; García Hernández *et al.*, 2013; Soltanipoor *et al.*, 2014) which will be considered for the updating of this review. One of the studies involves an anti-stretch mark cream with Centella asiatica triterpenes among other ingredients (García Hernández *et al.*, 2013). This is to be welcomed on two fronts; first, the product is a commercially available one and, secondly, the study involves Centella, which has been suggested for further investigation (Korgavkar & Wang, 2015; Farahnik *et al.*, 2017). However, since it is only one of the ingredients in the product, attributing any effect, if present, to specific ingredients or combination of ingredients will not be possible.

Our review recommended that well-planned, robust, randomised trials involving larger sample sizes be undertaken to evaluate the effects of topical preparations on the development and treatment of striae gravidarum, setting the background for the descriptive cross-sectional survey which constituted the second study in this thesis and supporting the planning of a pilot randomised trial to determine the feasibility of undertaking such a trial.

6.3.2 The use of anti-stretch-marks' products by women in pregnancy: a descriptive, cross-sectional survey

This large survey marked an important step towards developing the protocol for the later pilot trial. We were lacking information on use of anti-striae products by women in Ireland, frequency of product application, and the likelihood of women agreeing to take part in a trial to evaluate the effectiveness of a product to prevent or reduce striae gravidarum. We sought this information in the descriptive cross-sectional survey, using a questionnaire (Brennan *et al.*, 2016).

Our survey was the first to ask women specifically about their use of anti-stretch-mark products and related practices including, for example, application of the product and influences on women's decisions to use a product. While some researchers have reported on the use of anti-striae products (Bahrami *et al.*, 2012; Durmazlar & Eskioğlu, 2009; Kocaöz *et al.*, 2019), such studies focused commonly on risk factors or prevalence of striae gravidarum.

One study published in December 2015 (after our survey had been completed) includes some of the information we sought (Brennan *et al.*, 2016). This Polish study involving 299 postnatal Caucasian women who were six months or less post the birth of their baby assessed how effective topical products, in addition to massage, were in preventing striae gravidarum (Antoszewski *et al.*, 2015). Data were collected via a newly developed questionnaire and included demographic items, striae occurrence, use of anti-striae products and women's opinion of their effectiveness. The authors found from their correlation testing of striae gravidarum and frequency of cosmetic product application that cosmetic use of various types, at least twice daily, is significantly more effective in preventing striae gravidarum than once-a-day cosmetic use (63.7% vs. 77.6%). However, product effectiveness was self-assessed and retrospective in nature, and the study used an observational design.

The instrument used in Antoszewski *et al.* (2015) would certainly have contributed to the development of our instrument. However, we sought additional information beyond that available in Antoszewski *et al.* (2015), including specific information on types of product used, factors influencing women's decision on choice of anti-striae product, how likely they were to be influenced by findings from a research study, and how many would likely agree to participate in a trial to evaluate anti-striae products.

Both studies used convenience sampling. Our sample was larger (n=753 versus n=299) and included a small number of women (n=46) recruited via maternity advocacy groups that posted the survey link on their websites. Further, our sample included pregnant women in contrast to postnatal women included by Antoszewski *et al.* (2015). Other comparisons with our study are the process of

questionnaire development and testing. The development of the questionnaire (Brennan *et al.*, 2016) mirrored best practice (Boynton & Greenhalgh, 2004; Kelley *et al.*, 2003) and included the testing of content validity with a panel of experts. This could be seen as a strength of our study (Brennan *et al.*, 2016), as detail is given infrequently on instrument development or quality indexes such as reliability and validity in the literature considered in this thesis.

In relation to findings, similar percentages of women were using an anti-striae product in the two studies (Antoszewski *et al.*, 2015; Brennan *et al.*, 2016), with rates of 79.6% (n=238) and 78.2% (n=589) respectively, while both studies found that some women used more than one product.

Our survey is one of the largest cross-sectional observational studies undertaken on the topic of striae gravidarum. We identified 21 observational studies with smaller sample sizes (Antoszewski *et al.*, 2015; Atwal *et al.*, 2006; Bahrami *et al.*, 2012; Chang *et al.*, 2004; Davey, 1972; Durmazlar & Eskioğlu, 2009; Ersoy *et al.*, 2016; Ghasemi *et al.*, 2007; Kasielska-Trojan *et al.*, 2015; Kocaöz *et al.*, 2019; Lerdpienpitayakul *et al.*, 2009; Madlon-Kay, 1993; Mosbeh, 2019; Murphy *et al.*, 1992; Narin *et al.*, 2015; Nusrat *et al.*, 2019; Osman *et al.*, 2007; Poidevin, 1959; Thomas & Liston, 2004; Yamaguchi *et al.*, 2012; Yamaguchi *et al.*, 2014) and one study where the sample size exceeds ours (Picard *et al.*, 2015), with 800 hundred women included from three obstetric departments in Rouen in France.

We included an online version of our questionnaire, which was made available to women via a number of maternity care advisory groups. Similar access was not offered in other similar studies.

Although our sample was a large one with a high response rate (97%), it was not a representative sample and diverged from one of the principles of survey design in not capturing population diversity (Greener, 2011), which we were aware of during the planning stages. Therefore, against this background, we included the web-based electronic version of the questionnaire. Although it did not yield a representative sample, it was a strategy to capture the views of the

wider population, particularly as it is seen as potentially offering access to groups of people known to be interested in a particular topic (Polit & Beck, 2017). We recognised the use of a non-probability sample as a limitation of our study (Brennan *et al.*, 2016) and did not seek to make wider inferences.

Finally, with respect to the survey findings, it was evident from the survey that many women (n = 589, 78.2%) attending one large Irish maternity unit were using a topical product to prevent or reduce the development of striae gravidarum. Other studies also found that many women were using anti-striae products (Yamaguchi *et al.*, 2014, 77.6%, n=121, and Antoszewski *et al.*, 2015, 79%, n=238). Others found lower usage of anti-striae products by participants (Lerdpienpitayakul *et al.*, 2009, 69.9%, n=190; Osman *et al.*, 2007, 61%, n=67; Madlon-Kay 1993, 54%-63%, n=26-30; Kocaöz *et al.*, 2019, 40.9%, n=172). These studies and ours demonstrate that prevention of striae gravidarum is important to women.

6.3.3 The importance of preventing striae gravidarum

While acknowledging the importance of striae gravidarum prevention to women, it does not elicit the same attention as other physiological changes of pregnancy. Unlike other physiological changes, striae or other skin changes are not, for example, included in the current NICE guidelines for uncomplicated pregnancies (2008; 2019) nor are they included in the Australian Pregnancy Care Guidelines (Department of Health, 2019) or the WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience (WHO, 2016). Although there are variations in the minor disorders included in the different guidelines and recommendations, it is unclear as to why striae gravidarum are not included in light of their effects on women. They are a common physiological change affecting the skin, and do not disappear entirely after pregnancy (Atwal *et al.*, 2006; Murray, 1990; Muzaffar *et al.*, 1998; Vaughan Jones, 2007; Young & Jewell, 1996), can be seen as 'disfiguring' (Buchanan *et al.*, 2010; Chang *et al.*, 2004), and are known to affect women's quality of life (Mosbeh, 2019; Nusrat *et al.*, 2019; Ogrum & Dogru, 2019; Yamaguchi *et al.*, 2012). It has been suggested that their non-resolution may affect women psychologically and consequently their quality of life (Mosbeh, 2019). Their psychological effects can be weighty (Farahnik *et al.*,

2017) and distressing for some women (Yamaguchi *et al.*, 2014), while some may also have lack of self-confidence (Narin *et al.*, 2015). Overall, women with severe striae seem to be most affected, both physically due to the pruritus and irritation (Chang *et al.*, 2004) and in relation to quality of life (Nusrat *et al.*, 2019; Ogrum & Dogru, 2019).

While the reasons for this lack of attention remain unclear, they may be related to the fact that striae gravidarum are not a medical issue (Ersoy *et al.*, 2016) or do not present a health risk (Lerdpienpitayakul *et al.*, 2009; Osman *et al.*, 2008; Salter & Kimball, 2006). Striae gravidarum do seem to be perceived differently to other commonly occurring physiological changes and, although they are not a health problem, they do affect women's health and are an unwanted aspect of pregnancy (Salter & Kimball, 2006; Yamaguchi *et al.*, 2012). Women want to prevent them.

We found that product use was significantly more common in primigravid women. This concurs with the findings of Yamaguchi *et al.* (2014), the only other study we found that included both primiparae and multiparae. Most of the other studies on striae gravidarum limited their participants to nulliparous or primiparous women so that they could focus on the development of new striae or those developed during the current pregnancy. It is possible to speculate that first-time mothers may be less likely to have pre-existing striae, though to what extent is unclear as striae distensae are reported as being 'extremely common' (Al-Himdani *et al.*, 2014). This high prevalence can present challenges for trialists seeking to focus on newly developed striae, as in the case of Osman *et al.* (2008) who, despite including nulliparous women in their trial, found a high proportion of women had striae at enrolment. A possible solution here may be to exclude those with stretch marks, as done by Buchanan *et al.* (2010) who included both primigravidae and multigravidae, but without stretch marks.

Furthermore, though associated with a number of risk factors such as use of steroids and Cushing's syndrome, striae are most frequently reported in relation to adolescents and pregnancy (Al-Himdani *et al.*, 2014). We found in our study involving both primigravidae and multigravidae (Brennan *et al.*, 2016) that 46.3%

(n=342) of women had developed striae *before* the current pregnancy and 46.7% (n=344) had developed them *during* the current pregnancy. These findings were important in planning the trial. In particular, the findings on product use by primigravidae indicated that prevention of striae gravidarum is a topic of sufficient interest to first-time mothers and they would be interested in participating in a trial to evaluate the feasibility of conducting a large trial on the effectiveness of a moisturising oil (commercially available) compared to no treatment. In addition, our finding that 68.3% (n = 514) of women would think about participating in a future trial of a product to prevent or reduce striae gravidarum and that significantly more primigravid than multigravid women would think about it (78.1 versus 67.0% respectively, $p = 0.001$) (Brennan *et al.*, 2016) was important.

Our survey demonstrates that more than one-third of women (36.5%, n= 210) had used two or more products to prevent or reduce the development of striae gravidarum. Use of more than one anti-striae product is not unusual and has been identified by others. While Osman *et al.* (2007) found that 17% (n=19) had used more than one product, usually rates for proportion of using more than one product are not specified by researchers. Madlon-Kay (1993) says that most women are using both creams and lotions while, in the cross-sectional descriptive study by Kocaöz *et al.* (2019), various interventions or products were used. Unlike our findings, the proportion of women using both classic and specialist types were fewer in Antoszewski *et al.* (2015). Interestingly, women in the Antoszewski *et al.* study who used products from both classic and specialist groups were significantly more positive about the effectiveness of the products in preventing and treating striae. The observational nature of this study and the use of self-assessment of striae may have contributed to women's confidence in the products used (Antoszewski *et al.*, 2015).

We were aware from our survey (Brennan *et al.*, 2016) that many women were using more than one product. This may be a factor reducing interest in our trial evaluating one product. The finding in our survey that women also had a preference for some products over others was an important finding in the planning of the trial. We found that Bio-oil was the most frequently used product

(n = 351, 60.9%) by women in our study overall, in those women solely using it (n=189, 32.8%) and in those using it in addition to one or more product (n=162, 28.1%).

As we were seeking to shape a trial protocol, Bio-oil did seem like the choice of intervention for the trial. We knew anecdotally that it was used by many women and, whenever mentioning prevention of striae gravidarum, both women and midwives usually mentioned it; thus, while its use was not a surprise, the extent of its use was.

Bio-oil is manufactured by a South African-based company, Union Swiss, and is marketed as '*specialist moisturizing oil that helps improve the appearance of scars, stretch marks*', among other benefits. It consists of an oil base with added plant extracts and vitamins. The oils include mineral oil, sunflower and lavender oil, and the vitamins are E and A, in addition to fragrances such as Citronellol. The manufacturers recommend that it be '*applied twice daily*' and, in pregnancy, '*it should be applied from the start of the second trimester to areas that are prone to stretch marks such as the abdomen, breasts, lower back, buttocks, hips and thighs*' (All Star Health/Union Swiss, 2019). Its claimed benefits include that it assists in decreasing the chance of striae in '*teenage growth spurts, pregnancy and periods of rapid weight gain*' and also in ameliorating already existing striae.

Bio-oil is classified as a cosmetic by the manufacturers, and while they are not required to undertake clinical research, they cite research on its effectiveness (Bio-oil Professional, no year a). Two study summaries are provided on the Bio-oil professional website (Bio-oil Professional, no year b) in support of Bio-oils' claims for improving the appearance of stretch marks. The first (Photobiology Laboratory of MEDUNSA, Medical University of South Africa, 2005), involving 20 women with bilateral abdominal striae aged 18 to 55, evaluated the effectiveness of bio-oil for '*improving the appearance of stretch marks*' in a single-blind (assessor) randomised controlled trial. Due to the bilateral abdominal striae, they used a half-abdomen study design. Bio-oil was applied twice daily for three months to the abdominal area. Outcome assessments were completed at baseline and monthly intervals and Bio-oil was found to be

effective, with 50% of women noting that striae had improved by two months (Bio-oil Professional, no year b).

The second study was a double-blind, randomised, parallel group trial with the same objective as above and including 38 women of different ethnicities aged 18-65 with striae on the abdomen, thigh and hips, due to various causes including pregnancy. The spread of striae at the different locations allowed '*a half-half stretch mark application*'. Bio-oil was applied twice daily for two months without additional massaging of the area. Outcome assessments were at baseline, then two-weekly until four weeks and again at eight weeks. The Patient and Observer Scar Assessment Scale (POSAS) was used to evaluate the scars. This is a scale used frequently to evaluate scars, by both patients and professionals, but patients' views must be included for a full scar evaluation. The study was published first in 2004 (Draaijers *et al.*, 2004), revised in 2005 and is currently under revision (van Zuijlen, for the POSAS group, no year). The study found that Bio-oil is effective in improving stretch mark appearance, with a statistically significant result after two weeks in 95% of the participants. After eight weeks, all participants demonstrated an improvement. The authors report that there was '*a continuous improvement of POSAS*' over the study time (Bio-oil Professional, no year c). Neither of these small studies is found in the published peer-reviewed literature, nor are there other published trials.

Given the wide use of Bio-oil and manufacturers' claims of effectiveness, it seemed reasonable for it to be the prime target for a randomised trial evaluation. However, this proved problematic, as described in section 6.3.4 and Chapter 5.

