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VÄSTRA GÖTALANDSREGIONEN
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New versus Old Types of Pessaries and Gels as Contraceptives for Women
[Pessar och gel som preventivmedel för kvinnor]

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1. Abstract

Background

For more than a century female barrier contraceptives have been an important choice for women who want locally, rather than systemically acting, methods. Since the introduction of pessaries in the middle of the 20th century they were the only controlled contraceptive method for females for many years. Vaginal barriers with diaphragms or cervical caps are mostly combined with spermicidal gels or creams. Today, there is an increasing interest of hormone-free contraceptive methods.

Objectives

To evaluate whether new types of pessaries such as FemCap, Caya or equivalent products differ in prevention of pregnancy compared with older types of pessaries such as Milex or Ortho All-Flex, and whether different types of gels differ in prevention of pregnancy.

Methods

A systematic literature search was conducted in PubMed, Embase, the Cochrane Library, and HTA-databases. Two authors independently screened titles, abstracts and full-text articles for inclusion and extracted data. The certainty of evidence was graded according to the GRADE system.

Main results

Four RCTs and one cohort study were included in the assessment. One of the four RCTs was not available in ordinary databases, but data and quality assessment could be retrieved from a Cochrane review.

New types compared with old types of pessaries

Pregnancy

The 6-month pregnancy rate varied between 11%-15% in women who used a new type compared with 8%-12% in women who used an old type of pessary.

Conclusion: There may be little or no difference in pregnancy rate between new types and old types of pessaries. Low certainty of evidence (GRADE ⊕⊕◯◯).

Discontinuation

The discontinuation rate was 37% in users of new types of pessaries compared with 21% in users of old types of pessaries in the only RCT that reported such data.

Conclusion: The discontinuation rate may be higher with the new types compared with the old types of pessaries. Low certainty of evidence (GRADE ⊕⊕◯◯).

Acid buffering gel compared with nonoxynol-9 gel (PICO 2)

Pregnancy

The 6-month pregnancy rate was about 10% in women who used acid buffering gel with the pessary compared with about 12% in women who used the spermicidal nonoxynol-9 gel with the pessary.

Conclusion: There is probably little or no difference in pregnancy rate between acid buffering gel and nonoxynol-9 gel. Moderate certainty of evidence (GRADE ⊕⊕⊕◯).

Discontinuation

The discontinuation rate was significantly lower in women who used acid buffering gel compared with users of the nonoxynol-9 gel with a relative risk of 0.77 favouring acid buffering gel.

Conclusion: The discontinuation rate is probably lower when acid buffering gel is used than with non-oxynol-9 gel. Moderate certainty of evidence (GRADE⊕⊕⊕◯).

Concluding remarks

The pregnancy rates are rather high in women who use female barrier contraceptives. The new types of pessaries have not been shown to differ significantly from the old types in their efficacy to prevent pregnancies. Acid buffering gels do not differ from the spermicidal nonoxynol-9 gels with regard to pregnancies, but seem to be better tolerated by the women.

2. Svensk sammanfattning – Swedish summary

Bakgrund
Preventivmedlet pessar som kvinnlig barriärmetod har funnits i mer än ett sekel. Det har kombinerats med en spermiedödande gel eller kräm. Hormonella preventivmetoder har en stark ställning sedan introduktionen av p-piller på 50-talet. Av icke-hormonella alternativ är spiral vanligast, men det finns en viss efterfrågan på barriärmetoder som pessar, trots en sämre antikonceptionell effekt. Nyare typer av pessar har lanserats utanför det traditionella mottagningssystemet, och har istället sålts via internet och utan utprovning. Den spermiedödande gelen/krämen finns idag inte längre tillgänglig, varför man istället rekommenderar en surgörande gel i kombination med all pessaranvändning.

Syfte
Att utvärdera om nyare typer av pessar såsom FemCap, Caya eller likartade produkter skiljer sig från äldre pessartyper såsom Milex och Ortho All-Flex att förhindra graviditet, och om olika typer av gel även skiljer sig härvidlag.

Metoder
Under januari 2017 gjordes systematiska litteratursökningar i PubMed, Embase, the Cochrane Library, Cinahl, och HTA-databaser. Minst två författare granskade titlar, abstracts och fulltextartiklar, värderade studiekvalitet och extraherade data oberoende av varandra. Det vetenskapliga underlagets styrka bedömdes enligt GRADE-systemet.

Resultat
Fyra randomiserade, och en icke-randomiserad, kontrollerad studie inkluderades i rapporten. En av de randomiserade studierna var inte tillgänglig som originalpublikation utan data och kvalitetsbedömning baserades på information i en Cochrane översikt.

Nya jämfört med äldre typer av pessar (PICO 1)

Graviditet
Graviditetsfrekvensen under sex månader varierade mellan 11% och 15% hos kvinnor som använde en ny typ av pessar och mellan 8% och 12% hos kvinnor som använde en äldre typ.
Slutsats: Det är troligen en liten eller ingen skillnad i graviditetsfrekvens hos kvinnor som använder en ny jämfört med en äldre typ av pessar. Begränsat vetenskapligt underlag (GRADE ⊕⊕◯◯).

Avbrytande av användningen av pessar
Kvinnor som använde en nyare typ av pessar avbröt i större utsträckning sin användning, än kvinnor som använde en äldre typ (37% vs 21%) under en studietid av sex månader.
Slutsats: Andelen kvinnor som avbryter sin användning av pessar kan vara något högre hos de som startat med en nyare typ jämfört med de som använder en äldre typ. Begränsat vetenskapligt underlag (GRADE ⊕⊕◯◯).

Surgörande gel jämfört med nonoxynol-9 gel (PICO 2)

Graviditet
Graviditetsfrekvensen efter sex månader var ca 10% hos kvinnor som använde pessar tillsammans med en surgörande gel och ca 12% hos de som använde pessar tillsammans med nonoxynol-9 gel.
Slutsats: Det är sannolikt en liten eller ingen skillnad i graviditetsfrekvens hos kvinnor som använder en surgörande gel jämfört med nonoxynol-9 gel tillsammans med sitt pessar. Måttligt starkt vetenskapligt underlag (GRADE ⊕⊕⊕◯).

Avbrytande av användningen av pessar
Andelen kvinnor som avbryter sin användning av pessar var signifikant lägre hos de som använde en surgörande gel jämfört med de som använde nonoxynol-9 gel (relativ risk 0,77).
Slutsats: Användningen av en surgörande gel minskar troligen andelen kvinnor som slutar använda sitt pessar jämfört med nonoxynol-9 gel. Måttligt starkt vetenskapligt underlag (GRADE⊕⊕⊕◯).

Sammanfattande kommentar
Graviditetsfrekvensen är relativt hög hos kvinnor som använder pessar som preventiv metod. Nyare typer av pessar har inte visat sig skilja sig från äldre typer i effektivitet att förhindra graviditet. Surgörande gel skiljer sig inte heller avseende risk för graviditet, från den tidigare använda typen av gel som innehåller nonoxynol-9, men förefaller tolereras bättre.

The above summaries were written by representatives from the HTA-centrum. The HTA-report was approved by the Regional board for quality assurance of activity-based HTA. The abstract is a concise summary of the results of the systematic review. The Swedish summary is a brief summary of the systematic review intended for decision makers, and is ended with a concluding summary.

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3. Summary of Findings

Table 1. Comparison between new types and old types of pessaries.

