AANPAK VAN VAGINALE KLACHTEN: DE PLAATS VAN LASERAPPLICATIE VERGELEKEN MET MEER KLASSIEKE BEHANDELINGEN

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Vulvovaginale atrofie (VVA) / Genitourinary syndrome of menopause (GSM)

- **>50%** van de postmenopauzale vrouwen

- Veranderingen aan de urogenitale tractus door **hypo-oestrogenisme**

- **Droogte**
- Branderigheid
- Irritatie
- Ongemak / pijn
- Dyspareunie
- Urinaire klachten (stress-incontinentie, urge, dysurie, recidiverende UWI's)

“Meer klassieke” behandelingsopties

- Crèmes en glijmiddelen
- Hormonale therapie (lokaal en systemisch)
  - Oestrogenen
  - SERMs (Ospemifene)
  - DHEAS (Prasterone)
- US Food and Drug Administration (FDA) approved

Hormonale therapie (lokaal >> systemisch)

- >> **Lokaal (low dose) [80-90%] ; werkzaamheid, tolerantie en veiligheid**

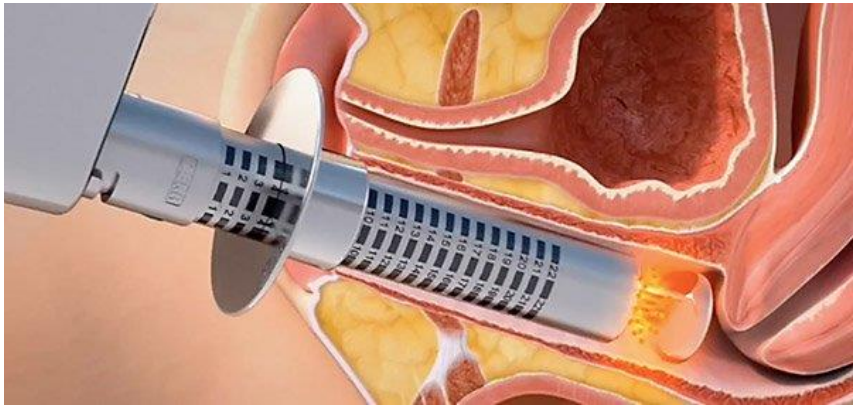
  Oestriol, Estradiol, Estrone,
  geconjugeerde equine oestrogenen

- **Systemisch** (indien geassocieerde climacterische klachten) [75%]

Laserapplicatie voor VVA

Vaginale laserapplicatie

- **Ablatieve CO_2 vs niet-ablatieve Erbium Yag.**
  - Collageen remodeling en neovascularisatie histologisch bewezen voor beide types



- **≥3 applicaties (5-10min) met 4-6 weken interval (ambulant)**

- **Geen analgesie vereist**

“Key Questions” voor klinische implementatie

- **Effectiviteit?**
- **Duurzaamheid?**
- **Veiligheid?**

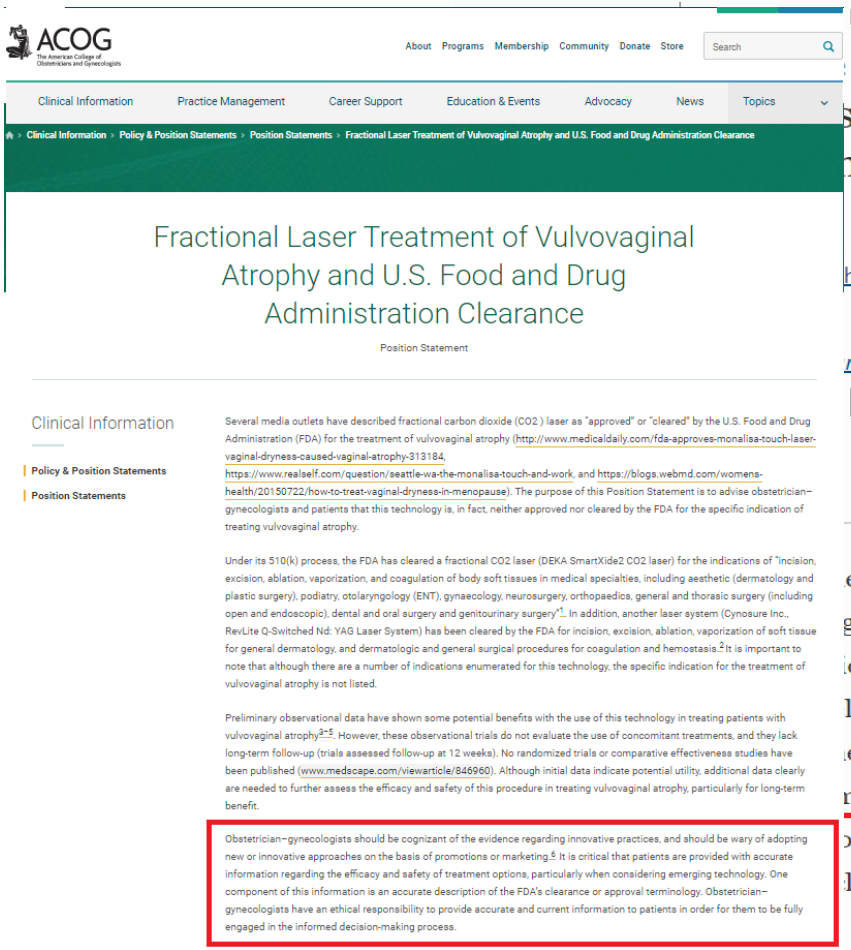
- **Kostprijs?**
- **Specifieke populatie?**