In summary, our large cross-sectional survey with a purposefully developed questionnaire (Brennan *et al.*, 2016) was unique in its focus and the information generated. It supported the importance of striae gravidarum prevention for women. Through informing the pilot trial (which will be discussed next), it brought to prominence the number of women who are taking preventative measures to prevent striae gravidarum in an Irish setting, how one product exceeded the popularity of all other products among women using anti-striae products during

pregnancy, and that primigravid women would be significantly more likely than multigravid women to consider participation in a future trial.

6.3.4 Prevention of striae gravidarum: study protocol for a pilot randomised controlled trial

Following from the conclusion of the Cochrane systematic review and informed by the cross-sectional descriptive survey findings, we developed the protocol for the pilot randomised trial to determine the feasibility of conducting the definitive trial to evaluate the effectiveness of a commercially available moisturising oil compared to no treatment for the prevention and reduction in severity of striae gravidarum (Brennan *et al.*, 2018).

The protocol was guided by the growing number of publications on pilot trial methodology (Arain *et al.*, 2010; Arnold *et al.*, 2009; Eldridge *et al.*, 2016a; Thabane *et al.*, 2010), reporting guidelines on randomised controlled trials extended to include feasibility and pilot studies (Eldridge *et al.*, 2016b), by the SPIRIT guidelines for designing and conducting a trial (Chan *et al.*, 2013a, 2013b & 2013c) and by protocols for other pilot trials. The protocol was also informed by methods used in other studies on striae gravidarum; for example, Soltanipour *et al.* (2014) and Davey (1972).

We considered the evaluation of Bio-oil in light of the survey findings (Brennan *et al.*, 2016) and the lack of published data as to its effectiveness. However, we noted that Bio-oil includes the ingredient Retinyl Palmitate (vitamin A), which is known to be teratogenic in pregnancy. I contacted the manufacturer but was unable to get further information on the type and amount of vitamin A used in Bio-oil. However, the Product Development Director stated that, *'taking absorption factors into account, an expectant mother would have to use more than 110ml of Bio-Oil per day, or almost two 60ml bottles, before exceeding the recommended daily maximum intake'*. Following this, I contacted a dermatologist in the UK who referred our query to a colleague in another UK university. His advice was that, due to the effects of oral vitamin A in animals, he would be concerned that *'chronic cutaneous application in pregnancy could have teratogenic potential. I would therefore not use anything containing retinyl*

palmitate in pregnancy'. I contacted the Irish Medicines Board who advised that '*studies with cosmetic products are outside of the scope of the CT Directive, therefore the IMB approval for such studies is not required*' (IMB, personal communication, 2012). In light of these findings and from an ethical perspective, I was not happy to proceed with Bio-oil as an intervention despite the survey findings.

The decision on choice of comparator in the trial was challenging. We were aware from our own study (Brennan *et al.*, 2016) and others (Antoszewski *et al.*, 2015; Yamaguchi *et al.*, 2014) of the high proportion of women using anti-striae products. I considered how I could design a pilot trial that would be attractive to women; i.e. all participants would apply a product. I was aware that the best control is use of a non-active treatment that could be blinded (Cummings *et al.*, 2007). However, I was unable to identify an appropriate placebo, which may be considered a weakness of the design. The chosen intervention (Johnson's baby oil®) could be considered an inactive product as it does not seem to have active ingredients that are readily evident (for example, vitamins), as is the case with other products such as olive oil. The oil base is a mineral one (Paraffinum liquidum), which is described as an emollient that hydrates the skin and retains moisture (Johnson & Johnson Consumer Inc., 2018). Isopropyl palmitate is also an emollient that moisturises the skin. So essentially, I was comparing a non-active moisturising oil with added perfume with no treatment. I followed the instructions on the oil for application which did not include massage, but, in hindsight, perhaps I should have included massage, as suggested by Young & Jewell (1996).

A no-treatment control group has been implemented by others (Soltanipoor *et al.*, 2012; Taavoni *et al.*, 2011; Wierrani *et al.*, 1992) and none of them mentions challenges with recruitment to their trials, which was reassuring.

However, this trial protocol experienced major recruitment challenges that are not unique to this study. Recruitment is one of the many challenges facing trialists (Thoma *et al.*, 2010), can be very difficult (Treweek *et al.*, 2018) and is frequently the most arduous task of the trial process (Friedman *et al.*, 2010) while

also being essential to overall trial success (Healy *et al.*, 2018). Failing to recruit sufficient numbers of participants within an acceptable timeframe has many serious implications for the integrity of the trial (Thoma *et al.*, 2010), while investigators can become disheartened (Friedman *et al.*, 2010), costs can be increased (Watson & Torgerson, 2006) and trials may be discontinued (Thoma *et al.*, 2010). Some of the main reasons for unsuccessful recruitment are overestimation of the number of eligible participants or deficient preparation (Friedman *et al.*, 2010). However, it is usually a complex issue (Walters *et al.*, 2017).

Challenges with recruitment to trials have been reported by others (Close *et al.*, 2016; Oude Rengerink *et al.*, 2015; Sananès *et al.*, 2017; Tooher *et al.*, 2008), while others have discontinued recruitment prematurely in the face of participant refusal to join a study (Mollart *et al.*, 2016). According to Treweek *et al.* (2018) the number of trials that recruit successfully is probably less than 50%. In addition, many trials have their recruitment period extended, with resultant cost implications (Treweek *et al.*, 2018). In the STEPS study (Campbell *et al.*, 2007), it is reported that less than a third of trials in an epidemiological review of a cohort of trials funded by the UK's Medical Research Council (MRC) and Health Technology Assessment (HTA) recruited their planned number of participants within the planned timeframe.

The magnitude of the concern for the current recruitment problems is evident from the findings of an online Delphi survey involving 48 UK Clinical Research Collaboration-registered Clinical Trials Units, which stated that the top priority for trials' methodological research was '*research into methods to boost recruitment in trials*' (Tudur Smith *et al.*, 2014:1). More recently, the PRioRiT_y (Priority Setting Partnership) study identified and prioritised 10 important unanswered trial recruitment questions or uncertainties for research (Healy *et al.*, 2018). This large, multi-stage, collaborative project, assisted by the James Lind Alliance (UK), included public representatives, health professionals and researchers with experiences in trial design, methodology and methods. Methods included surveys and a face-to-face workshop where the priorities were agreed. All 10 priorities will be instrumental in influencing the future research

agenda to improve trial recruitment strategies and ultimately promote trial participation (Healy *et al.*, 2018).

Further support for dealing with the challenges of recruiting to trials is evident in the review by Frew *et al.* (2014). Using a socioecological model, they sought out barriers and facilitators to the recruitment of pregnant women to trials over time, highlighting some of the challenges to both recruiting and retaining pregnant women in clinical research trials. They reviewed studies between 1994 and 2014, and included 86 articles in the review. Barriers identified included drug-related safety issues in pregnancy, restrictive protocols, not knowing about research in their community, accessibility and transport issues, and personal factors such as time. They found that using '*integrative sampling and recruitment methods*' that are supported by antenatal healthcare providers will trump challenges to recruitment. They recommend that through strong engagement with community-based groups pregnant woman can be retained in cohort studies in future (Frew *et al.*, 2014).

In our trial, I planned to recruit 40 mothers over a three- to four-month period, based on the number of first-time mothers (circa 80) attending for their first antenatal booking appointment at the maternity unit over a four-week period. During the planning of the pilot trial, I believed this projection to be feasible, based on the attendance at the clinic, though bearing in mind that, with recruitment challenges, it could take longer than expected. In hindsight I was over-optimistic, which trialists are cautioned against (Walters *et al.*, 2017) but may have been misguided by the success of the survey participation (Brennan *et al.*, 2016), which is very different in terms of burden for the woman.

I met with clinical staff in advance of starting recruitment to elicit support for the trial (Friedman *et al.*, 2010), knowing the importance of having their support (Frew *et al.*, 2014). Staff were aware of the pilot trial and the eligibility criteria for recruitment, and agreed to inform eligible women about it and link the women with me accordingly. With the support of the administrative staff, I was able to access the numbers of first-time mothers expected at each of the clinics each week. I was not competing with other researchers, which can be a factor in

determining successful recruitment (Friedman *et al.*, 2010) and I was present and available actively in the clinic waiting area at each clinic during the recruitment period.

However, soon after commencing recruitment in July 2017, it was apparent that recruitment was going to be challenging. Initially, it was difficult to identify all the first-time mothers, as sometimes staff omitted to link the women with me. I overcame that by sitting in the clinic where I could easily approach potentially eligible women when it was appropriate. The women overall were interested in the trial, but during the two initial weeks of recruitment it was evident that most women had already decided on using a product to prevent striae gravidarum and in some cases had actually started using the product. Further, some of the women were outside the 12-14-week gestation inclusion criterion.

Due to personal and work commitments, I was unable to continue further with recruitment in 2017 and re-commenced recruitment in February 2018. Prior to this, and following discussion with my supervisor, I sought ethical approval to extend the 12-14-week gestation inclusion criterion to 12-16 weeks in the hope of promoting recruitment. I also met with the clinic staff, senior midwives, clinical placement coordinators, the community midwifery team and the staff in the ultrasound scanning department to get their advice on overcoming the recruitment issues I had experienced previously. The plan to try to recruit in the community clinics was not supported by the team as women are at a later gestation when seen at the clinics and, in their experience, those who have decided to use an anti-striae product are already doing so. But from talking to the ultrasound scanning staff, there were opportunities to meet women for the study, as women tended to move between the antenatal clinic and the ultrasound scanning department during their first hospital visit. Further, they offered to give me an indication each morning of the numbers expected in attendance. Finally, I also had a meeting with my midwifery colleagues and talked to other experienced researchers in the school about how I might recruit to the pilot trial. Areas identified were how I was communicating and what I was communicating with the women about the trial. Following their advice, I reviewed my recruitment information and made some changes. I also recorded myself,

and made some improvements to how I was communicating the information. This increased my confidence and made me less hesitant than previously. Though I had started out confidently, I was less so by the end of the two weeks due to my lack of success and had been somewhat '*discouraged*', as identified by Friedman *et al.* (2010:183).

Thus, re-prepared with my revised presentation skills for approaching women, I actively tried to recruit eligible women over a four-week period, moving between the antenatal clinic and the ultrasound scanning department in February 2018. Despite my commitment and enthusiasm, I did not succeed in engaging women sufficiently to consider participation in the trial. Suggestions for slow recruitment, such as accepting a smaller number of participants or less stringent inclusion criteria (Friedman *et al.*, 2010), were not appropriate in the context of this pilot trial due to the small sample being sought and the relevance of the inclusion criteria. In addition, due to the time constraints on this trial, it was not possible to extend the recruitment period further. Difficulties in recruitment of women to this pilot trial meant it was not possible to fulfil the study aim of testing the feasibility and acceptability of undertaking a larger trial (Arnold *et al.*, 2009) or to inform the protocol for a future definitive trial. Moreover, it would not be possible to pursue a trial involving the commercially available moisturising oil compared to no treatment.

In summary, the pilot trial sought to determine the feasibility of conducting a definitive trial to evaluate the effectiveness of a commercially available moisturising oil compared to no treatment for the prevention and reduction in severity of striae gravidarum. The protocol was informed by the findings of the cross-sectional survey (Brennan *et al.*, 2016), other trials on prevention of striae gravidarum and trial methodological literature. However, this pilot trial was unsuccessful in recruitment and, with the exception of revealing how many could be recruited, it did not achieve the other pilot trial objectives. Nevertheless, against a background of maintaining '*a philosophy of continual improvement*' and trying to perfect '*every aspect of the research and development process*' (Fogel, 2018:156), we explored the factors influencing recruitment to the pilot trial using a qualitative design. This qualitative part is important as it may guide

future research on this topic while also adding to the body of evidence on the challenges of recruiting pregnant women to trials.

6.3.5 A qualitative study of the factors influencing recruitment to a pilot trial on the prevention of striae gravidarum

The qualitative study identified four themes and 12 categories related to the factors influencing recruitment to the pilot trial. Here, the findings have been discussed in the context of other striae gravidarum studies (eg. Kocaöz *et al.*, 2019; Osman *et al.*, 2007; Osman *et al.*, 2008), the earlier studies covered in this thesis (Brennan *et al.*, 2012; Brennan *et al.*, 2016) and the literature on the recruitment to trials in maternity care and in general. Our study (Brennan *et al.*, 2019, under review) reiterated the importance of striae gravidarum prevention to women and supported the high use of anti-striae products by women, as identified in our survey (Brennan *et al.*, 2016). Many women believed that it was best to apply a product to the skin during pregnancy (even if it was not known to be effective) rather than not applying anything.

6.3.5.1 Similarities and differences with other trials

Many women had made their choice of anti-striae product before first contact with the midwife. This presents challenges for future trials, even though a trial involving a well-known intervention product may be more likely to be accepted by women and may promote recruitment (Brennan *et al.*, 2019 under review). Our recruitment gestation period of 12-16 weeks is similar to others. Buchanan *et al.* (2010), for example, enrolled women at 16 weeks' gestation, García Hernández *et al.* (2013) at 12+/-2 weeks' gestation and Osman *et al.* (2008) during the first trimester, and women started applying the product between 12 and 18 weeks' gestation. Contrasting with our study (Brennan *et al.*, 2019 under review) and others (Buchanan *et al.*, 2010; García Hernández *et al.*, 2013; Osman *et al.*, 2008), other trialists have used a later recruitment gestation period (Soltanipour *et al.*, 2014; Soltanipour *et al.*, 2012; Taavoni *et al.*, 2011) and, while Soltanipour *et al.* (2014) highlight their recruitment gestation period of 18-20 weeks as a trial limitation, this was not done by the other studies.

However, our work and that of others (Lerdpienpitayakul *et al.*, 2009) indicates that, by the time women present for first point of care during pregnancy, i.e. in the primary healthcare setting, some will already be using a topical preparation for the prevention of striae. Lerdpienpitayakul *et al.* (2009) report how 18.9% (n=36) were applying the product from before pregnancy while the majority had commenced use of an anti-striae product by ≤ 16 weeks (55%, n=105).

A reason for the early use of anti-striae products identified by our study (Brennan *et al.*, 2019 under review) may be that women today are more informed about striae gravidarum and the available products. Thus, in general they are not influenced by their general practitioner, who is usually their first point of care in pregnancy, as was evident in our study findings, where only 3.4% (n=19) identified the general practitioner as influencing their product choice.