Outcomes	Study design Number of studies	Relative effect (95% CI)	Absolute effect	Certainty of evidence GRADE
Pregnancy	2 RCT	OR = 1.24 (0.89; 1.74) aRR = 1.96[2]	15.0% vs 12.4% 13.5% vs 7.9%	⊕⊕◯◯ [1]
	1 Cohort		11.3% vs 10.7%	⊕⊕◯◯
Discontinuation	1 RCT		63% vs 79% p<0.001	⊕⊕◯◯[3]

Footnotes:
1. Very serious study limitations with unclear randomisation procedure and high withdrawal rate in one RCT and some uncertainty in directness.
2. 95% confidence interval not reported.
3. Serious study limitations with high withdrawal rate after randomisation, and some uncertainty in directness due to unclear method of recruitment of study subjects.

Abbreviations: OR = Odds Ratio, aRR = adjusted Relative Risk.

Table 2. Comparison between Acid-buffering gel and Nonoxynol-9-gel.

Outcomes	Study design Number of studies	Relative effect (95% CI)	Absolute effect	Certainty of evidence GRADE[1]
Pregnancy	2 RCT		10.1% vs 12.3% 9.6% vs 12.5%	⊕⊕⊕◯[1]
Discontinuation	2 RCT	RR =0.77 (95% CI: 0.68;0.86)	61% vs 49% 58% vs 46%	⊕⊕⊕◯[2]

Footnotes:
1. Some study limitations with 10-15% withdrawal rate after randomisation, some uncertainty in directness due to unclear method of recruitment.
2. Some uncertainty in directness due to unclear method of recruitment of study subjects.

Abbreviation: RR = Relative Risk

Certainty of evidence

High certainty ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty ⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty ⊕⊕◯◯	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty ⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

4. Abbreviations/Acronyms

aRR = adjusted Relative Risk
CPP = Cumulative Pregnancy Probability
FU = Follow-up
HIV = Human Immunodeficiency Virus
ITT = Intention to treat
MITT = Modified intention to treat
NS = Not significant
OR = Odds ratio
PP = Per protocol
PU = Perfect use
RCT = Randomised clinical trial
TU = Typical use
UTI = Urinary tract infection
VGR = Region Västra Götaland
Δ = difference

5. Background

For more than a century the female barrier contraceptives have been an important choice for women who want locally, rather than systemically, acting and rapidly reversible methods.

The previously used spermicides with barrier contraceptives were all based on detergents, most commonly nonoxynol-9, which potently disrupt the cell membranes of the sperm, as well as those of some sexually transmitted pathogens (Hillier et al., 2005, Hicks et al., 1985). Nowadays the spermicidal gel (nonoxynol-9) is no longer produced. The acid-buffering lactate- and cellulose-based gels are the currently available alternatives (Contra gel and Caya gel).

Today, there is an increasing interest in hormone-free contraceptive methods. This has been spread via the internet and has led to an increased awareness of and demand for hormone-free alternatives. If these methods turn out to be less effective there is a risk for unwanted pregnancies. Therefore, there is a need for new recommendations for how, and when, to use pessary with presently available gels as a preventive method. Also, there is a need for clear information to the prescribing medical professionals in Sweden, and to patients from the Swedish health care system internet website (1177).
Through the present report, the term *pessary* is used instead of the terms *diaphragm* and *cap*.

Prevalence and incidence

Since the introduction of pessaries in the middle of the 20th century they were the only contraceptive method for women for many years. Nowadays the use of pessaries has declined since more effective contraceptive methods are available. In 2015 vaginal barrier methods (including pessaries and spermicidal foams; jelly, cream and sponges) are reported to be used among married or in-union women aged 15 to 49 years, at a prevalence of 0.1% and 0.9% worldwide and in Europe, respectively (United Nations, 2015). The number of pregnancies per 100 women and year when pessaries such as Ortho-All-flex and Milex are used correctly in combination with nonoxynol-9 gel (“perfect use”), and when they are used “typically” have been reported to be 6 and 12 per year, respectively (Trussell, 2011).

Present use of pessary

The types of pessaries that presently are available over the counter are Milex, Caya and FemCap. Milex, which is the type of pessary that followed after Ortho-All-flex, has been on the market for many decades, and it is subsidised by the Region Västra Götaland (VGR). The newer types of pessaries, Caya and FemCap, are not subsidised.

The normal pathway through the health care system and current wait time for assessment

Women who choose the Milex pessary as contraceptive method need a consultation with a midwife at a midwife center (i.e. Barnmorskemottagning) or at a youth clinic (i.e. Ungdomsmottagning) or with a gynaecologist. The size will then be checked for a correct fit prior to a prescription. The FemCap and Caya pessaries are available at internet websites. Thus, these products will not be checked for a perfect fit by a health professional prior to their use. The woman has to follow written instructions in order to find the correct size and learn by herself how to insert and remove the pessary.

Annual sales of pessaries

The number of women who use pessaries as contraceptives is difficult to estimate. During 2015 and 2016, and until mid-April 2017 88, 49 and 19 Milex pessaries, respectively, were sold by the company Solann in VGR. The corresponding quantities for the entire Sweden were 503, 301 and 78.

There is no sales statistics publicly available for the pessaries FemCap and Caya. According to the responsible salesman who has the exclusive right to sell them through an internet website, 39 FemCap and 61 Caya pessaries were ordered during the first three months of 2017 by the four health care regions (Stockholm, Värmland, Norrbotten, Blekinge) that subsidise pessaries to women below 26 years of age. An unknown number of women in these regions have ordered the pessaries by themselves through the website. Data on the number of FemCap or Caya users in other parts of Sweden are not available.

Present recommendations from medical societies or health authorities

The current national recommendations from the Swedish Medical Products Agency regarding contraception, May 2014, do not have any specific recommendations of the use of pessary with the currently available pessary gels.

6. Pessaries and gels

The mode of action of all female barrier methods is to prevent the passage of sperms into the uterus by creating a physical barrier between the sperm and the uterus, as well as to provide a reservoir that can hold the spermicidal cream or gel close to the cervical ostium.

The Milex pessary is a silicone rubber diaphragm available in six sizes between 60 and 85 mm in diameter. It should be inserted into the vagina with the posterior part in the posterior fornix and its anterior part right under the pubic rim. Thereby, it will entirely cover the cervix. It requires a trained provider to assess that it is correctly fitted to each woman. In VGR this is currently done by a gynaecologist or a midwife.

The FemCap pessary is a cervical cap made of silicone rubber that is shaped like a sailor´s hat. The dome is designed to cover the cervix, the rim to fit into the vaginal fornices, and the brim to adhere and conform to the vaginal walls. It is available in three sizes; small (22 mm) designed for nulliparous women, medium (26 mm) for women who have been pregnant, but have not had a vaginal delivery, and large (30 mm) for women who have experienced a vaginal delivery. Due to initial problems with removal the first version of the device was redesigned and a removal strap has been added to the device.

The Caya pessary is a ”single-sized” diaphragm with an anatomical shaped, contoured rim (outer diameter 67 mm x 75 mm) surrounding a silicone membrane that loosely covers the cervix. In the anterior part there is a small cup (“fingertip removal dome”) to help to get a good grip for removal.

Women who choose Caya and FemCap have to search for these products on internet websites. The women have only written instructions when to choose the right size of the device as well as how to insert it.

The recommendations in Sweden have been to use the pessary in conjunction with a spermicide. Contra gel and Caya gel are identical acidic gels based on lactate and cellulose. The mechanism of action of lactate is to maintain low vaginal pH in the presence of relatively alkaline semen. Low vaginal pH has been shown to inactivate sperms. The cellulose component elevates the viscosity of the gel, which creates a matrix that impedes sperm motility (Williams 2007).
The gel is certified for use, and is recommended by the producer, to be used as a contraceptive gel along with the pessary to get contraceptive effectiveness.

7. Objective

The questions at issue:
1) Is there a difference between the new and old types of pessaries in prevention of pregnancy?
2) Is there a difference between acid-buffering gel combined with a pessary and nonoxynol-9 gel combined with a pessary in prevention of pregnancy?
3) Is there a difference between acid-buffering gel combined with a pessary and pessary without any gel in prevention of pregnancy?

PICO (P = Patients, I = Intervention, C = Comparison, O = Outcome variables)

PICO 1	
P	Fertile women who use pessary together with gels for contraception
I	New types of pessary (in Sweden: Femcap, Caya or equivalent products in other countries)
C	Milex or Ortho All-Flex
O	Critical for decision making Pregnancy Important but not critical for decision making Discontinuation (only in RCT) Complications

PICO 2	
P	Fertile women who use pessary for contraception
I	Acid-buffering gel (Lactate and cellulose gel)
C	Nonoxynol-9
O	Critical for decision making Pregnancy Important but not critical for decision making Discontinuation (only in RCT) Complications

PICO 3	
P	Fertile women who use pessary for contraception
I	Acid-buffering gel (Lactate and cellulose gel)
C	No gel
O	Critical for decision making Pregnancy Important but not critical for decision making Discontinuation Complications

8. Methods

Systematic literature search (appendix 1)

During January 2017 two authors (TS, ACE) performed systematic literature searches in PubMed, Embase, the Cochrane Library, and Cinahl. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to all the participants of the project group. All authors read the articles independently of one another and it was finally decided in a consensus meeting which articles should be included in the assessment.

Critical appraisal and certainty of evidence

The included studies, their design and patient characteristics are presented in Appendix 2. The excluded studies and the reasons for exclusion are presented in Appendix 3. The included studies have been critically appraised using a checklist for assessment of randomised clinical trials and cohort studies, modified from SBU by HTA-centrum. The results and the assessed quality of each article have been summarised per outcome in Appendices 4.1-4.3. Data were extracted by at least two authors per outcome. RevMan 5.2 was used to pool data in meta-analyses. A summary result per outcome and the associated certainty of evidence are presented in Summary-of-findings tables (page 7). The certainty of evidence was defined according to the GRADE system (Atkins et al., 2004; GRADE Working Group).

Ongoing research

A search was performed in Clinicaltrials.gov 2017-03-24 using the search terms: ((gel OR contragel OR (caya gel) OR microbicide OR microbicides OR spermicide OR spermicides OR spermicidal OR spermatocide OR spermatocides OR spermatocidal agents OR nonoxynol-9) AND (diaphragm OR diaphragms OR pessary OR pessaries OR cervical cap OR femcap OR caya OR milex OR ortho all-flex)) OR ((diaphragm OR diaphragms OR pessary OR pessaries OR cervical cap OR femcap OR caya OR milex OR ortho all-flex) AND (contraception OR contraceptive)).

A search was performed in WHO International Clinical Trials Registry Platform (ICTRP) 2017-03-24 using the search terms: diaphragm OR diaphragms OR pessary OR pessaries OR (cervical cap) OR femcap OR caya OR milex OR (ortho all-flex) in the Intervention field.

The retrieved registered studies were checked for eligibility and those fulfilling the PICO criteria are presented in the report.

9. Results

Literature search (Appendix 1)

The literature search identified 2,112 articles after removal of duplicates. After reading the abstracts 2,054 articles were excluded. Another 33 articles were excluded by two authors after reading the articles in full text. The remaining 25 articles were sent to all participants of the project group, and five articles were finally included in the assessment (Appendix 2). One of the four RCTs was not possible to retrieve from available databases, but data and quality assessment could be retrieved from a Cochrane review (Gallo et al, 2002). Another RCT included a second part, which was handled as a separate cohort study. One additional cohort study was included in the assessment.

New compared with old types of pessaries (PICO I)

Critical outcome for decision-making

Pregnancy (Appendix 4.1)

Two RCTs and one cohort study had pregnancy rate as the primary outcome variable. The RCTs were Bernstein et al. (1986), a superiority study (data extracted from Gallo et al., 2002), and Mauck et al. (1999), a non-inferiority study. The former study compared the Prentif Cap pessary, which has a design that is very similar to the new FemCap pessary but is no longer available, with the Ortho All Flex pessary. The Mauck study compared the new pessary FemCap with the Ortho All Flex. Nonoxynol-9 gel was used in both studies. The trials had severe study limitations due to high withdrawal rates after randomisation. Furthermore, the randomisation procedure was not clearly presented in one of them. The cohort study by Schwartz et al. published in 2015 compared the new pessary single-size Caya with the Ortho All-flex.

The Bernstein RCT reported no difference in the cumulative pregnancy rates between the two devices. In the Mauck study the adjusted risk (the point estimate) of pregnancy among FemCap users was 1.96 times higher that among Ortho All-Flex users, and non-inferiority could not be shown. The cohort study found no significant difference in the 6-month pregnancy rate between the single-size Caya (11.3%) and the Ortho All Flex diaphragm (10.7%).

Conclusion: There may be little or no difference in pregnancy rate when new types of pessaries are compared with old types. Low certainty of evidence (GRADE ⊕⊕◯◯).

Important outcome for decision-making

Discontinuation (Appendix 4.2)

Only the RCT by Mauck et al. reported on discontinuation. It had serious study limitations with a high withdrawal rate after the randomisation. One reason was device fitting problems. More women reported problems with the FemCap compared with the Ortho All-Flex pessary with regard to inability to fit the device (FemCap 4.7% vs. Ortho All-Flex 0.5%, $p<0.001$) as well as inability to insert or remove it (FemCap 10.4% vs. Ortho All-Flex 0.7%, $p<0.001$).
Conclusion: The discontinuation rate may be higher with new compared with old types of pessaries. Low certainty of evidence (GRADE ⊕⊕◯◯).

Complications (Appendix 4.3)

Two RCTs and one cohort study reported complications. User discomfort and urinary tract infection were less frequently reported among users of the “new” types of pessaries.
Conclusion: It is uncertain whether the frequency of complications is different with new pessaries compared with old types. Very low certainty of evidence (GRADE⊕◯◯◯).

Acid buffering gel compared with nonoxynol-9 gel (PICO 2)

Critical outcome for decision-making

Pregnancy (Appendix 4.1)

Two RCTs had pregnancy rate as the primary outcome variable. One of them had a non-inferiority design. Both studies had some study limitations with withdrawals before as well as after randomisation, and some problems with regard to directness. The non-inferiority trial did demonstrate that the acid-buffering gel was not less effective in preventing pregnancies. The other trial reported similar pregnancy rates and provided no statistical analysis.

Conclusion: There is probably little or no difference in pregnancy rate between acid buffering gel used with a pessary and nonoxynol-9 gel used with a pessary.

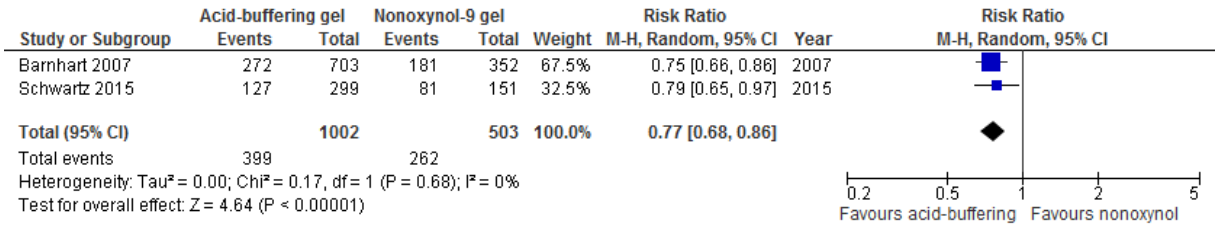
Moderate certainty of evidence (GRADE ⊕⊕⊕◯).