The prevention of striae gravidarum is often portrayed as a cosmetic issue (Bahrami *et al.*, 2012; Ersoy *et al.*, 2016; Lerdpienpitayakul *et al.*, 2009; Muallem & Rubeiz, 2006; Osman *et al.*, 2007) and one that is addressed away from a healthcare setting. Support for this view is evident from the theme 'Who knows best' (Brennan *et al.*, 2019, under review) and the two categories, '*family and friends* and *retail and advertising*'. This is consistent with the earlier survey undertaken as part of this thesis (Brennan *et al.*, 2016) and is consistent with Mallol *et al.* (1991) who found that women are using topical products frequently for striae prevention independent of their healthcare professional's advice. Therefore, some women may be influenced greatly by advertising by cosmetic manufacturing companies either directly or indirectly. Moreover, these companies do not require approval for their products before launching them on the market (HPRA, 2014), and are not obliged to publish their scientific data in the published literature, where it is open to evaluation and public scrutiny, and in most cases the product effectiveness is at best unknown.

6.3.5.2 *Trial recruitment*

The findings contribute to the body of literature in relation to recruitment to trials and specifically in relation to women in pregnancy, a group that was excluded in the past from research (Ballantyne *et al.*, 2017) and is still not represented

adequately (Frew *et al.*, 2014). Both randomisation and equipoise were identified as important factors in the context of trial recruitment. It was evident from the interview data that women did not think that equipoise existed in our trial. Furthermore, they did not want to be allocated to the no-treatment group and would not be prepared to discontinue their current product. Our findings emphasise the criticality of the choice of intervention (Cummings *et al.*, 2007) followed by the importance of the choice of the control intervention (Cheah *et al.*, 2018).

When considering randomisation, it is worth considering the forecast of Gross & Fogg (2001) at the beginning of this century. They found that there would be a reluctance by 21st century health consumers to participate in trials due to an *'unwillingness to agree 'to random assignment... assessments that are too lengthy, intrusive or irrelevant', or 'comply with protocols that do not meet their needs'* (Gross & Fogg, 2001:530). Moreover, random allocation is seen as not meeting *'individual needs'* as consumers are asked to give up control over the type of treatment they receive which, according to Gross & Fogg (2001:531), is contrary to the current drive in 'health care consumerism', citing Haugh (1999) who talks about how the babyboom generation are more inclined to be independent thinkers and less influenced by the old order than previous generations. They assume that they have a choice and are unlikely to engage in any healthcare activity *'that restricts options or control'* (Gross & Fogg, 2001:531). Despite these challenges to recruitment in trials (Thoma *et al.*, 2010; Treweek *et al.*, 2018), some trials do recruit, as evident in the recent review by Walters *et al.* (2017).

Our finding that *'trial requirements should fit with my routine'* (Brennan *et al.*, 2019 under review), under the theme 'Influencers on current trial participation', relates to the findings of Strömmer *et al.* (2018) who investigated the underpinning reasons for women's non-participation in a pregnancy trial involving nutritional supplementation. They also sought to identify ways to increase recruitment. Strömmer *et al.* (2018) recruited women (n=340) who had been involved in one of two UK trials involving nutritional supplementation (MAternal Vitamin D Osteoporosis Study (MAVIDOS) and the Southampton

PRegnancy Intervention for the Next Generation (SPRING)). Women who chose not to participate (referred to as decliners) from the SPRING trial (n=296, 62%) completed a questionnaire, while non-participants (n=30) and participants in both trials (n=44) were interviewed to examine the influences on their decisions to participate or not in a trial. Strömmer *et al.* (2018) identified the theme 'Barriers to taking part', which included both 'attitudes' and 'practical considerations', both of which relate to our finding that 'trial requirements should fit with my routine', which captures participants' willingness or not to comply with the pilot trial requirements, such as daily showering before application of the oil and the keeping of a paper diary during the study to record the use of the oil application. Most of the non-participants in the Strömmer *et al.* (2018) study did not see benefits of the study, focused more on the challenges of meeting the study requirements and were apprehensive about coping with the study demands. Similarly, in our study some women would have found it challenging to adhere to the study requirements of keeping a diary and having a daily shower and their concern was evident in the findings, though for others it fitted with their routine. Unlike the Strömmer *et al.* (2018) findings, some of our participants were concerned about the implications of non-adherence for the integrity of the study (Brennan *et al.*, 2019 under review).

Our findings on influences on future trial participation yielded a somewhat different focus to that of Strömmer *et al.* (2018). The focus of our findings related to trial processes such as randomisation, which the participants were not attracted to, and to the choice of intervention. Women in our study would be more interested in a study that involved the testing of a known anti-stretch mark or a specific type of product. Strömmer *et al.* (2018:79) found that women who chose not to participate indicated a wish '*for more explanation and reassurance from trusted sources*', while both non-participants and participants highlighted the importance of participants meeting with a healthcare professional working on the trial in improving recruitment experience. This relates more to the interpersonal aspects of recruitment in contrast to our findings (Brennan *et al.*, 2019 under review). Other important points made by both groups were the importance of effective advertisement, '*testimonials from previous participants, and making it easy and worthwhile to participate through offering flexible*

appointments and something concrete in return for taking part (p.79). These aspects were not reflected in our qualitative findings (Brennan *et al.*, 2019 under review). This may, at least in part, be due to our inclusion of only women who had declined to join the pilot trial (Brennan *et al.*, 2019 under review) in contrast to Strömmer *et al.* (2018) who included both women who chose and women who chose not to take part. Strömmer *et al.* (2018) caution how the women who chose not to participate might not be representative of all women who chose not to participate in trials, but are important in informing further trial research, particularly as the decliners are an unconsidered or forgotten group in trial recruitment literature.

6.3.5.3 *Understanding of trial design*

Our findings (Brennan *et al.*, 2019 under review) further the perspective that some participants do not understand trial design (Kenyon *et al.*, 2006; Oude Rengerink *et al.*, 2015). Earlier writers have highlighted this issue. In 1997, Snowdon *et al.* (1997) highlighted a lack of understanding of the essence of trials by parents of critically ill babies who were being asked to consent to inclusion of their baby in a UK collaborative neonatal trial of *extracorporeal membrane oxygenation (ECMO)*, which involved the comparison of two methods of life support for babies with respiratory failure that could be reversed. Parents who were being interviewed had agreed for their baby to participate in the trial. The study found that parents often did not understand what the trial entailed nor the use of random assignment or the reason for it. This is not unique to research in pregnancy and childbirth. Based on their interviews with men with benign prostatic disease, Featherstone & Donovan in 2002 note that most patients will find it difficult to understand the different aspects of participating in a trial. Similarly, Robinson *et al.* (2005) reported on the challenges lay people have in understanding trial design and in particular equipoise and randomisation. From six investigations using theoretical scenarios, most of the participants considered '*the random allocation methods*' objectionable when undertaking a trial, while most participants also objected to a doctor suggesting that chance decide a treatment for a patient when the best treatment is unknown.

Robinson *et al.* (2005) propose giving a readily understandable explanation of the scientific advantages of randomisation but also helping the participants to think about the information they are given and in particular how the trial will further knowledge. They recommend deliberation on ascertaining the most effective ways of including both written and oral information for potential participants, how best to assist participants think about the aim of furthering knowledge and developing participant leaflets according to the best evidence.

In summary, this qualitative study identified four themes and 12 categories related to the factors influencing recruitment to the pilot trial. The findings are important from a topic and methodological perspective. This study reiterated the significance of striae gravidarum prevention to women and the popularity of anti-striae topical product use during pregnancy. Women did not seem to be actively seeking evidence in support of the effectiveness of their chosen product, and many believed that it was good to apply a product to the skin during pregnancy despite the effectiveness of this being unknown. Offering women the opportunity to be part of a trial that would be of low burden and would test a well-known product may optimise recruitment. However, reluctance to be randomised because of the possibility of being allocated to the no-intervention control group suggests that further work is needed in this field. Recruitment in the primary healthcare setting is unlikely to be successful due to the limited influence of healthcare practitioners on women's decision-making (Brennan *et al.*, 2016).

6.4 Conclusion

The four studies that make up this thesis represent a planned and sequential investigation to address the prevention of striae gravidarum in primigravid women. The thesis systematically reviewed the evidence in support of the prevention of striae gravidarum (study one) and surveyed women (study two) on their use of anti-striae products. These studies informed the design of a pilot trial (study three). Although a majority of the women surveyed indicated that they would consider participating in a future trial of a product to prevent or reduce striae gravidarum, this was not the case when recruiting to the pilot trial (study three) for a number of reasons and as identified in study four of the thesis.

This thesis was undertaken against a background of increasing publications relating to striae gravidarum. While studies looking at risk factors for striae among different populations continue to be popular either as a particular focus or alongside another aspect, there is an increasing body of literature on quality of life and body image in relation to striae gravidarum. There is now evidence that striae and in particular severe striae can adversely affect women's quality of life. Although women may see striae gravidarum prevention as a cosmetic issue and, as with other skin care, choose to focus on it away from a healthcare setting, they stand to benefit from large trials appropriately designed to evaluate the effects of topical products in the prevention of striae gravidarum in the future. As reported in the qualitative study (Brennan *et al.*, 2019 under review), a trial involving a well-known intervention may be more acceptable to women and encourage recruitment.

6.4.1 Strengths and limitations of the thesis

This thesis has a number of strengths and limitations in addition to the ones mentioned in the four studies. A key strength is the planned and sequential nature of the investigation to address the topic using appropriate methodologies. It contributes substantially to the body of literature on striae gravidarum. The Cochrane systematic review synthesised best evidence for the prevention of striae gravidarum. The large survey was unique in its focus on the use of anti-striae products by women during pregnancy to prevent or reduce the development of striae gravidarum, and was instrumental in the design of the pilot randomised controlled trial. Furthermore, the focus on issues around application of the anti-striae product, cost incurred and influences on women's decisions to use a product is unique. Other strengths of this work include generation of evidence to demonstrate the importance of striae prevention to women and the need for the products commonly used by women to be evaluated. Finally, this thesis demonstrated that it is not feasible to undertake a large trial on the effectiveness of a moisturising oil (commercially available) compared to no treatment for the prevention and reduction in severity of striae gravidarum in Ireland (question 3).

The main limitation of the thesis results from the difficulties in recruiting women to the pilot trial and the resultant non-achievement of the trial objectives. In the event of planning another trial, a further pilot study is strongly advised in order to determine the feasibility of a large trial and guide its processes. A second limitation is the choice of experimental and control intervention for the planned trial, which was a significant factor in our unsuccessful recruitment. Women did not think that equipoise existed in our trial. Furthermore, they did not want to be allocated to the no-treatment group and would not be prepared to discontinue their current product. It is evident from our research that a control intervention is essential in any future trial in Ireland due to most women wishing to apply some type of moisturiser to their skin, particularly during pregnancy (even if it is not known to be effective). Use of a well-known product may be attractive to women. Thus, trials on the prevention of striae gravidarum involving topical products require access to commercial products and specifically an appropriate placebo, which was not possible in this study.

6.4.2 Implications for clinical practice

As highlighted above, the Cochrane review findings undertaken as part of this thesis *'found no high-quality evidence to support the use of any of the topical preparations in the prevention of stretch marks during pregnancy'*. This conclusion will guide clinicians in discussing striae gravidarum and their prevention with women during pregnancy. Although we know that striae gravidarum prevention is important to women, some may have researched the topic and may not seek advice on it from healthcare professionals.

6.4.3 Implications for further research

1. Our Cochrane systematic review is due for updating to include the studies undertaken in the meantime.
2. There is a need for rigorous and well-designed randomised trials to evaluate the different commercially available products used by women to prevent striae gravidarum. Such research requires access to appropriate placebos and may necessitate co-operation with industry. Future trials should consider products in use so as to increase the acceptability of the planned study to women during pregnancy. A pilot study is paramount to determine feasibility

of the main trial.

3. Women did not seem to be seeking evidence actively in support of the effectiveness of their chosen product and many believed that it was good to apply a product to the skin during pregnancy despite its effectiveness being unknown. It is important to explore, in greater depth, factors influencing women's use of anti-striae products despite lack of knowledge of their effectiveness.
4. It is important that research continues into strategies to promote trial recruitment both in general and specifically in relation to pregnant women.

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Appendix 1

Paper 1: Topical preparations for preventing stretch marks in pregnancy: Copyright Clearance Agreement

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Appendix 2

Paper 2: The use of anti stretch marks' products by women in pregnancy: a descriptive, cross-sectional survey: Survey questionnaire

SURVEY QUESTIONNAIRE

The use of skin products to prevent or reduce the development of stretch marks in pregnancy.

Thank you for taking the time to complete this questionnaire on the use of skin products for the prevention or reduction of stretch marks in pregnancy.

By completing the questionnaire I confirm that:

- I have read and understand the information sheet for the above study.
- I have had the opportunity to read and consider the information.
- I understand that I am participating voluntarily in this study.
- I understand that the researcher will store all information and data securely and in confidence.
- I understand that data arising from completion of the questionnaire will be kept confidential and anonymous.
- I have the researcher's name and contact details if I require further information.
- I consent to participate in the study.

Questions about you

1. How many weeks pregnant are you? _____ (please give number)
2. How many children have you given birth to? _____ (please give number)
3. What is your nationality?
 - Irish 1
 - Other (please specify below) 2_____

Questions on the use of skin products to prevent or reduce the development of stretch marks during this pregnancy

4. Did you or are you applying any product to your skin during this pregnancy to try to prevent or reduce the development of stretch marks?
 - 1 Yes
 - 2 No → Go to question 13

Appendices

5. Which of the following products did you apply or are you applying to your skin?
(please tick all that apply)

- Cocoa butter cream 1
- Cocoa butter lotion 2
- Olive oil 3
- Bio Oil 4
- Germ oil 5
- Revitol stretch mark cream 6
- Mama Mio tummy rub stretch mark oil 7
- Other (please specify below) 8

6. Which of the following information sources, if any, helped you to decide which product to use? (please tick all that apply)

- Advice from friends 1
- Advice from a family member 2
- Advice from my GP 3
- Advice from my obstetrician 4
- Advice from a midwife 5
- Advice from a pharmacist 6
- Product advertisement 7
- Internet 8
- Information in newspapers/health supplements 9
- Other (please specify below) 10

7. How many weeks pregnant (approximately) were you when you started to apply a product to your skin to prevent or reduce the development of stretch marks?
_____ (please give number of weeks)

Appendices

8. How often during the week do you or did you, on average, apply the product?

(please tick one)

- One day a week
- Two days a week
- Three days a week
- Four days a week
- Five days a week
- Six days a week
- Seven days a week
- Other (please specify below)

9. How many times during the day did you or do you, on average, apply the product?

(tick one)

- Once a day
- Twice a day
- Three times a day
- Four times a day
- Five times a day
- Other (please specify below)

10. What was, or is, the average length of time you spent/spend per day applying the product?

_____ (please give number of minutes)

Appendices

11. Did you or do you usually have a shower before applying the product? (please tick one box)

- Always 1
- Sometimes 2
- Seldom 3
- Never 4

12. How much money have you spent on skin products to prevent or reduce the development of stretch marks during **this pregnancy**? (please tick one box)

- Less than €5 1
- €5-€10 2
- €11-€15 3
- €16-€20 4
- €21-€30 5
- €31-€40 6
- €41-€50 7
- ≥ €51 8

Questions on the development of stretch marks during this pregnancy
--

13. Had you developed stretch marks on your skin (for example, on your abdomen, breasts, thighs or buttocks) **prior** to this pregnancy?