Important outcomes for decision-making

Discontinuation (Appendix 4.2, Figure 1)

Two RCTs reported on discontinuation. Both studies had some study limitations (see above). The discontinuation rate with the acid-buffering gel was lower for acid-buffering compared to nonoxynol-9 gel in both studies (when pregnancy and lost to follow-up were excluded). The rate of discontinuation varied from 39% to 51% and from 43% to 54% for acid-buffering gel and nonoxynol-9 gel, respectively, in the two trials. A summary estimate in a meta-analysis demonstrated a significant difference between the gels with a relative risk of 0.77 (95% confidence interval 0.68; 0.97), Figure 1.

Figure 1.
Meta-analysis comparing acid-buffering gel with nonoxynol-9 gel.
Outcome: Discontinuation (excluding patients with pregnancy and lost to follow-up).



Conclusion: The discontinuation rate is probably lower when acid buffering gel is used compared with nonoxynol-9. Moderate certainty of evidence (GRADE⊕⊕⊕◯).

Complications (Appendix 4.3)

Two RCTs reported complications. User discomfort was common for both gels. Symptomatic urinary tract infections were less frequent among users of the acid-buffering gel compared with the nonoxynol-9 gel ($p<0.01$).

Conclusion: There is probably little or no difference in user discomfort between the two gels. Urinary tract infection are probably less frequent among users of the acid-buffering gel compared with the nonoxynol-9 gel. Moderate certainty of evidence (GRADE⊕⊕⊕◯).

Acid buffering gel compared with no gel (PICO 3)

No study that compared efficacy and safety between acid-buffering gel and no gel was found in the literature search.

10. Ethical issues (Appendix 5)

There is only one subsidised pessary and the availability differs across the country. The other two pessaries on the market are available only through the internet and the patients have to purchase them without any professional guidance. There is also a difference in cost between the currently available pessaries, which might have an impact on women's possibility to choose between similar products. If different types of pessaries are not subsidised similarly the recommendations by healthcare professionals may be affected by lack of knowledge of new products that are sold only via the internet.
It is an ethical issue whether pessaries should be subsidised at all, given the poor contraceptive effect compared with other types, mainly hormonal contraceptives. However, that is beyond the scope of this report.

11. Organisational aspects

Present use of pessaries in Region Västra Götaland

The Milex diaphragm is prescribed by gynaecologists and by midwifes at midwife centres and some of the Youth clinics in VGR. The Caya and Femcap are sold through the internet.

Consequences of introduction of the "new" type of pessaries for personnel

If Caya and FemCap were to be subsidised by VGR and made available as a contraceptive free of charge, midwifes have to be trained how to insert, and to teach the woman how to insert and remove the pessary. This will require further education and training of personnel.

Consequences for other clinics or supporting functions in the Region Västra Götaland

The present capacity in Midwife centres is currently sufficient to handle all women who want to try out a pessary. There will be no consequences for other clinics.

12. Economic aspects

Present costs

During 2016, 49 Milex pessaries were prescribed at the midwife centres and youth clinics in VGR. It is currently subsidised in VGR and the cost per pessary is 344 SEK. A gel is also recommended, but it is not subsidised. The cost of a 30 minute visit to a midwife is 274 SEK. Hence, the total cost per Milex is 618 SEK and the total cost for the 49 Milex pessaries that were prescribed was 30,300 SEK.

Expected costs of the new types of pessaries

The expected cost for VGR for the new alternatives, Femcap and Caya, is the cost of the product and the cost of two 30 minutes visits to a midwife. The cost of Femcap is 799 SEK and the cost of Caya is 449 SEK. Hence, the total cost per sold Femcap would be 1,350 SEK and the total cost per sold Caya would be 1,000 SEK. If the 49 Milex that were sold during 2016 would be replaced by Femcap, the total cost would be approximately 66,000 SEK and 49,000 SEK if Milex were replaced by Caya.

Further, a set with samples of pessaries in different sizes would have to be purchased by each clinic that would prescribe to product for a cost of 375 SEK. For the 123 clinics in VGR, the total cost would be 18,700 SEK.

The cost of abortion of unwanted pregnancies is not included in the economic aspects since there was no difference in the pregnancy rate.

Possibility to prescribe the new types of pessaries within the present budget

The extra costs can be handled within the present budget.

Available economic evaluations or cost advantages/disadvantages

There are no available economic evaluations on the topic.

13. Discussion

This HTA analysis was performed to compare and assess the efficacy and safety of previously conventional barrier contraceptive methods (the old types of pessaries) and nonoxynol-9 gel with pessaries with an altered design (the new types of pessaries) and a new acid-buffering gel.

The pregnancy rates were relatively high with about 10% to 15% of the pessary-users that conceived during 6 months follow-up. In our analysis the new types of barrier contraceptive methods were not found to be better than the old types with regard to contraception. The discontinuation rate was higher for the recently introduced pessaries. Furthermore, we found that there is probably no difference in pregnancy rate between acid buffering gel and nonoxynol-9 gel. However a meta-analysis showed that women who used the acid-buffering gel had lower discontinuation rates.

There was a limited number of studies. Only four studies, two that compared new with old types of pessaries and two that compared acid buffering-gel with nonoxynol-9, were identified in the systematic literature search. This low number of performed and published studies may be explained by difficulties to recruit a sufficient number of individuals to these kind of studies, since participating women will be exposed to a risk of unwanted pregnancy.

A problem with the included studies was their high withdrawal and discontinuation rates. The latter was due to difficulties in inserting and removing the pessary as well as with their dislodgement. This was mostly noted among Caya and FemCap users (both for strapped and unstrapped pessaries) and could be explained by variations in the anatomy of the cervix and vagina among women. A trained provider who initially could have assessed the fitness of the pessary for each woman might have increased the compliance and safety of these two methods of barrier contraception.

The literature search did not identify any study that compared the efficacy and safety between acid-buffering gel and no gel. In the excluded Schwartz study (2008) the measured outcome was not in accordance with the PICO (number of progressive sperm in the postcoital test, comparing SILCS (Caya) with and without nonoxynol-9). The study demonstrated that the presence of the nonoxynol-9 gel reduced the average number of progressively motile sperm, suggesting an increased contraceptive effect of the acid-buffering gel.

14. Future perspective

Scientific knowledge gaps

The contraceptive effect of the new pessaries needs to be further studied.

Ongoing research

The search in clinicaltrials.gov 2017-03-24 identified 88 trials. Two of them are relevant for the question at issue. One is an RCT, with a passed completion date and the other one is a prospective case series with unclear completion date.

The search in WHO International Clinical Trials Registry Platform (ICTRP) identified 269 trials. No relevant trials that were not duplicates with clinicaltrials.gov were identified.

NCT nr	Country	Study design	Number of subjects (n)	Intervention	Outcome variables	Planned completion date
NCT 02309554	USA Dominican republic	RCT	27	The SILCS Diaphragm Used With 3% N-9 Gel, ContraGel®, or No Gel	Primary: Sperm mobility Secondary: Emergent adverse experiences among female participants and among male partners	March 2016
NCT 00397670	No information	Single Group	200	Open Label Study of the Safety and Contraceptive Efficacy of BufferGel® With Diaphragm	Contraceptive efficacy (pregnancy rate) at six months (183 days).	No information

15. Participants in the project

The question was nominated by
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Declaration of interest
None of the authors has any conflict of interest to declare.

Project time
HTA was accomplished during the period of 2016-12-12 – 2017-05-31.
Literature searches were made in March 2017.

The question at issue:
1) Is there a difference between the new and old types of pessaries in prevention of pregnancy?
2) Is there a difference between acid-buffering gel combined with a pessary and nonoxynol-9 gel combined with a pessary in prevention of pregnancy?
3) Is there a difference between acid-buffering gel combined with a pessary and pessary without any gel in prevention of pregnancy?

PICO (P = Patients, I = Intervention, C = Comparison, O = Outcome variables)

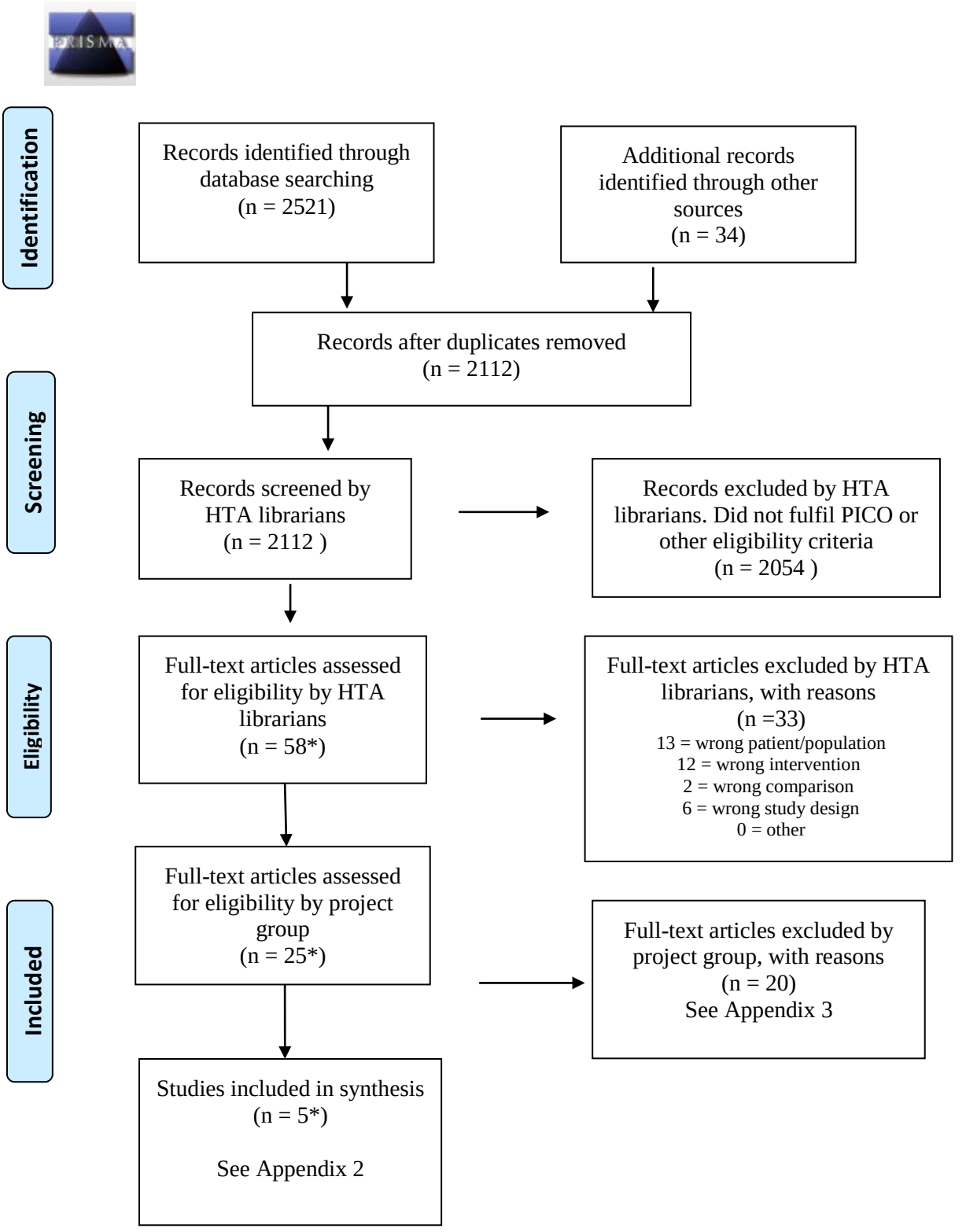
PICO 1	
P	Fertile women who use pessary together with gels for contraception
I	New types of pessary (in Sweden: Femcap, Caya or equivalent products in other countries)
C	Milex or Ortho All-Flex
O	Critical for decision making Pregnancy Important but not critical for decision making Discontinuation (only in RCT) Complications

PICO 2	
P	Fertile women who use pessary for contraception
I	Acid buffering gel (Lactate- and cellulose gel)
C	Nonoxynol-9
O	Critical for decision Pregnancy Important but not critical for decision making Discontinuation (only in RCT) Complications

PICO 3	
P	Fertile women who use pessary for contraception
I	No gel
C	Acid buffering gel (Lactate- and cellulose gel)
O	Critical for decision making Pregnancy Important but not critical for decision making Discontinuation Complications

Study design:
Systematic reviews
Randomised controlled trials
Non-randomised controlled studies
Case-series ≥ 200
Publication year: -
Language: English, Swedish, Norwegian, Danish, Finnish, German and French

Selection process – flow diagram



* This includes the reference by Bernstein, 1986. The original article has not been identified but data from Gallo, 2002, has been used in the analysis.

Search strategies

Database: PubMed
Date: 2017-01-10
No of results: 674

Search	Query	Items found
#10	**Search #6 NOT #9**	**674**
#9	Search #7 OR #8	5789799
#8	Search ((animals[mh]) NOT (animals[mh] AND humans[mh]))	4311890
#7	Search Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp]	1537503
#6	Search #4 OR #5	688
#5	Search femcap[tiab] OR caya[tiab] OR milex[tiab] OR ortho all-flex[tiab]	47
#4	Search #1 AND #2 AND #3	656
#3	Search gel[tiab] OR microbicide[tiab] OR microbicides[tiab] OR spermicide[tiab] OR spermicides[tiab] OR spermicidal[tiab] OR spermatocide[tiab] OR spermatocides[tiab] OR spermatocidal agents[tiab] OR nonoxynol-9 OR "Spermatocidal Agents"[Pharmacological Action] OR "Spermatocidal Agents"[Mesh]	265120
#2	Search "Contraception"[Mesh] OR contraception[tiab] OR contraceptive[tiab]	64783
#1	Search ((("Contraceptive Devices, Female"[Mesh] OR diaphragm[tiab] OR diaphragms[tiab] OR pessary[tiab] OR pessaries[tiab] OR cervical cap[tiab] OR femcap[tiab] OR caya[tiab] OR milex[tiab] OR ortho all-flex[tiab]	39361

Database: Embase 1974 to 2017 January 09 (OvidSP)
Date: 2017-01-10
No of results: 1570