- 1 Yes
- 2 No

Appendices

14. Did you develop stretch marks on your skin (for example, on your abdomen, breasts, thighs or buttocks) during **this** pregnancy?

1 Yes

2 No → Go to question 19

15. Where did the stretch marks **mainly** occur on your body during **this** pregnancy?
(please tick one)

- Abdomen 1
- Breasts 2
- Thigh 3
- Buttocks 4
- Other (please specify below)

16. How would you quantify the amount of stretch marks you got during this pregnancy?
(please tick one box)

- A few 1
- Quite a lot 2
- A lot 3
- Extensive 4

Questions on how stretch marks affect you and impact on your lifestyle

17. My stretch marks often make me feel less confident about my body (please tick one of the boxes)

Strongly ¹ Agree Agree ² Neither Agree ³ nor Disagree Disagree ⁴ Strongly ⁵ Disagree

18. Did the presence of stretch marks on your skin prevent you from participating in any of the following activities? (please tick all that apply (if not please go to next question (question 19))

- Swimming 1
- Gymnasium activities/aerobics 2
- Other 3

Questions about what influences you when making decisions about your health and wellbeing

19. Which of the following influences you most in making health care related decisions? (tick all that apply)

- Advice from friends 1
- Advice from a family member 2
- Advice from my GP 3
- Advice from my obstetrician 4
- Advice from a midwife 5
- Advice from a pharmacist 6
- Product advertisement 7
- Internet 8
- Information in newspapers/health supplements 9
- Other (please specify below) 10

Appendices

20. Would your decision on whether or not you used a product for preventing or reducing stretch marks in pregnancy be influenced by the findings of a research study?

1 Yes

2 No

21. During a future pregnancy, would you consider participating in a study to evaluate the effectiveness of a product to prevent or reduce stretch marks in pregnancy?

1 Yes

2 No

Thank you for taking time to complete this questionnaire

Appendix 3

Paper 2: The use of anti stretch marks' products by women in pregnancy: a descriptive, cross-sectional survey: Cover letter for expert panel member

Appendices

Cover letter for expert panel member

Dear panel member,

Thank you for agreeing to help determine the content validity of this instrument on the use of skin products to prevent or reduce the development of stretch marks in pregnancy. You were asked to join the expert panel due to your clinical and or research experience and your help is appreciated.

Stretch marks commonly occur during pregnancy and many women use a variety of anti-stretch mark products to try and prevent or reduce their occurrence. The purpose of this survey is to ascertain what topical products are commonly used by women during pregnancy to prevent or reduce the development of stretch marks in pregnancy, and to ascertain their willingness to participate in a future study to evaluate the effectiveness of an anti-stretch mark product.

I have developed the tool with my supervisors based on the literature on stretch marks in pregnancy, and from consumer advice. The questionnaire consists of 22 questions which are mainly closed ended. On the attached form, as a panel member you are required to evaluate each question on the questionnaire and the full questionnaire according to the following criteria:

- Relevance of the question (on a 4 point scale of 1=not relevant, 2=somewhat relevant, 3=quite relevant, 4=very relevant);
- Clarity of the wording of the questions for pregnant women (please recommend word changes as necessary) (on a 4 point scale of 1=not clear, 2=somewhat clear, 3=quite clear, 4=very clear);
- Completeness of the entire instrument and if any additional questions are necessary;
- Number of questions and the need for questions to be removed.

An item or question content validity index will be computed based on the number of experts who give a rating of three or four for relevancy for each question. This number will then be divided by 12 (number of experts) to give the proportion of agreement for each question. An acceptable content validity index will be achieved by 10 of the experts rating a question as 3 or 4. Finally the content validity for the full instrument will be determined using the content validity index average (CVI/Ave) method (Polit et al., 2007) or the proportion of the items judged relevant across the tool with the goal of reaching 0.90 or greater.

Thank you for assisting me in this endeavour.

Yours sincerely

Miriam Brennan

PhD student

Appendix 4

Paper 2: The use of anti stretch marks' products by women in pregnancy: a descriptive, cross-sectional survey: Content validity testing instrument

The use of skin products to prevent or reduce the development of stretch marks in pregnancy

Content Validity Testing

Thank you for agreeing to help determine the content validity of this instrument on the use of skin products to prevent or reduce the development of stretch marks in pregnancy.

Stretch marks commonly occur during pregnancy and many women use a variety of anti-stretch mark products to try and prevent or reduce their occurrence. The purpose of this survey is to ascertain what topical products are commonly used by women during pregnancy to prevent or reduce the development of stretch marks in pregnancy and to ascertain their willingness to participate in a future study to evaluate the effectiveness of an anti-stretch mark product. The survey consists of 22 questions.

I would appreciate if you would:

1. Rate the relevance and clarity of each question as follows:

Relevance of the question

- 1=Item is not relevant to the purpose of the survey
- 2=Item is somewhat relevant to the purpose of the survey but is in need of major revision
- 3=Item is quite relevant to the purpose of the survey but is in need of minor revision
- 4=Item is very relevant to the purpose of the survey.

Clarity of the question

- 1=Item is not clear
- 2=Item is somewhat clear but is in need of major revision
- 3=Item is quite clear but is in need of minor revision
- 4=Item is very clear.

Where you rate the item as a 1, 2 or 3, please comment on your reasons for your rating and/or on the revisions required.

2. Evaluate the completeness of the entire instrument and indicate if:
 - Additional questions are required.
 - Questions need to be removed.

Thank you for your help.

The use of skin products to prevent or reduce the development of stretch marks in pregnancy.

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions about you		
Q1 How many children have you given birth to? (please give number)	Rating = Comment:	Rating = Comment:
Q2 How many weeks pregnant are you? (please give number)	Rating = Comment:	Rating = Comment:
Questions on stretch marks in pregnancy and the use of skin products to prevent or reduce stretch marks.		
Q3 Did you or are you applying any skin product to your skin during this pregnancy to try to prevent or reduce the development of stretch marks? -Yes -No→ please go to Q13	Rating = Comment:	Rating = Comment:

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions on stretch marks in pregnancy and the use of skin products to prevent or reduce stretch marks Continued		
Q4 Which of the following products did you apply to your skin? (please tick all that apply)) -Cocoa butter cream - Cocoa butter lotion -Olive oil - Bio Oil - Germ oil - Revitol stretch mark cream - Mama Mio tummy rub stretch mark oil -other (please specify)	Rating = Comment:	Rating = Comment:
Q5 Which of the following helped you to decide which product to use (please tick appropriate response(s)) -Advice from friends -Advice from a family member -Advice from my GP -Advice from my obstetrician -Advice from a midwife -Advice from a pharmacist -Product advertisement -Information in newspapers or other parts of the media -Other (please specify)	Rating = Comment:	Rating = Comment:

Appendices

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions on stretch marks in pregnancy and the use of skin products to prevent or reduce stretch marks Continued		
Q6 How many weeks pregnant were you when you started to apply the product? (please give number)	Rating = Comment:	Rating = Comment:
Q7 How often during the week did you apply the product? (please tick one) -One day a week -Two days a week -Three days a week -Four days a week -Five days a week -Six days a week -Seven days a week	Rating = Comment:	Rating = Comment:

Appendices

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions on stretch marks in pregnancy and the use of skin products to prevent or reduce stretch marks Continued		
Q8 How many times during the day did you apply the product? (please tick one) -Once a day -Twice a day -Three times a day -Four times a day -Five times a day Other (please specify)	Rating = Comment:	Rating = Comment:
Q9 Did you have a shower before applying the product? (please tick one) -Always -Sometimes -Seldom -Never	Rating = Comment:	Rating = Comment:
Q10 What was the average length of time you spent per day applying the product? (please give number of minutes)	Rating = Comment:	Rating = Comment:

Appendices

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions on stretch marks in pregnancy and the use of skin products to prevent or reduce stretch marks Continued		
Q11 How many weeks pregnant were you when you stopped applying the product? (please give number)	Rating = Comment:	Rating = Comment:
Q12 How much money have you spent on skin products to prevent or reduce the development of stretch marks during this pregnancy? (please tick one) - Less than €5 -€5-€10 -€11-€15 -€16-€20 -€21-€30 -31-€40 -€41-€50 -≥ €51-	Rating = Comment:	Rating = Comment:
Q13 Did you develop stretch marks on your skin (for example, on your abdomen, breasts, thighs, or buttocks) <u>prior</u> to this pregnancy? -Yes -No	Rating = Comment:	Rating = Comment:

Appendices

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions on stretch marks in pregnancy and the use of skin products to prevent or reduce stretch marks Continued		
Q14 Did you develop stretch marks on your skin (for example, on your abdomen, breasts, thighs, or buttocks) during <u>this</u> pregnancy? -Yes -No →please go to Q19	Rating = Comment:	Rating = Comment:
Q15 Where were the stretch marks mostly located on your body during this pregnancy? (please tick appropriate one) -Abdomen -Breasts -Thigh -Buttocks	Rating = Comment:	Rating = Comment:
Q16 How would you quantify the amount of stretch marks you got during the pregnancy? -Very small amount -Small amount -Moderate amount -Severe amount -Very severe amount	Rating = Comment:	Rating = Comment:

Appendices

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions on stretch marks in pregnancy and the use of skin products to prevent or reduce stretch marks Continued		
Q17 Did you experience any of the following symptoms with the stretch marks? (please tick all that apply) -Burning sensation -Itching sensation -Stress -Anxiety -Worry -Other (please list)	Rating = Comment:	Rating = Comment:
Q18 Did the presence of stretch marks on your skin prevent you from participating in any of the following activities? -Swimming -Gymnasium/aerobics Yes or No Other (please list other activities that you were prevented from participating in)	Rating = Comment:	Rating = Comment:

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions about what influences you when making decisions about your health and wellbeing.		
Q19 Which of the following influences you the most in making health care related decisions? - Advice from friends -Advice from a family member -Advice from my GP -Advice from my obstetrician -Advice from a midwife -Advice from a pharmacist -Product advertisement -Information in newspapers or other parts of the media -Other (please specify)	Rating = Comment:	Rating = Comment:
Q20 Would you be influenced by the results of a high quality study indicating how good or bad a product was in preventing or reducing stretch marks in pregnancy? -Yes -No	Rating = Comment:	Rating = Comment:
Q21 Would you consider using a product found by a high quality study to be good at preventing or reducing stretch marks in pregnancy? -Yes -No	Rating = Comment:	Rating = Comment:

Appendices

	Relevance	Clarity
	1=Item is not relevant to the purpose of the survey	1=Item is not clear
	2=Item is somewhat relevant to the purpose of the survey but is in need of major revision	2=Item is somewhat clear but is in need of major revision
	3=Item is quite relevant to the purpose of the survey but is in need of minor revision	3=Item is quite clear but is in need of minor revision
	4=Item is very relevant to the purpose of the survey	4=Item is very clear
Questions about what influences you when making decisions about your health and wellbeing Continued		
Q22 During a future pregnancy, would you consider participating in a study to evaluate the effectiveness of a product to prevent or reduce stretch marks in pregnancy? -Yes -No	Rating = Comment:	Rating = Comment:

Evaluation of the entire instrument

1. Do you consider the instrument to be complete, i.e. it has the correct questions to achieve the aim of the survey (to ascertain what topical products are commonly used by women during pregnancy to prevent or reduce the development of stretch marks and to ascertain their willingness to participate in a future study).

Yes

No

If No please suggest questions that may be included:

2. Do you consider some questions as unnecessary and therefore should be removed from the instrument?

Yes

No

If Yes please suggest questions that may be removed:

Appendix 5

Paper 2: The use of anti stretch marks' products by women in pregnancy: a descriptive, cross-sectional survey: Content validity testing results

Appendices

Content validity testing																		
Relevance of Questions													Total No. of Experts		12			
	E 1R	E 2R	E 3R	E 4R	E 5M	E 6M	E 7M	E 8M	E 9W	E 10W	E 11W	E 12W	Experts in Agreement : rating 4 or 3		Sum		I-CVI	
													4	3				
Q1	4	4	4	3	4	4	4	4	4	4	4	4	11	1	12	12	1.000	
Q2	4	4	4	4	4	4	4	4	4	4	4	3	11	1	12	12	1.000	
Q3	4	4	4	4	4	4	4	4	4	4	4	4	12	0	12	12	1.000	
Q4	4	4	4	4	4	3	4	3	4	4	4	4	10	2	12	12	1.000	
Q5	4	4	4	4	4	3	4	3	4	4	4	4	10	2	12	12	1.000	
Q6	4	4	4	4	4	3	4	4	4	4	4	4	11	1	12	12	1.000	
Q7	4	4	4	4	4	3	4	4	4	4	4	4	11	1	12	12	1.000	
Q8	4	4	2	4	4	4	4	4	4	4	4	4	11	0	11	12	0.917	
Q9	4	4	1	4	4	3	4	3	1	4	4	4	8	2	10	12	0.833	
Q10	4	4	2	3	4	3	4	4	4	4	4	4	9	2	11	12	0.917	
Q11	4	4	4	3	4	3	4	4	4	4	4	4	10	2	12	12	1.000	
Q12	4	4	4	3	4	4	4	3	4	4	4	4	10	2	12	12	1.000	
Q13	4	4	4	4	3	3	4	4	4	4	4	4	10	2	12	12	1.000	
Q14	4	4	4	3	3	4	4	4	4	4	4	4	10	2	12	12	1.000	
Q15	4	4	4	3	3	3	4	3	4	4	4	4	8	4	12	12	1.000	
Q16	4	4	4	3	4	3	4	4	4	4	4	4	10	2	12	12	1.000	
Q17	4	4	4	3	3	2	2	3	4	4	4	4	7	3	10	12	0.833	
Q18	4	4	4	4	4	3	4	3	4	4	4	4	10	2	12	12	1.000	
Q19	4	4	2	2	3	3	4	3	4	4	4	4	7	3	10	12	0.833	
Q20	4	4	4	2	2	2	4	4	4	4	4	4	9	0	9	12	0.750	Question changed/ Polit say revision of item less than .78
Q21	4	4	2	2	2	2 or 1	4	3	4	4	4	4	7	1	8	12	0.667	Question deleted
Q22	4	4	4	3	3	2	4	4	4	4	4	4	9	2	11	12	0.917	
Average																0.939		

Appendix 6

Paper 2: The use of anti stretch marks' products by women in pregnancy: a descriptive, cross-sectional survey: Participant letter of invite

Appendices

Letter of invite

Dear participant,

I am a midwife and a PhD student in the National University of Ireland, Galway. As part of my PhD, I am undertaking a survey of antenatal women on the use of skin products to prevent or reduce the development of stretch marks in pregnancy. The survey findings will assist me in developing a future research study, to evaluate the effectiveness of a skin product used to prevent or reduce the development of stretch marks in pregnancy.

I am seeking to recruit women who are 36 weeks pregnant or more to participate in this study.

Please find enclosed:

1. Participant information sheet
2. Questionnaire
3. Card for name and address (if you would like a copy of the results).

Please place the completed questionnaire in the box on the Antenatal Clinic reception desk, labelled 'Stretch Marks' Study Questionnaires'.

Thank you for your help.

Yours sincerely

Miriam Brennan

PhD student

National University of Ireland Galway.

Contact details

e mail: brennanm@nuigalway.ie

Telephone number: 091 493651

Appendix 7

Paper 2: The use of anti stretch marks' products by women in pregnancy: a descriptive, cross-sectional survey: Participant information sheet

Participant information sheet

If you would like to take part in a research study it is important that you understand why the research is being done and what it will involve.

Please take time to carefully read the following information. Your responses are very important so please ask if you do not understand any of the information or would like more information. I can be contacted at the contact details given below.

Study title

The use of skin products to prevent or reduce the development of stretch marks in pregnancy.

What is the purpose of the study?

Stretch marks commonly develop during pregnancy, especially in the third trimester. They affect between 50% and 90% of women. They appear as red lines or streaks on the skin, then fade slowly to leave pale lines but they do not fade entirely. The abdomen, breasts and thighs are the parts of the body most commonly affected. Stretch marks can affect or concern women in different ways. Some women might see them as changing how they look and will try to prevent or reduce them by using the different products readily available on the market. Other women may not think this and do not take any action to prevent or reduce them.

While there are many skin products used by women to prevent or reduce the development of stretch marks, many of the products have not been evaluated in high quality research studies. It is therefore unclear as to how effective the products are.

The aim of this survey is to determine what skin products are commonly used by women during pregnancy to prevent or reduce the development of stretch marks during pregnancy.

Why have I been chosen?

You have been chosen for inclusion in this study as you are at 36 weeks of pregnancy or more.

Who is undertaking and overseeing the study?

Miriam Brennan, a PhD student of the School of Nursing & Midwifery, National University of Ireland Galway. My supervisor Professor Declan Devane of the School of Nursing & Midwifery, National University of Ireland Galway is overseeing the study.

What will happen to me if I participate in the study?

If you participate in the study you will be required to complete the questionnaire. The questionnaire will take approximately 10 minutes to complete.

Are there any disadvantages in taking part in this study?

There are no known disadvantages associated with participating in this study.

What are the possible risks of taking part in this study?

There are no known risks associated with participating in this study.

What are the possible benefits of taking part in this study?

You will not receive any direct benefit during this pregnancy from participating in this study. However, information obtained from the study will inform a future study to evaluate the effectiveness of a skin product used to prevent or reduce the development of stretch marks in pregnancy and which subsequently may benefit women during pregnancy.

Appendices

Confidentiality – who will know I am taking part in the study?

You are not required to include your name on the questionnaire and will therefore not be identifiable. All information from the completed questionnaire will be stored safely on a password-protected laptop and it will be encrypted. All completed questionnaires will be stored securely. Miriam Brennan, the researcher is the only one who will have access to the questionnaires. My supervisor Professor Declan Devane will see the data analysis as part of the supervision process.

Hospital Ethics Committee Approval

This study was granted ethical approval by the University Hospital Galway Ethics Committee and the Research Ethics Committee of the National University of Ireland Galway.

What will happen to the results of the study?

As the survey is anonymous, it will not be possible to send a copy of the results to each participant. However, if you would like a copy of the results, please complete the enclosed card with your name and address and place the card into the box with the completed questionnaire. Please do not attach the card to your completed questionnaire. In addition, the results will also be written up in the academic journals and included in my thesis. If you are participating online, you will be given a separate URL where you can register your email address to receive a copy of the findings of the survey.

Who do I contact if I require further information?

If you require further advice or information please contact me at the contact details below.

Voluntary participation

If you decide to participate your participation is voluntary, and you may decide not to complete the questionnaire at any point without giving a reason and without any disadvantage.

Contact Details

<p>Principal investigator Miriam Brennan E mail: brennanm@nuigalway.ie Telephone number: 091 493651</p>
--

Thank you

Appendix 8

Paper 2: The use of anti stretch marks' products by women in pregnancy: a descriptive, cross-sectional survey: Ethical approval letters - Galway University Hospitals



Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive



Merlin Park University Hospital
Ospidéal na h-Ollscoile, Páirc Mheirlinne
GALWAY UNIVERSITY HOSPITALS

Clinical Research Ethics Committee
Main Administration Building
Merlin Park Hospital
Galway.

24th June, 2013.

*Ms. Miriam Brennan
Lecturer in Midwifery
School of Nursing & Midwifery
National University of Ireland
Galway.*

*Ref: C.A. 921 - The use of skin products to prevent or reduce the development of
stretch marks in pregnancy*

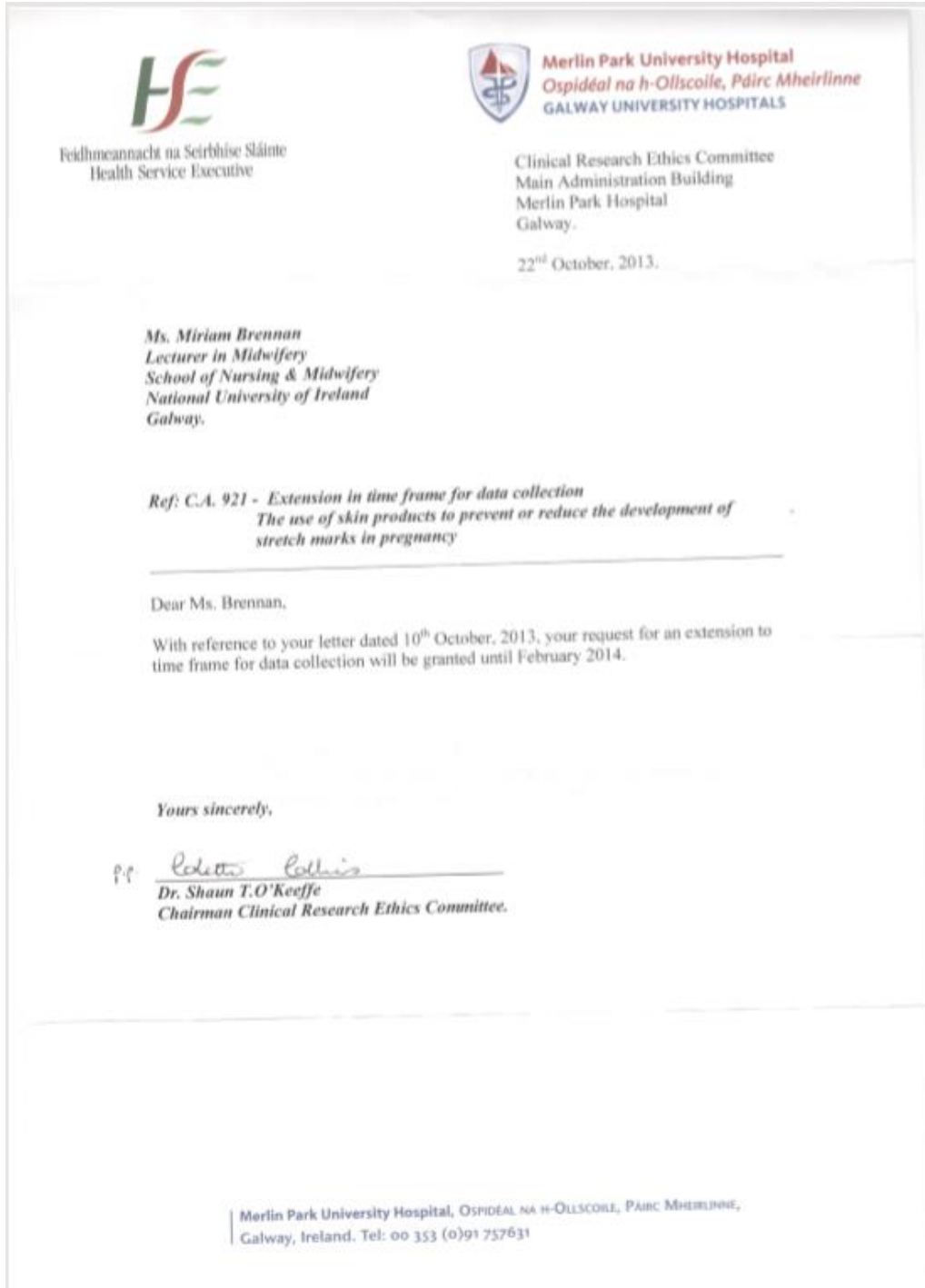
Dear Ms. Brennan,

I have considered the above project, and I wish to grant Chairman's approval to proceed.

Yours sincerely,

PP. 
Dr. Shaun T. O'Keeffe
Chairman Clinical Research Ethics Committee.

Merlin Park University Hospital, OSPIDÉAL NA H-OLLSCOILE, PÁIRC MHEIRLINNE,
Galway, Ireland. Tel: 00 353 (0)91 757631



 <p>Feidhmeannacht na Seirbhíse Sláinte Health Service Executive</p>	 <p>Merlin Park University Hospital Ospidéal na h-Ollscoile, Páirc Mheirlinne GALWAY UNIVERSITY HOSPITALS</p>
	<p>Clinical Research Ethics Committee Main Administration Building Merlin Park Hospital Galway.</p>
	<p>13th March, 2013</p>
	<p>2014</p>
<p>Ms. Miriam Brennan Lecturer in Midwifery School of Nursing & Midwifery National University of Ireland Galway.</p>	
	<p><i>Ref: C.A. 921 - The use of skin products to prevent or reduce the development of stretch marks in pregnancy</i></p>
	<p>Dear Ms. Brennan,</p>
	<p>Please see confirmation that we have received your letter dated 3rd February, 2014 with regard to data collection delays for the above study.</p>
	<p>Thanking you,</p>
	<p>Yours sincerely,</p>
	<p>PA  Dr. Shaun T. O'Keeffe Chairman Clinical Research Ethics Committee.</p>
	<p>Merlin Park University Hospital, OSPIDÉAL NA H-OLLSCOILE, PÁIRC MHEIRLINNE, Galway, Ireland. Tel: 00 353 (0)91 757631</p>

Appendix 9

Paper 2: The use of anti stretch marks' products by women in pregnancy: a descriptive, cross-sectional survey: Ethical approval letter-NUI Galway



Leas-Uachtarán
um Thaighde

Vice President
for Research

Date: 11th July 2013

Ref: 13/JUNE/10

Ms Miriam Brennan
School of Nursing and Midwifery
Aras Moyola
NUI Galway

Dear Ms Brennan

Re. Ethics Application: The use of skin products to prevent or reduce the development of stretch marks in pregnancy

I write to you regarding the above proposal which was submitted for Ethical review. Having reviewed your response to my letter, I am pleased to inform you that your proposal has been granted **APPROVAL**.

All NUI Galway Research Ethic Committee approval is given subject to the Principal Investigator submitting annual and final statements of compliance. The first statement is due on or before 30th June 2014. Please see section 7 of the REC's Standard Operating Procedures for further details which also includes other instances where you are required to report to the REC.

Yours Sincerely

Allyn Fives
Chair, Research Ethics Committee

OÉ Gaillimh,
Bóthar na hOllscoile,
Gaillimh, Éire

NUI Galway,
University Road,
Galway, Ireland

T +353 91 495 312
F +353 91 494 595

www.nuigalway.ie/research/vp_research

Appendix 10

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Intervention group diary**

Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial (ISRCTN76992326)

Diary (Intervention group)

Thank you for agreeing to participate in the study on the prevention of stretch marks in pregnancy.

Study ID. _____

Please bring the diary and the empty oil bottles to your clinic appointment when you are 38 weeks gestation or to the later appointments at weeks 39-41.

Appendices

Instruction for completion

Please remember to complete this diary each day after you have applied the oil for the duration of the study.

If you forget to complete the diary please do so as soon as you remember.

It will take less than 5 minutes to complete and is an important part of the study data.

You will receive two weekly reminder texts to remind you to complete the daily study diary.

Example of how to complete the diary

Week 12 of pregnancy			Week beginning 16/06/2017	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday	√		√	
Tuesday	√			√- spilled some on ground. No action taken
Wednesday	√		√	
Thursday	√		√	
Friday	√		√	
Saturday	√		√	
Sunday	√		√	

Appendices

Please complete the diary each day as per the example above

Week 12 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 13 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 14 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 15 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 16 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 17 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 18 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 19 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 20 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 21 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 22 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 23 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 24 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 25 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 26 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 27 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 28 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 29 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 30 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 31 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 32 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 33 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 34 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 35 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 36 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 37 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 38 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 39 of pregnancy			Week beginning ____/____/____	
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendices

Week 40 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Week 41 of pregnancy				Week beginning ____/____/____
Day	Applied oil		Problems -No	Problems -Yes <i>Please write what they are & any action taken</i>
	Yes	No		
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Appendix 11

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Control group diary**

Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial (ISRCTN76992326)

Diary (Control group)

Thank you for agreeing to participate in the study on the prevention of stretch marks in pregnancy.