#	Searches	Results
1	**exp uterine cervix cap/**	**342**
2	female contraceptive device/ or vagina pessary/	3101
3	contraceptive device/ or female contraceptive device/	2332
4	(diaphragm or diaphragms or pessary or pessaries or cervical cap or femcap or caya or milex or ortho all-flex).ab,dv,ti.	32685
5	1 or 2 or 3 or 4	35644
6	exp contraception/	150517
7	(contraception or contraceptive).ab,ti.	56723
8	6 or 7	173150
9	exp spermicidal agent/ or exp nonoxinol 9/ or exp contraceptive agent/ or exp microbicide/	150430
10	(gel or microbicide or microbicides or spermicide or spermicides or spermicidal or spermatocide or spermatocides or spermatocidal agents or nonoxynol-9).ab,ti,tn.	287011
11	9 or 10	432739
12	5 and 8 and 11	1723
13	(caya or femcap or milex or ortho all-flex).ab,dv,ti.	108
14	12 or 13	1800
15	(animal not (animal and human)).sh.	1326543
16	14 not 15	1799
17	limit 16 to (article or conference paper or note or "review")	1570

Database: The Cochrane Library
Date: 2017-01-10
No of results: 79
Cochrane reviews 5
Other reviews 1
Trials 73
Technology assessments -
Economic evaluations -

ID	Search	Hits
#1	MeSH descriptor: [Contraceptive Devices, Female] explode all trees	796
#2	diaphragm or diaphragms or pessary or pessaries or cervical cap or femcap or caya or milex or ortho all-flex:ti,ab,kw (Word variations have been searched)	1198
#3	#1 or #2	1929
#4	MeSH descriptor: [Contraception] explode all trees	388
#5	contraception or contraceptive:ti,ab,kw (Word variations have been searched)	4829
#6	#4 or #5	4868
#7	MeSH descriptor: [Spermatocidal Agents] explode all trees	96
#8	gel or microbicide or microbicides or spermicide or spermicides or spermicidal or spermatocide or spermatocides or spermatocidal agents or nonoxynol-9:ti,ab,kw (Word variations have been searched)	7676
#9	#7 or #8	7676
#10	**#3 and #6 and #9**	**79**

Database: CINAHL (EBSCO)
Date: 207-01-10
No of results: 198

#	Query	Results
S7	**S3 AND S6**	**198**
S6	S4 OR S5	10,213
S5	TI (contraception OR contraceptive) OR AB (contraception OR contraceptive)	7,886
S4	(MH "Contraception")	5,101
S3	S1 OR S2	1,388
S2	TI (diaphragm OR diaphragms OR pessary OR pessaries OR cervical cap OR femcap OR caya OR milex OR ortho all-flex) OR AB (diaphragm OR diaphragms OR pessary OR pessaries OR cervical cap OR femcap OR caya OR milex OR ortho all-flex)	1,246
S1	(MH "Diaphragms, Contraceptive") OR (MH "Cervical Caps")	207

Reference lists
A comprehensive review of reference lists brought 34 new records

Reference lists

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Project: New versus Old Types of Pessaries and Gels as Contraceptives for Women
Appendix 2. Characteristics of included studies

Author, Year, Country	Study Design	Study duration	Length of follow-up	Study Groups; Intervention vs control	Diaphragm type	Patients (n)	Mean Age (years)	Outcome variables
Barnhart, 2007 USA	RCT PICO 2	2001-2004	6 months	Lactate gel vs Nonoxynol-9	Ortho All-Flex	1055	28	Pregnancy Compliance Complications
Bernstein, 1986 USA (based on data from Gallo 2002)	RCT PICO 1	Not reported	6-24	Prentif cavity rim cervical cap (I) vs Ortho diaphragm (C)	Prentif cavity rim cervical cap, Ortho diaphragm	1529	Not reported Inclusion age18-40	Pregnancy Compliance Complications
Mauck , 1999, USA	RCT PICO 1	1995-1999	6 months	FemCap (I) vs Ortho All-Flex (C), (+nonxynol-9)	Fem cap, Ortho All-Flex	755	29	Pregnancy Complications
Mauck, 2006, USA	Two case series (from a cohort study)	Not reported	8 weeks	Strapped-FemCap vs Unstrapped-FemCap.	FemCap	539	29	Complications Compliance
Schwartz, 2015 Part 1, USA	RCT PICO 2	2008-2009	190 days and 6 menstrual cycles	Acid-buffering gel vs. nonoxynol-9	Caya	421	29	Pregnancy
Schwartz, 2015 Part 2, USA	Cohort PICO 1	Not reported	Not reported	Caya vs Ortho diaphragm	Caya	1529+421	Not reported	Pregnancy

Project: New versus Old Types of Pessaries and Gels as Contraceptives for Women

Appendix 3. Excluded articles

Study author, publication year	Reason for exclusion
Bounds, 1995	Wrong comparison (Nonoxynol-9 vs no gel)
Cagen, 1986	Case series (n 620) using Prentif Cavity-Rim Cervical Cap not available today
Coffey, 2008	No outcome data according to PICO (Only acceptability)) Ortho All Flex vs SILCS diaphragm (Caya)
Eliot, 1985	No extractable data on pregnancy and compliance (Vimule cap –Cavity Rim cap)
Johnson, 1984	Case series n<200 using an old type of cervical cap (Prentif®) not available today
Gallo, 2012	Systematic review including 2 RCTs,already included as original articles
Gollub, 1989	Secondary re-analysis of Bernstein 1986
Kaufman, 1960	Case series n<200 using diaphragms of different brands with Lanesta Gel
Koch, 1982	Case series (n 413) using Prentif Cavity-Rim Cervical Cap not available today
Lauersen, 1986	Case series (n 217) using Prentif Cavity-Rim Cervical cap not available today
Lehfeldt, 1984	Case series n<200 using Prentif cervical cap with Delfen spermicidal cream/Ramses Jelly (N-9,5%)
Lepine, 2015	Cost-effectiveness study using a mathematical model. No data available.
Mauck, 1996	Wrong comparison (Nonoxynol-9 vs no gel) Lea's shield
Powell, 1986	Case series (n 617) using Prentif Cavity-Rim Cervical Cap and Vimule caps (15) not available today
Richwald, 1989	Case series (n 3433) using Prentif Cavity-RimCervical cap not available today
Shihata, 1992	Case series n<200 (106 women using FemCap assessing acceptability)
Shihata, 1991	Case series n<200 (106 women using **FemCap** + nonoxynol 3%)
Schwartz, 2008	No outcome data according to PICO (Postcoital test, comparing SILCS (Caya) with and without nonoxynol-9
Trussel, 1993	Re-analysis of two clinical studies
Williams, 2007	Wrong population (not using diaphragm as contraception).Phase I safety trial on different microbicide gels.

Project: New versus Old Types of Pessaries and Gels as Contraceptives for Women
Appendix 4.1
Outcome variable: Pregnancy rate

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients (n)	Lost to follow-up (n)	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention (I)	Control (C)				
PICO 1 **New vs old types of pessary**				**New type of pessary**	**Old type of pessary**				
Bernstein, 1986, USA	RCT superiority	1529	305	<u>Prentif Cap</u> 87/581 (15.0 %) OR=1.24 (95% CI 0.89;1.74)	71/572 (12.4 %)	Prentif Cap not available today	-	-	?
Mauck, 1999, USA	RCT non-inferiority	I=419 C=422	I=13 C=17	<u>FemCap</u> <u>CPP:</u> TU: 13.5% aRR 1.96 (above non-inferiority limit <1.73) PU: 11.1% (above non-inferiority limit)	<u>Ortho All flex diaphragm</u> <u>CPP:</u> TU: 7.9% PU:7.4%		?	-	?
Schwartz, 2015, USA	Cohort	I=450 C=1055	I=19 C=198	<u>Single size Caya</u> <u>6m CPP:</u> TU:11.3% Δ 0.7 (95% CI -3.6; 4.9)	<u>Ortho All flex diaphragm</u> <u>6m CPP:</u> TU:10.7%	Control group was historical controls derived from one of the treatment groups in the study of Barnhart 2007	+	?	+