Study ID. _____

Please bring the diary to your clinic appointment when you are 38 weeks gestation or to the later appointments at weeks 39-41.

Appendices

Instruction for use

Please remember to complete this diary each day.

In order to help you remember it may be helpful to put a reminder in your phone.

If you forget to complete it please do so as soon as you remember.

It will take less than 5 minutes to complete and is an important part of the study data.

You will receive two weekly reminder texts to remind you to complete the daily study diary.

Example of how to complete the diary.

Week 12 of pregnancy		Week beginning 16/08/2016	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday	√		
Tuesday	√		
Wednesday	√		
Thursday	√		
Friday	√		
Saturday	√		
Sunday	√		

Appendices

Please complete the diary each day as per the example above

Week 12 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 13 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 14 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 15 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 16 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 17 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 18 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 19 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 20 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 21 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 22 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 23 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 24 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 25 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 26 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 27 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 28 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 29 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 30 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 31 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 32 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 33 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 34 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 35 of pregnancy		Week beginning ___/___/___	
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 36 of pregnancy			Week beginning ____/____/____
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 37 of pregnancy			Week beginning ____/____/____
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 38 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 39 of pregnancy			Week beginning ___/___/___
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendices

Week 40 of pregnancy			Week beginning ____/____/____
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Week 41 of pregnancy			Week beginning ____/____/____
Day	Did Not apply any skin product to my abdomen	Applied a skin product to my abdomen	Comment <i>Name and amount of product applied</i>
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Appendix 12

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Outcomes assessment form**

Prevention of striae gravidarum: a pilot trial (ISRCTN76992326)

Outcomes Assessment at 38-41 weeks gestation

1. Study ID Number	
2. Group assignment	
3. Gestation	
4. Current weight in Kg	
5. Weight gain during pregnancy (% & absolute)	%:
	Absolute:
6. Height in metres	
7. BMI	
8. Mid abdominal circumference in cm	

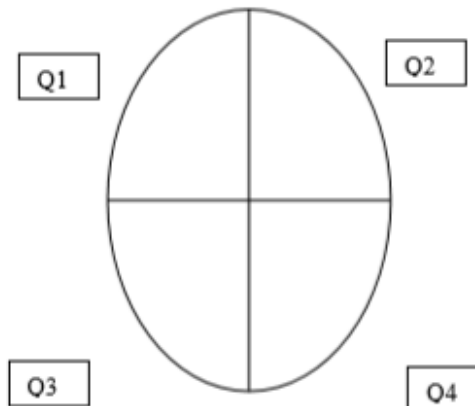
9. Presence of abdominal striae (as reported by mother) Yes No

10. Development of polyhydramnios Yes No

11. Gestational week of onset of striae _____

12. Number of striae

Quadrants	Number of striae 0=no striae; 1=striae do not affect quadrant completely; 2=striae affect quadrant completely
Quadrant 1	
Quadrant 2	
Quadrant 3	
Quadrant 4	
Total Score	



Appendices

13. Striae scoring and grading

Striae scoring	Striae score	Striae grading
No striae=0		None
Mild striae = 1-3		Mild striae
Moderate =4-6		Moderate striae
Severe =7-8		Severe striae

14. Final grading based on striae score (tick one)

None Mild Moderate Severe

15. Woman's perception of the severity of striae gravidarum

None Mild Moderate Severe

16. Development of striae in other body areas

Yes No

If control group participant - proceed to Q19

17. Adherence of Intervention group to protocol guidelines

Adherence of intervention Group (Tick 1 box)

Yes (applied the oil daily over approx. 26 weeks as per protocol)	<input type="checkbox"/>
No (applied the oil less than daily for 26 weeks)	<input type="checkbox"/>
No (applied the oil less than ten times over the course of the study)	<input type="checkbox"/>

18. Reason(s) for non-adherence

Intervention group participant - proceed to Q21

19. Adherence of Control group to protocol guidelines

Did not apply a product to the abdomen during study

Yes No

Appendices

20. Reason(s) for non-adherence _____

21. Undesirable effect

Occurrence of undesirable effect Yes

22. If **Yes** when did the undesirable effect occur (gestation, in relation to oil application) (Undesirable event form & HPRA form to be completed) _____

23. Woman's rating of the tolerability/acceptability of the oil (Tick appropriate box)

How would you rate your <u>tolerability/acceptability</u> of the oil on a scale of 0-3?	
Poor (0)	
Medium (1)	
Good (2)	
Excellent (3)	

24. Woman's rating of the effectiveness of the oil (Tick appropriate box)

How would you rate the <u>effectiveness</u> of the oil on a scale of 0-3?	
Poor (0)	
Medium (1)	
Good (2)	
Excellent (3)	

Birth Related Outcomes

25. Gestational week at birth _____

26. Weight of infant _____ Kgs

Appendix 13

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Trial register form**

Appendices

12. Consent for 'prevention of striae gravidarum study' Yes No

13. Randomisation
Intervention arm Control arm

14. Study ID number _____

15. Person recruiting the woman

Signature

Print name

____/____/____
Date

Appendix 14

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Participant letter of invite (1)**

**Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial
(ISRCTN: 76992326)**

Letter of Invite (1)

Dear participant,

I am a PhD student in the National University of Ireland Galway. As part of my PhD, I am undertaking a pilot trial on the use of a moisturising oil compared to no treatment for the prevention and reduction of stretch marks in pregnancy.

I am seeking to recruit women who are attending for their first antenatal booking appointment and are **12-14 weeks pregnant**.

Please find enclosed 'Participant information leaflet' with details of the study.

Thank you for your help.

Yours sincerely

Miriam Brennan

PhD student

National University of Ireland Galway.

Contact details

e mail: miriam.brennan@nuigalway.ie

Telephone number: 091 493651

Appendix 15

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Participant letter of invite (2)**

Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial
(ISRCTN: 76992326)

Letter of Invite (2)

Dear participant,

I am a PhD student in the National University of Ireland Galway. As part of my PhD, I am undertaking a pilot trial on the use of a moisturising oil compared to no treatment for the prevention and reduction of stretch marks in pregnancy.

I am seeking to recruit women who are attending for their first antenatal booking appointment and are **12-16 weeks pregnant**.

Please find enclosed 'Participant information leaflet' with details of the study.

Thank you for your help.

Yours sincerely

Miriam Brennan

PhD student

National University of Ireland Galway.

Contact details

e mail: miriam.brennan@nuigalway.ie

Telephone number: 091 493651

Appendix 16

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Participant information leaflet**

**Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial
(ISRCTN76992326)**

Participant Information Leaflet

If you would like to take part in a research study it is important that you understand why the research is being done and what it will involve.

Please take time to carefully read the following information and ask me if you do not understand any of the information or would like more information. I can be contacted at the contact details given below.

Study title: Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial.

What is the purpose of the study?

Stretch marks commonly develop during pregnancy, especially in the third trimester. They affect between 50% and 90% of women. They appear as red lines or streaks on the skin, then fade slowly to leave pale lines but they do not fade entirely. The abdomen, breasts and thighs are the parts of the body most commonly affected. Stretch marks can affect or concern women in different ways. Some women might see them as changing how they look and will try to prevent or reduce their severity by using different products readily available on the market. Other women may not think this and do not take any action to prevent or treat them.

While there are many skin products used by women to prevent or reduce the development of stretch marks, many of the products have not been evaluated in high quality research studies. It is therefore unclear as to how effective the products are.

The aim of this pilot trial is to evaluate the possibility of doing a larger trial to evaluate the effects of a moisturising oil on the prevention and reduction of stretch marks in pregnancy.

Why have I been chosen?

You have been chosen for inclusion in this study as you are attending the antenatal clinic at 12-14 weeks of pregnancy and you are expecting your first baby.

Who is undertaking and overseeing the study?

Miriam Brennan, a PhD student of the School of Nursing & Midwifery, National University of Ireland Galway.

My supervisor Professor Declan Devane of the School of Nursing & Midwifery, National University of Ireland Galway is overseeing the study.

What will happen to me if I participate in the study?

If you participate in the study:

1. You will be required to answer some preliminary questions and to have an assessment of your abdomen for stretch marks to see if you are eligible to participate in the trial or not.
2. You will be required to agree to be randomly allocated to either the intervention group or the no treatment group. If allocated to the intervention group you will be required to:
Apply ~2ml of the moisturising oil (= 2 pumps) after showering and before drying your skin, daily to your abdominal area. Following this you are required to 'pad it dry' so it is absorbed into the skin.

Appendices

If allocated to the no treatment group you will be required **Not to apply any skin product to your abdomen** during pregnancy.

3. You will also be required to answer some questions and to have some assessments (e.g. weight, and height) undertaken at recruitment to the trial and again at one of the 38-41 weeks of pregnancy clinic appointments.
4. You will also be required to complete a **diary on your daily application of the moisturising oil or not** as advised by the researcher.
5. You will receive two weekly reminder texts to keep the study diary.
6. If you are allocated to the group which requires you to apply the moisturising oil to your abdomen, you will be asked to bring the empty oil bottles back to the researcher at one of the 38-41 weeks of pregnancy clinic appointments.

Are there any disadvantages in taking part in this study?

There are no known disadvantages associated with participating in this trial.

What are the possible risks of taking part in this study?

There are no known risks associated with participating in this trial. However, in the event of a woman having an undesirable effect associated with the moisturising oil, they are advised to discontinue the oil and to contact their general practitioner.

What are the possible benefits of taking part in this study?

By being part of the study you will help to advance the research into the prevention of stretch marks in pregnancy, which may subsequently benefit women during pregnancy.

Confidentiality – who will know I am taking part in the study?

Following recruitment to the trial a note will be put in your hospital records to indicate your participation in the study. Consequently the obstetrician(s) and midwife/midwives who are caring for you will be aware that you are participating in the trial.

All information collected from you will be stored safely in electronic and paper form. Electronic data will be anonymised based on your individual participant trial ID number and stored in a password protected file on a password protected, encrypted laptop.

This data will be accessible only to the researcher, her supervisor, a research assistant, and a statistician.

All completed paper forms will be stored in a locked cabinet in the researcher's home for a period of 5 years. Only the researcher will be able to access these.

All data will be kept secure by the researcher for a period of five years.

Hospital Ethics Committee Approval

This study was granted ethical approval by the University Hospital Galway Ethics Committee.

What will happen to the results of the study?

The study results will be published in one of the academic journals as part fulfilment for the researcher's PhD requirements.

Who do I contact if I require further information?

If you require further advice or information please contact me the researcher at the contact details below.

Appendices

Voluntary participation

If you decide to participate your participation is voluntary. You may decide to withdraw from the study at any point without giving a reason and without any disadvantage. If you wish to withdraw please contact me, the researcher at the number or e mail below.

Contact Details

Principal investigator

Miriam Brennan

E mail: brennanm@nuigalway.ie

Telephone number: 091 493651

Thank you

Appendix 17

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Consent form**

**Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial
(ISRCTN76992326)**

Consent Form

First Name <small>Use BLOCK Capitals please</small>	
Surname <small>Use BLOCK Capitals please</small>	
Address <small>Use BLOCK capitals please Or addressograph</small>	

Date of birth / /
Day Month Year

In order to participate in the stretch mark prevention in pregnancy pilot study you must place a tick (✓) in the box beside the three statements below.

<ul style="list-style-type: none"> • I confirm that I have read, and understand the study information for the stretch mark prevention in pregnancy study. 	
<ul style="list-style-type: none"> • I confirm that I have had the opportunity to ask questions and that my questions were answered to my satisfaction. 	
<ul style="list-style-type: none"> • I understand that participation in this study is voluntary and that I am free to withdraw from the study at any time without my care or legal rights being affected. 	

To indicate your willingness and consent to being involved in this study, please place a tick (✓) in the box beside how you would like to take part in this study; that is choose 1 OR 2 from below

<p>1. <u>Stretch mark prevention in pregnancy study participation</u> I am willing and agree to take part in the stretch mark prevention in pregnancy study. I am aware that this means, I will complete a diary of my daily application or not of the moisturising oil as advised by the researcher. I agree to receiving two weekly reminder texts to complete the daily study diary and I also agree to the researcher accessing my health records and those of my baby.</p>	
OR	
<p>2. <u>Access to healthcare information only of a non participant</u> I Do NOT wish to take part in the stretch mark prevention in pregnancy study but I give permission for the study researcher to use anonymised data in reporting on women who did not want to participate in the study.</p>	

Appendix 18

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Consent on withdrawal form**

Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial
(ISRCTN76992326)

Consent on Withdrawal Form

First Name Use BLOCK Capitals please	
Surname Use BLOCK Capitals please	
Address Use BLOCK capitals please Or addressograph	

Study ID Number _____

<p>1. <u>Retention of data collected prior to my withdrawal from the study and the inclusion of data collected routinely</u> In the event of my withdrawal from the study, I give permission for the study researcher to include the anonymised data collected prior to my withdrawal and to include any relevant data collected routinely, for example, infant birth weight.</p>	
OR	
<p>2. <u>Retention of data collected prior to my withdrawal from the study</u> In the event of my withdrawal from the study I give permission for the study researcher to include the anonymised data collected prior to my withdrawal.</p>	
OR	
<p>3. <u>Complete withdrawal</u> In the event of my withdrawal from the study I do not give permission for the study researcher to include any of my data in the study analysis.</p>	

Signature of researcher

Print Name

Date

(copy to be send to participant).

Appendix 19

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Demographic and baseline
characteristics' data form**

**Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial
(ISRCTN76992326)**

Demographic & Baseline Characteristics' Data Form

1. Date: ___/___/___

2. Study ID Number: _____

3. Date of Birth

DAY	MONTH	YEAR
-----	-------	------

4. Occupation: _____

5. What is your ethnic or cultural background?

White

Irish

Irish Traveller:

Any other white background:

Black or Black Irish

African

Any other Black background

Asian or Asian Irish

Chinese

Any other

Other

(including mixed background)

Asian Background

6. Gestation	
7. Weight prior to pregnancy in Kg	
8. Weight at recruitment (Kg)	

9. Height in metres	
10. BMI	
11. Mid abdominal circumference (cm)	

12. Do you have any medical condition? Yes

No Proceed to Q14

13. If Yes list conditions:

Appendices

14. Are you taking any **prescribed medications**? Yes
No Proceed to Q16

15 If Yes please list medications and indication for use

Medication	Indication for use
1.	
2.	
3.	
4.	
5.	