CPP=cumulative pregnancy probability, ns=not significant, ITT=intent to treat, MITT =modified intent to treat, PP = Per protocol, TU= typical use, PU =perfect use, aRR=adjusted risk ratio, Δ=difference

Project: New versus Old Types of Pessaries and Gels as Contraceptives for Women
Appendix 4.1
Outcome variable: Pregnancy rate

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients (n)	Lost to follow-up (n)	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention (I)	Control (C)				
PICO 2 **Acid-buffering vs Nonoxynol-9 gel**				**Acid-buffering gel**	**Nonoxynol-9 gel**				
Barnhart, 2007, USA	RCT non-inferiority	N=1055 I=621 C1=300	I=125 C1=73	<u>6 m CPP:</u> ITT 10.3% Δ-0.7 (95% CI-0.5;3.8) PP 10.1% Δ-2.2 (95% CI-7.7;3.3) PU 4.7% Δ-1.4% (-8.4;5.6)	<u>6 m CPP:</u> ITT 11.0% PP 12.3% PU 6.1% (within stated non-inferiority limits)	Per protocol (MITT) is defined as: "randomly assigned subjects with at least one act of coitus while using the assigned study product and for whom there was at least one report of pregnancy status. PU is described as correct and consistent use	+	+	+
Schwartz, 2015 USA	RCT	I=299 C1=151	I=11 C1=8	<u>6m CPP:</u> TU: 9.6% (5.5;13.6) <u>6 cycles CPP:</u> TU: 10.9% (5.3;16.5) PU: 4.4% (0;10.0)	<u>6 m CPP:</u> TU: 12.5% (5.4;19.5) <u>6 cycles CPP:</u> TU: 14.0% (2.5;25.1) PU: 14.9% (0.2;29.7)		?	+	+

CPP=cumulative pregnancy probability, ns=not significant, ITT=intent to treat, MITT =modified intent to treat, PP = Per protocol, TU= typical use, PU =perfect use, Δ=difference

Project: New versus Old Types of Pessaries and Gels as Contraceptives for Women
Appendix 4.2
Outcome variable: Discontinuation rate

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients (n)	Lost to follow-up (n)	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention (I)	Control (C)				
PICO 1 **New vs old types of pessary**				**FemCap**	**Ortho All-Flex**				
Mauck, 1999 USA	RCT	I=419 C1=422	I=13 C1=17	156/419* (37.0%) Reasons for discontinuation: Inability to fit device 20/419* (4.7%) Inability to insert/remove 44/419* (10.4%) Non-safety device related 17/419* (4.0%) Non-safety not related 27/419* (6.4%) Protocol violation 29/419* (6.6%)	85/422* (20.8%) Reasons for discontinuation: 2/422* (0.5%) 3/422* (0.7%) 6/422* (1.5%) 26/422* (6.4%) 25/422* (6.1%)	Discontinuation excluding pregnancy and lost to FU *manual calculation from Fig 2	?	-	?
PICO 2 **Acid-buffering vs Nonoxynol-9 gel**				**Acid-buffering gel**	**Nonoxynol-9 gel**				
Barnhart, 2007 USA	RCT	N=1055 I=621 C1=300	I=125 C1=73	272/703* (38.7%)	181/352* (51.4%)	Discontinuation excluding pregnancy and lost to FU *manual calculation from Fig 1	+	+	+
Schwartz, 2015 USA	RCT	I=299 C1=151	I=11 C1=8	127/299* (42.5%)	81/151* (53.6%)	Discontinuation excluding pregnancy and lost to FU *manual calculation from Fig 2	?	+	+

FU=Follow-up, ns = not significant

2017-06-09

Project: New versus Old Types of Pessaries and Gels as Contraceptives for Women
Appendix 4.3
Outcome variable: Complications.

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients (n)	Lost to follow-up (n)	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention (I)	Control (C)				
PICO 1 **New vs old types of pessary**				**New types of pessary**	**Old types of pessary**				
Bernstein 1986 USA Data extracted from and MF Gallo 2002	RCT superiority	1529	305	Prentif Cap Overall: Not reported User discomfort 5/604 (0.8%) OR 0.31; 95% CI 0.14;0.71 P=0.0057 UTI 14.8	Ortho All-Flex diaphragm Overall: Not reported User discomfort 18/597 (3%) UTI 16.5 Ratio 0.9*	Prentif Cavity Rim Cervical Cap is not available today. User discomfort includes vaginal ulcerations or lacerations. *UTI total episodes per 100women/year not available data to be tested for significance	-	-	?
Mauck 1999 USA	RCT non-inferiority	I=419 C=422	I=13 C=17	FemCap Overall: Not calculable User discomfort 46/350(13.1%) Partner discomfort 25/350 (7.1%) Blood found in the device 31/346 (9.0%) UTI 26/346 (7.5%) p = 0.028	Ortho All-Flex diaphragm Overall: Not calculable User discomfort 67/398 (16.8%) Partner discomfort 10/398 (2.5%) Blood found in the device 16/396 (4.0%) p = 0.006 UTI 49/396 (12.4%)	User discomfort includes vaginal symptoms, spotting/bleeding, device uncomfortable and coital pain.	?	-	?
Schwartz 2015 USA	Cohort	I=450 C=1055	I=19 C=198	Single size Caya Overall: Not reported Urogenital adverse event Δ -23.6 (95% CI -29.1; -18.1) Product related adverse event Δ -24.0 (95% CI -28.3;-19.6) UTI Δ -6.4 (95% CI -8.9;-4.09)	Ortho All flex diaphragm Overall: Not reported Urogenital adverse event Product related adverse event UTI	Control group was historical controls derived from one of the treatment groups in the study of Barnhart 2007	+	+	+

UTI=urinary tract infection

Project: New versus Old Types of Pessaries and Gels as Contraceptives for Women
Appendix 4.3
Outcome variable: Complications.

* + No or minor problems
? Some problems
- Major problems

Author, year, country	Study design	Number of patients (n)	Lost to follow-up (n)	Results		Comments	* Directness	* Study limitations	* Precision
				Intervention (I)	Control (C)				
Mauck 2006 USA	Case series			Strapped Fem Cap User discomfort 27% Partner discomfort 14%	Unstrapped Fem Cap User discomfort 12% Partner discomfort 4%				
PICO 2 **Acid-buffering vs Nonoxynol-9 gel**				**Acid-buffering gel**	**Nonoxynol-9 gel**				
Barnhart 2007 USA	RCT non-inferiority	N=1055 I=621 C1=300	I=125 C1=73	Overall* N=621 User discomfort 68% Symptomatic UTI 9% p=0.03 Partner discomfort 12%	Overall* N=300 User discomfort 69% Symptomatic UTI 14% Partner discomfort 10%	User discomfort includes, bacterial vaginosis, symptomatic yeast vaginitis and irritation. *Outcome was only expressed as percent	+	+	+
Schwartz 2015 USA	RCT	I=299 C1=151	I=11 C1=8	Overall 185/278 (66.5%) User discomfort 178/278 (64%) Symptomatic UTI 7/278 (2.5%) Not significant between study groups	Overall 92/137 (67.2%) User discomfort 85/137 (62%) Symptomatic UTI 7/137 (5.1%)	User discomfort includes pain, irritation, pruritus, abnormal bleeding and symptomatic vaginal infection (urogenital adverse events).	+	+	+

UTI=urinary tract infection

Project: Efficacy and Safety of Barrier Contraceptives for Women
Appendix 5. Ethical aspects.