16. Are you taking any **un prescribed/over the counter medications**?

Yes

No

17. Are you taking any **other drugs**?

Yes

No

18. Do you **drink alcohol**

Yes

No Proceed to Q20

19. If Yes what is current intake weekly _____.

20. Do you **smoke cigarettes** Yes

No Proceed to Q22

21. If Yes how many per day _____

Striae/stretch mark history

22. Do you have any **previous history of striae** Yes

No Proceed to Q23

23. If Yes where did they occur? (tick all that apply)

Abdomen Thighs Other
Breasts Buttocks

Appendices

24. Did any first degree relative (mother or sister) develop stretch marks during pregnancy

Yes

No

25. Skin type based on Fitzpatrick classification Questionnaire

Score		0	1	2	3	4
	What is the natural colour of your hair?	Sandy red	Blond	Chestnut, dark blond	Dark brown	Black
	What is your eye colour?	Light blue, gray, green	Blue, gray, green	Blue	Dark brown	Brownish black
	What is the colour of sun unexposed skin areas?	Reddish	Very pale	Pale with beige tint	Light brown	Dark brown
	How many freckles on unexposed skin areas?	Many	Several	Few	Incidental	None
	What happens when you are in the sun Too long without sun block?	Painful redness, blistering peeling	Blistering followed by peeling	Burns sometimes followed by peeling	Rarely burns	Never had a problem
	How well do you turn brown?	Hardly or not at all	Light colour tan	Reasonable tan	Tan very easily	Turn dark very quickly
	Do you turn brown within one day of sun exposure?	Never	Seldom	Sometimes	Often	Always
	How does your face respond to the sun?	Very sensitive	Sensitive	Normal	Very resistant	Never had a problem
	When did you last expose yourself to the sun or artificial sun treatments?	More than 3 months ago	2-3 month ago	1-2 months ago	Less than 1 month ago	Less than 2 weeks ago
	Do you expose the area to be treated to the sun?	Never	Hardly ever	Sometimes	Often	Always

Appendix 20

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Undesirable effect record form**

Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial
(ISRCTN76992326)

Undesirable Effect Record Form

Participant information (as per HPRa form):

1. Study ID Number: _____

2. Date: ____ / ____ / ____

3. Participant's initials: _____

4. Age (at time of undesirable effect): _____

5. Date of birth (dd/mm/yyyy): _____

6. Country of residence of the consumer: _____

Description of the undesirable effect (as per HPRa form)

7. Date the first symptoms of the undesirable effect were experienced/started (dd/mm/yyyy)

____ / ____ / ____

8. Length of time between first use of oil & the first symptoms of the undesirable effect (Please insert a number & then tick the appropriate box)

____ Minutes Hours Weeks Months Years

9. Location of the undesirable effect:

- skin (please specify location: _____)
- Scalp
- Hair
- Eyes
- Teeth
- Nails
- Lips
- Mouth (please specify location: _____)
- Other (please specify location: _____)

Appendices

10. To what parts of the body was the product applied? Please specify all areas that it was applied to _____

11. Description of symptoms experienced: _____

12. Have you used any treatment for the undesirable effect, including products purchased without visiting your doctor? If so please complete the table below.

Yes Please list below

No Proceed to Q14

13. Product used list

Name of product	Number of times/taken/administered per day	Duration of use of product

14. Participant's assessment of the severity of the effect

How would you rate the severity of the effect on a scale of 0-3?(tick correct box)	1	2	3
Mild			
Moderate			
Severe			

Further Information on the Suspected Product

15. Date of first ever use of the product (if date is unknown, please submit an approximate month/year estimate)(dd/mm/yy): _____

16. Frequency of use (please insert a number and then tick the appropriate box):

_____ times per day month week year

Appendices

17. Is the cosmetic product for professional use ? (should be stated on the product labelling, tick yes also if applied by a professional):

Yes No

18. Date of stopping product use (dd/mm/yyyy): _____

19. Full product name: _____

20. Company name: _____

21. Batch number and /or bar code (if applicable): _____

22. Expiry date (if applicable):

23. Precautions stated on the packaging: _____

24. Address on pack (underlined EU address): _____

25. Name & address of retail premises where product was purchased:

26. Details of other cosmetic products used at the same time: _____

****attach photograph of the product packaging if possible****

Other Relevant Medical History

(Include health care professional report if applicable)

27. Description of allergies (past & present, if applicable): _____

28. Description of type and result of patch test performed for the cosmetic product (if applicable): _____

Appendices

29. Description of other underlying disease or conditions (if applicable):

30. If you use any medication (including products purchased without prescription), please complete the table below:

Name of product	Number of times applied/taken/administered per day	Duration of use of medication

Please complete a HPRA form also for this participant

Appendix 21

Paper 3: Prevention of striae gravidarum: study protocol for a pilot randomised controlled trial: Undesirable effect report log

Prevention of striae gravidarum (stretch marks in pregnancy): a pilot trial (ISRCTN76992326)

Undesirable Effect Record Log

No	Date	Study ID	Date of effect	Nature of effect	Participant's assessment of severity of effect mild, moderate or severe	Action taken	Outcome	Related to trial Not related Unlikely Related possibly or probably related	HPRA form completed	Researcher's signature

Appendix 22

Paper 3: Prevention of striae gravidarum: study protocol for a pilot randomised controlled trial: Health Products Regulatory Authority (HPRA) Undesirable Effect Report Form for Cosmetic Products

Undesirable Effect Report Form for Cosmetic Products

Please complete all relevant sections of this form in confidence and return to Cosmetics Section, Health Products Regulatory Authority, Earlsfort Centre, Earlsfort Terrace, Dublin 2, D02 XP77. Telephone 353-1-6764971, e-mail cosmetics@hpra.ie

A privacy notice in relation to the personal data collected on this form is available on the HPRA website (www.hpra.ie) under 'Report an Issue' and 'Medicine Quality Issue/Defect'.

Reporter name: [REDACTED]		
Address: [REDACTED]		
E-mail: [REDACTED]		
Telephone number: [REDACTED]		
If you are not the consumer, state profession: [REDACTED]		
If reporter is not consumer, insert consumer initials: [REDACTED]	Sex: <input type="checkbox"/> M <input type="checkbox"/> F	Age: [REDACTED]
Suspected product(s) (include full name and brand): [REDACTED]		
Batch number and expiry date if present on pack: [REDACTED]	Product reference number/shade/colour (if applicable): [REDACTED]	
Dates/duration of use: [REDACTED]		
Address on pack (EU address): [REDACTED]		
Is the product for professional use only? <input type="checkbox"/> Yes <input type="checkbox"/> No (should be stated on the pack)		
Precautions stated on the pack: [REDACTED]		
Name and address of retailer of the product: [REDACTED]		
Details of reaction: (brief description of the reaction including location of the reaction, location of application of the product) [REDACTED]		

Appendices

Time to first signs of reaction: (seconds/days) █	Date of occurrence of reaction: █	Duration of reaction: █
Treatment given/action taken: █		
Use of product discontinued: <input type="checkbox"/> Yes <input type="checkbox"/> No Improvement on discontinuation: <input type="checkbox"/> Yes <input type="checkbox"/> No Subsequently reapplied: <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, outcome: █		
Details of other cosmetics used at the same time: █		
Description of allergies (past and present, if applicable): █		
If a patch test was performed <u>prior to use</u> of the cosmetic product, describe the type of test used and the results of the patch test: █		
Description of any other underlying disease, conditions or medication (if applicable): █		
Was a healthcare professional consulted? <input type="checkbox"/> Yes <input type="checkbox"/> No		
Contact details of the healthcare professional (note the healthcare professional may be contacted in the case of a serious undesirable effect): █		
<i>Include healthcare professional report and photos of the product if possible.</i>		

Signature:

Date:

Thank you for taking the time to complete this form.

Appendix 23

**Paper 3: Prevention of striae gravidarum: study protocol for a pilot
randomised controlled trial: Ethical approval letters -Galway
University Hospitals**



Ospidéal na h-Ollscoile, Páirc Mheirlinne
Merlin Park University Hospital
GALWAY UNIVERSITY HOSPITALS

Clinical Research Ethics Committee
Room 59
1st Floor
HR Building
Merlin Park Hospital
Galway.

8th June, 2017.


Ms. Miriam Brennan
Lecturer in Midwifery
School of Nursing & Midwifery
Aras Moyola
National University of Ireland
Galway.

Ref: C.A. 1770 - Prevention of Striae Gravidarum: A Pilot Trial

Dear Ms. Brennan,

I have considered and reviewed the above project, and I am happy to confirm Chairman's approval to proceed.




Yours sincerely,



Professor B. Gerard Loftus
Chairman Clinical Research Ethics Committee.

c.c. Professor Declan Devane, Professor of Midwifery, School of Nursing & Midwifery
Aras Moyola, National University of Ireland, Galway.

Ospidéal na h-Ollscoile, Páirc Mheirlinne, MERLIN PARK UNIVERSITY HOSPITAL,
Galway, Ireland. Tel: 00 353 (0)91 757631

 <p>Saolta Grúpa Oideolaí Cúram Sáinní University Health Care Group</p>	 <p>Ospidéal na h-Ollscoile, Páirc Mheirlinne Merlin Park University Hospital GALWAY UNIVERSITY HOSPITALS</p>
<p>Clinical Research Ethics Committee Room 59 1st Floor HR Building Merlin Park Hospital Galway.</p>	
<p>13th July, 2017.</p>	
<p>Ms. Miriam Brennan Lecturer in Midwifery School of Nursing & Midwifery Aras Moyola National University of Ireland Galway.</p>	
<p><u>Ref: C.A. 1770 - Prevention of Striae Gravidarum: A Pilot Trial</u></p>	
<p>Dear Ms. Brennan,</p>	
<p>The Chairman's decision to approve the above study was ratified at the Clinical Research Ethics Committee meeting on Wednesday 12th July, 2017.</p>	
<p>Yours sincerely,</p>	
<p> _____ Professor B. Gerard Loftis Chairman Clinical Research Ethics Committee.</p>	
<p>c.c. Professor Declan Devane, Professor of Midwifery, School of Nursing & Midwifery Aras Moyola, National University of Ireland, Galway.</p>	
<p>Ospidéal na h-Ollscoile, Páirc Mheirlinne, Merlin Park University Hospital, Galway, Ireland. Tel: 00 353 (0)91 757631</p>	

 <p>Saolta Grúpa Ollscoile Cúram Sláinte University Health Care Group</p>	 <p>Ospidéal na h-Ollscoile, Páirc Mheirlinne Merlin Park University Hospital GALWAY UNIVERSITY HOSPITALS</p>
	<p>Clinical Research Ethics Committee Room 59 1st Floor HR Building Merlin Park Hospital Galway.</p>
	<p>21st July, 2017.</p>
<p>Ms. Miriam Brennan Lecturer in Midwifery School of Nursing & Midwifery Aras Moyola National University of Ireland Galway.</p>	
	<p>Ref: C.A. 1770 - <i>Prevention of Striae Gravidarum: A Pilot Trial</i> <i>Amendment to Protocol - submitted and approved 21st July, 2017</i></p> <hr/>
	<p>Dear Ms. Brennan,</p>
	<p>I have considered the above amendment, and I wish to confirm Chairman's approval to proceed.</p>
	<p>Yours sincerely,</p>
	<p> _____ Professor B. Gerard Loftus Chairman Clinical Research Ethics Committee.</p>
	<p>c.c. Professor Declan Devane, Professor of Midwifery, School of Nursing & Midwifery Aras Moyola, National University of Ireland, Galway.</p>
	<p>Ospidéal na h-Ollscoile, Páirc Mheirlinne, MERLIN PARK UNIVERSITY HOSPITAL, Galway, Ireland. Tel: 00 353 (0)91 757631</p>



Ospidéal na h-Ollscoile, Páirc Mheirlinne
Merlin Park University Hospital
GALWAY UNIVERSITY HOSPITALS

Clinical Research Ethics Committee
Room 59
1st Floor
HR Building
Merlin Park Hospital
Galway.

25th January, 2018.

Ms. Miriam Brennan
Lecturer in Midwifery
School of Nursing & Midwifery
Aras Moyola
National University of Ireland
Galway.


*Ref: C.A. 1770 - Prevention of Striae Gravidarum: A Pilot Trial
Amendment to Extend Duration of Data Collection and Extend
Gestational age of women at recruitment submitted 24th January,
2018*

Dear Ms. Brennan,

I have considered the above amendment, and I am happy to confirm Chairman's approval to proceed.

- Extend Duration of Data Collection by 6 months
- Extend Gestational age of women at recruitment from 12-14 weeks to 12-16 weeks

Yours sincerely,


Professor G. Gerard Loftus
Chairman Clinical Research Ethics Committee.

c.c. Professor Declan Devane, Professor of Midwifery, School of Nursing & Midwifery
Aras Moyola, National University of Ireland, Galway.

Ospidéal na h-Ollscoile, Páirc Mheirlinne, MERLIN PARK UNIVERSITY HOSPITAL,
Galway, Ireland. Tel: 00 353 (0)91 757631



Ospidéal na h-Ollscoile, Páirc Mheirlinne
Merlin Park University Hospital
GALWAY UNIVERSITY HOSPITALS

Clinical Research Ethics Committee
Room 59
1st Floor
HR Building
Merlin Park Hospital
Galway.

24th July, 2018.

Ms. Miriam Brennan
Lecturer in Midwifery
School of Nursing & Midwifery
Aras Moyola
National University of Ireland
Galway.

*Ref: C.A. 1770 - Prevention of Striae Gravidarum: A Pilot Trial
Amendment submitted 20th July, 2018
Extension of Data Collection Period for Pilot Trial
from 25th July to the 31st August, 2018*

Dear Ms. Brennan,

I have considered the above amendment, and I wish to confirm Chairman's approval to proceed.

Yours sincerely,



Professor B. Gerard Loftus
Chairman Clinical Research Ethics Committee.

c.c. Professor Declan Devane, Professor of Midwifery, School of Nursing & Midwifery
Aras Moyola, National University of Ireland, Galway.

Ospidéal na h-Ollscoile, Páirc Mheirlinne, MERLIN PARK UNIVERSITY HOSPITAL,
Galway, Ireland. Tel: 00 353 (0)91 757631

Appendix 24

Paper 4: A qualitative study of the factors influencing recruitment to a pilot trial on the prevention of striae gravidarum: Participant letter of invite

Appendices

Title of Study: A qualitative descriptive study of the factors influencing recruitment to a pilot trial on the prevention of stretch marks in pregnancy

Letter of Invite

Dear participant,

I am a midwife and PhD student in the National University of Ireland, Galway. As part of my PhD, I am undertaking a study of the factors influencing recruitment to a pilot trial on the prevention of stretch marks in pregnancy. I am seeking to interview women who are 12-16 weeks pregnant attending for their booking visit in the Maternity Unit of University Hospital Galway.