The effect of the intervention on health	
Q1: Health: How does the intervention affect patients' health in terms of quality of life and life-length (including adverse effects)?	Quality of life has not been studied.
Q2: Knowledge gaps: If there is lack of scientific evidence for the effect of the intervention, are there ethical and/or methodological problems with future research in order to strengthen this evidence.	Yes, there are knowledge gaps, particularly regarding the efficacy of the new types of pessary. There was only one RCT on a pessary that is available today. The study was old (1999), had major study limitations and did not demonstrate non-inferiority for the new type of pessary studied.
Q3: Degree of severity: What degree of severity has the condition the intervention is supposed to treat?	The degree of severity of an unplanned pregnancy may differ widely between individuals.
Q4: Third parties: How does the intervention affect the health of third parties	Partner health is not affected although partner discomfort was reported in comparisons of both pessaries and gel. Partner discomfort was reported more often among users of FemCap compared with Ortho All-Flex, while the rates were similar in comparison of gels.
Summary: How is the benefit/risk – ratio for the intervention (given the answers of Q1-Q4)?	The benefit/risk ratio for the new types of pessary seem to be negative, considering contraceptive effect, user and partner discomfort.
The compatibility of the intervention with ethical values	
Q5: Equality and justice: Is there a risk that access to the intervention violates the Human Dignity principle or the Swedish Discrimination Act?	No
Q6: Autonomy: Can the intervention affect patients' and others' participation in decisions and their ability to make informed and relevant decisions about the intervention?	No
Q7: Privacy: How does the intervention affect patient's and others' physical and personal privacy?	Awareness about the differences between the contraceptive methods and their efficacy will increase the women's choices and might decrease the number of unwanted pregnancies. The positive effect may be that the women will be aware of the differences between the methods and the contraceptive efficacy and this may secondarily positively affect the relationship towards the partner.
Q8: Cost effectiveness: Is the balance between the cost and effects of the intervention reasonable?	The difference in the price between the currently available pessaries might have an impact on women's possibility to choose between similar products. If different types of pessaries are not subsidised similarly the recommendations by healthcare professionals may be affected by lack of knowledge of new products that only are sold via the internet. If Caya and FemCap were to be subsidised by VGR and available as a contraceptive method free of charge, the midwifes should receive training in how

	to choose the right size, insert and remove the pessary as well as teach the woman how to insert and remove it.
Summary: Is the use of the intervention compatible with ethical values (given the answers of Q5-Q8)?	Yes
Structural factors that can affect the use and consequences of the intervention	
Q9: Resources and organization: Are there resource- or organizational limitations that can affect who will get access to the intervention or that can lead to less access to other care if the intervention is used?	The Milex pessary is prescribed by gynaecologists and midwifes at midwife centres and some of the Youth clinics in the Region Västra Götaland. The Caya and Femcap are sold via the internet.
Q11: Stake holder interests: Are there stake holder interests that can influence the use of the intervention and thereby lead to unequal access?	Maybe when new products are sold via the internet.
Summary: Are there reason to believe that an equal access to the intervention (or other care interventions) can be affected (given the answers to Q9-Q11)?	Yes
Long-term ethical consequences	
Q12: Long-term consequences: Can the use of the intervention result in more long-term consequences?	No
Overall summary	
How can the ethical aspects regarding the intervention be summarised? Does this summary indicate that the intervention should be modified or that there should be special requirements associated with offering the intervention?	There are no major ethical aspects regarding the use of new versus old types of pessaries and gels. However, the products are available through different sources and the present subsidy includes only the old type of pessary.

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA

HTA

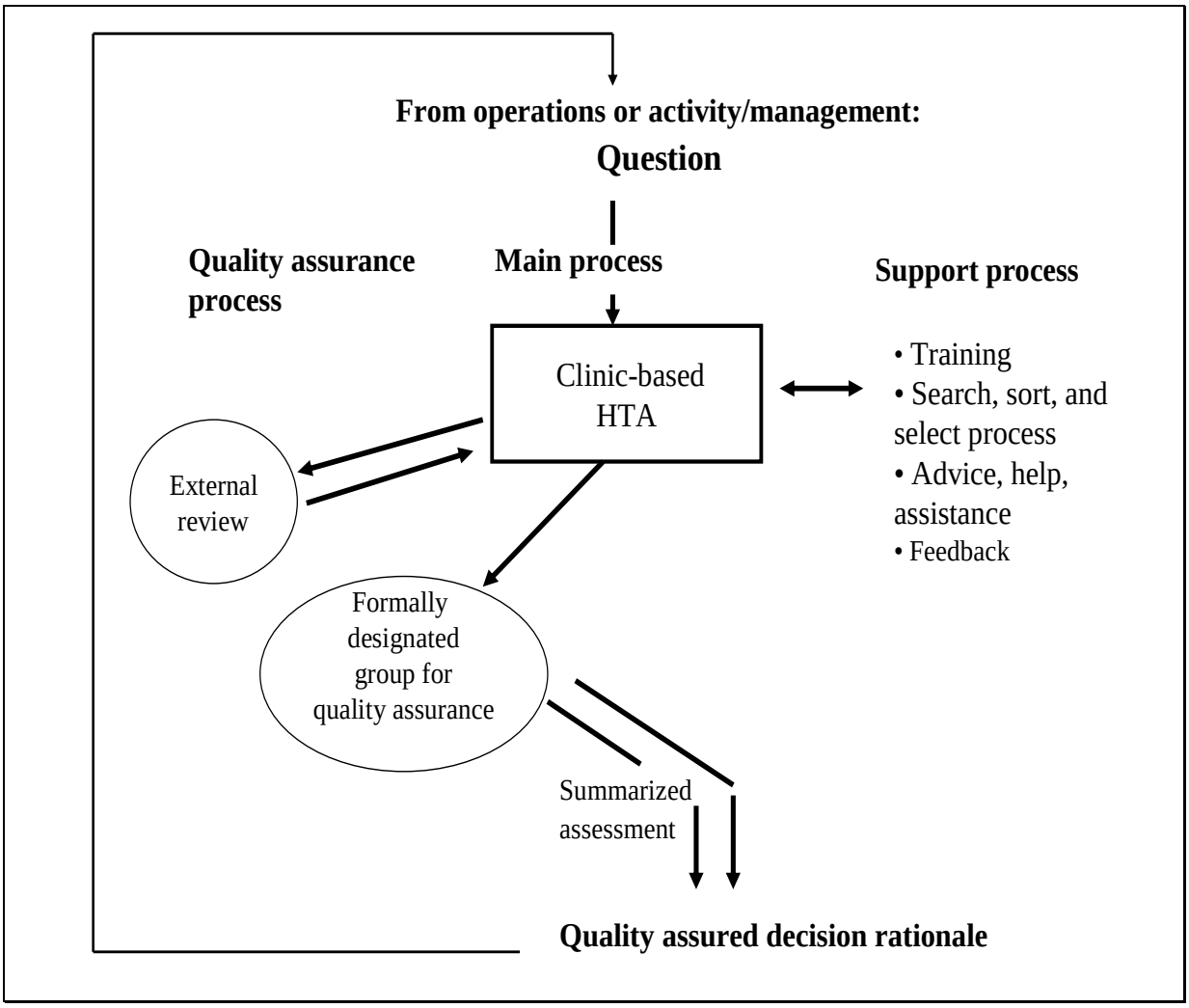
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕O)
Low quality of evidence	= (GRADE ⊕⊕OO)
Very low quality of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

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