Please find enclosed 'Participant information sheet' with details of the study.

Thank you for your help.

Yours sincerely

Miriam Brennan

Lecturer in Midwifery and PhD student

National University of Ireland Galway.

Contact details

e mail: miriam.brennan@nuigalway.ie

Telephone number: 091 493651

Appendix 25

Paper 4: A qualitative study of the factors influencing recruitment to a pilot trial on the prevention of striae gravidarum: Participant information sheet

Title of Study: A qualitative descriptive study of the factors influencing recruitment to a pilot trial on the prevention of stretch marks in pregnancy

Participant Information sheet

If you would like to take part in a research study it is important that you understand why the research is being done and what it will involve.

Please take time to carefully read the following information and ask me if you do not understand any of the information or would like more information.

Study title: A qualitative descriptive study of the factors influencing recruitment to a pilot trial on the prevention of stretch marks in pregnancy.

What is the purpose of the study?

Stretch marks commonly develop during pregnancy, especially in the third trimester. They affect between 50% and 90% of women. They appear as red lines or streaks on the skin, then fade slowly to leave pale lines but they do not fade entirely. The abdomen, breasts and thighs are the parts of the body most commonly affected. Stretch marks can affect or concern women in different ways. Some women might see them as changing how they look and will try to prevent or reduce their severity by using different products readily available on the market. Other women may not think this and do not take any action to prevent or treat them.

While there are many skin products used by women to prevent or reduce the development of stretch marks, many of the products have not been evaluated in high quality research studies. It is therefore unclear as to how effective the products are. I am currently inviting pregnant women to participate in a pilot trial to evaluate if a moisturising oil compared to no treatment would be effective in preventing stretch marks in pregnancy. The aim of this part of the study is to explore factors influencing recruitment to this pilot trial.

Why have I been chosen?

You have been chosen for inclusion in this study as you are 12-16 weeks pregnant and attending for your booking appointment at the Antenatal Clinic of the Maternity Unit of University Hospital Galway.

Who is undertaking and overseeing the study?

Miriam Brennan, a PhD student of the School of Nursing & Midwifery, National University of Ireland Galway.

My supervisor Professor Declan Devane of the School of Nursing & Midwifery, National University of Ireland Galway is overseeing the study.

What will happen to me if I participate in the study?

If you participate in the study you will agree to be interviewed over the phone by the researcher Miriam Brennan about the factors influencing recruitment to the pilot trial.

Are there any disadvantages in taking part in this study?

There are no known disadvantages associated with participating in this study.

Appendices

What are the possible risks of taking part in this study?

There are no known risks associated with participating in this study.

What are the possible benefits of taking part in this study?

By being part of the study you will help to advance and guide the research into the prevention of stretch marks in pregnancy which may subsequently benefit women during pregnancy. You will also illuminate factors influencing women's decisions to participate in trials.

Confidentiality – who will know I am taking part in the study?

The researcher, Miriam Brennan, will know you are taking part in the study. All information collected from you will be stored safely on a password protected lap top. Your interview data will be coded and the record of this coding will be stored separately on a password protected file on a password protected laptop. All information including consent forms will be stored safely for a period of 5 years. Only the researcher will be able to access these.

Hospital Ethics Committee Approval

The full study was granted ethical approval by the University Hospital Galway Ethics Committee.

What will happen to the results of the study?

The study results will be published in an academic journal and this will also form part of the requirements for the researcher's PhD.

Who do I contact if I require further information?

If you require further advice or information please contact Miriam Brennan at the contact details below.

Voluntary participation

If you decide to participate your participation is voluntary. You may decide to withdraw from the study at any point without giving a reason and without any disadvantage. If you wish to withdraw please contact me at the number or e-mail below.

Contact Details

<p>Principal investigator Miriam Brennan E mail brennanm@nuigalway.ie Telephone number: 091 493651</p>
--

Thank you

Appendix 26

Paper 4: A qualitative study of the factors influencing recruitment to a pilot trial on the prevention of striae gravidarum: Consent form

Appendix 27

**Paper 4: A qualitative study of the factors influencing recruitment
to a pilot trial on the prevention of striae gravidarum: Interview
guide**

A qualitative descriptive study of the factors influencing recruitment to a pilot trial on the prevention of stretch marks in pregnancy

Interview guide

Introduction.

Brief outline of the study and its aims.

Turn on recorder.

You agreed to participate in the pilot trial; Can you tell me your reasons for participating in the pilot trial?

Participants who refer to quality of information communicated by the recruiter...

Probe questions re information communicated as follows:

- You said that the information presented was very clear. Can you tell me what made it so clear?
- You said the 'amount of information provided' was also one of the reasons for participating in the pilot trial. Can you elaborate more on what you mean by the amount of information provided?
- You also mention the recruiter's manner; again what was it about the recruiter's manner?

Participants who refer to deriving some benefit from participating in the trial...

Probe questions re benefit as follows:

- You mention that you might get some benefit from participating in the trial. Can you tell me what you mean by this?
- What do you see as a benefit?

Participants who mention the value or the importance of research...

Probe questions re value or the importance of research as follows:

- You mention how participating in research is valuable. Can you elaborate on what you mean by valuable?
- You mention about the importance of participating in research or the importance of research. Can you elaborate on what you mean by this?
- You mention about wanting to help other women. Can you explain what you mean by this?

Prompts

Appendices

- What do they feel about being part of a study that might provide better evidence for you in a future pregnancy or for other pregnant women?
- Do you see any advantages of participating in the trial? If so what are they
- Do you see any disadvantages of participating in the trial? If so what are they
- Have you been asked by other doctors or midwives to participate in other studies during this pregnancy, and if so how many times were you asked to consider joining a research study?

Or

You declined to participate in the pilot trial. Can you talk to me about your reasons for not participating in the pilot trial?

Participants who refer to a product already in use or planned to use...

Probe questions re product choice as follows:

- What influenced your decision to use product X? (Probe: media, friends, HC professionals)
- How confident are you that it will work?
- When did you start to use product X or when do you intend to start using it?
- Can you talk to me about the influence of cost/price of the product on your choice of product?
- In a future stretch mark product study, what other products would encourage you to change your mind and to participate in the study? For example a more expensive one.
- In a future stretch mark product study, what incentive(s) if any, would encourage you to participate in the study?

Participants who do not want to be randomised to one of two groups...

Probe questions re randomisation as follows:

- Can you talk to me a little about what you understand by 'random allocation of women to different groups'
- What is your understanding of why we do this in a study like this one ?
- As you know this study involved randomly assigning women to either apply a moisturising oil or no treatment. Do you see any advantages or disadvantages of being in one group over the other and if so what are they?

Prompts

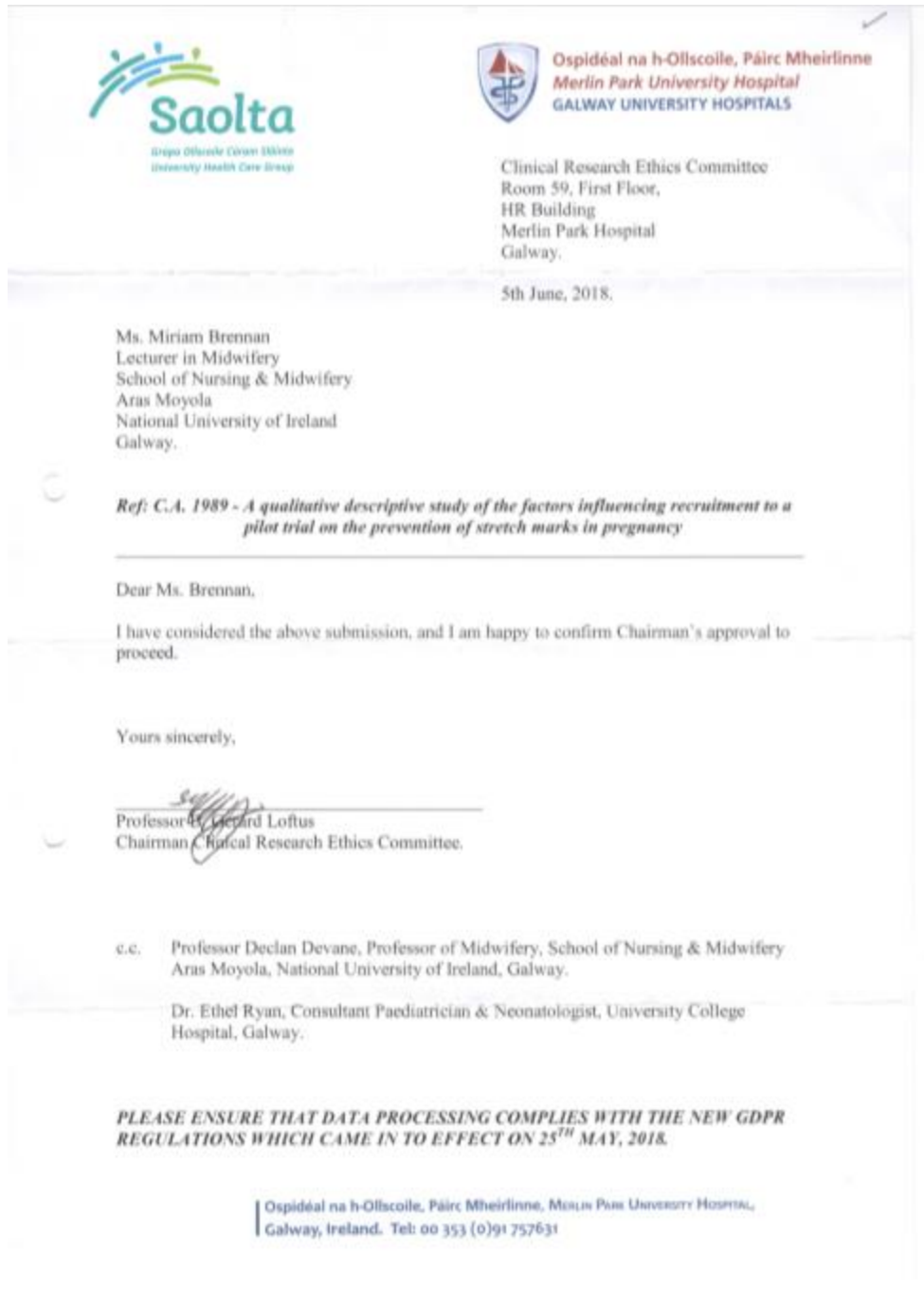
- Did the practice in the trial of randomising women to one of two groups influence your decisions to not participate in the trial?
- Do you have any objections to being randomised to one of two groups? If so what are they?




Appendices

- Do you have views on any of the other aspects of the trial? (for example what participants are being required to do, for example like the application of the oil after a shower or completion of the diary)?
- What would you feel about being part of a study that might provide better evidence for you in a future pregnancy or for other pregnant women?
- Have you been asked by other doctors or midwives to participate in other studies during this pregnancy, and if so how many times were you asked to consider joining a research study?
- Finally can you give me some suggestions for a future stretch mark study that would motivate you to participate in it?

Appendix 28

**Paper 4: A qualitative study of the factors influencing recruitment
to a pilot trial on the prevention of striae gravidarum: Ethical
approval letters -Galway University Hospitals**



 <p>Saolta Grúpa Oibríoch Cúram Sláinte University Health Care Group</p>	 <p>Ospidéal na h-Ollscoile, Páirc Mheirlinne Merlin Park University Hospital GALWAY UNIVERSITY HOSPITALS</p>
<p>Clinical Research Ethics Committee Room 59, First Floor, HR Building Merlin Park Hospital Galway.</p>	
<p>29th June, 2018.</p>	
<p>Ms. Miriam Brennan Lecturer in Midwifery School of Nursing & Midwifery Aras Moyola National University of Ireland Galway.</p>	
<p>Ref: C.A. 1989 - A qualitative descriptive study of the factors influencing recruitment to a pilot trial on the prevention of stretch marks in pregnancy Amendment 1 submitted 29th June, 2018 - Text Communication and Professional Transcriber</p>	
<p>Dear Ms. Brennan,</p>	
<p>I have considered the above amendment, and I am happy to confirm Chairman's approval to proceed.</p>	
<p>Yours sincerely,</p>	
<p> _____ Professor B. Gerard Loftus Chairman Clinical Research Ethics Committee.</p>	
<p>c.c. Professor Declan Devane, Professor of Midwifery, School of Nursing & Midwifery Aras Moyola, National University of Ireland, Galway.</p>	
<p>Dr. Ethel Ryan, Consultant Paediatrician & Neonatologist, University College Hospital, Galway.</p>	
<p>PLEASE ENSURE THAT DATA PROCESSING COMPLIES WITH THE NEW GDPR REGULATIONS WHICH CAME IN TO EFFECT ON 25TH MAY, 2018.</p>	
<p>Ospidéal na h-Ollscoile, Páirc Mheirlinne, MERLIN PARK UNIVERSITY HOSPITAL, Galway, Ireland. Tel: 00 353 (0)91 757631</p>	



Ospidéal na h-Ollscoile, Páirc Mheirlinne
Merlin Park University Hospital
GALWAY UNIVERSITY HOSPITALS

Clinical Research Ethics Committee
Room 59, First Floor,
HR Building
Merlin Park Hospital
Galway.

13th July, 2018.

Ms. Miriam Brennan
Lecturer in Midwifery
School of Nursing & Midwifery
Aras Moyola
National University of Ireland
Galway.

Ref: C.A. 1989 - A qualitative descriptive study of the factors influencing recruitment to a pilot trial on the prevention of stretch marks in pregnancy

Dear Ms. Brennan,

The Chairman's decision to approve the above study was ratified at the Clinical Research Ethics Committee meeting on Wednesday 11th July, 2018.

Yours sincerely,


Professor B. Gerard Lofthus
Chairman Clinical Research Ethics Committee.

c.c. Professor Declan Devane, Professor of Midwifery, School of Nursing & Midwifery
Aras Moyola, National University of Ireland, Galway.

Dr. Ethel Ryan, Consultant Paediatrician & Neonatologist, University College
Hospital, Galway.

Ospidéal na h-Ollscoile, Páirc Mheirlinne, MERLIN PARK UNIVERSITY HOSPITAL,
Galway, Ireland. Tel: 00 353 (0)91 757631