Effectiviteit anno 2018

7 observationele studies (prospectief):

- **Geen bijwerkingen** gerapporteerd
- **Significante afname van de VVA-symptomen** in alle studies tot einde follow-up
- **Significant beter seksueel functioneren**
- **Grote patiënten tevredenheid**: 92% na 6 maanden, sterke afname effect na 18 maanden (Cave spontane vs oncologische menopause!)

(Perino, Calligaro et al. 2015)(Salvatore, Nappi et al. 2014)(Sokol and Karram 2016)(Pitsouni, Grigoriadis et al. 2016)(Pieralli, Bianchi et al. 2017)(Gaspar, Brandi et al. 2017)



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Fractional Laser Treatment of Vulvovaginal Atrophy and U.S. Food and Drug Administration Clearance

Position Statement

Clinical Information

Policy & Position Statements

Position Statements

Several media outlets have described fractional carbon dioxide (CO2) laser as "approved" or "cleared" by the U.S. Food and Drug Administration (FDA) for the treatment of vulvovaginal atrophy (http://www.medicaldaily.com/fda-approves-monalisa-touch-laser-vaginal-dryness-caused-vaginal-atrophy-313184, https://www.realself.com/question/seattle-wa-the-monalisa-touch-and-work, and https://blogs.webmd.com/womens-health/20150722/how-to-treat-vaginal-dryness-in-menopause). The purpose of this Position Statement is to advise obstetrician–gynecologists and patients that this technology is, in fact, neither approved nor cleared by the FDA for the specific indication of treating vulvovaginal atrophy.

Under its 510(k) process, the FDA has cleared a fractional CO2 laser (DEKA SmartXide2 CO2 laser) for the indications of "incision, excision, ablation, vaporization, and coagulation of body soft tissues in medical specialties, including aesthetic (dermatology and plastic surgery), podiatry, otolaryngology (ENT), gynaecology, neurosurgery, orthopaedics, general and thorasic surgery (including open and endoscopic), dental and oral surgery and genitourinary surgery"[1]. In addition, another laser system (Cynosure Inc., RevLite Q-Switched Nd: YAG Laser System) has been cleared by the FDA for incision, excision, ablation, vaporization of soft tissue for general dermatology, and dermatologic and general surgical procedures for coagulation and hemostasis.[2] It is important to note that although there are a number of indications enumerated for this technology, the specific indication for the treatment of vulvovaginal atrophy is not listed.

Preliminary observational data have shown some potential benefits with the use of this technology in treating patients with vulvovaginal atrophy[3–5]. However, these observational trials do not evaluate the use of concomitant treatments, and they lack long-term follow-up (trials assessed follow-up at 12 weeks). No randomized trials or comparative effectiveness studies have been published (www.medscape.com/viewarticle/846960). Although initial data indicate potential utility, additional data clearly are needed to further assess the efficacy and safety of this procedure in treating vulvovaginal atrophy, particularly for long-term benefit.

Obstetrician–gynecologists should be cognizant of the evidence regarding innovative practices, and should be wary of adopting new or innovative approaches on the basis of promotions or marketing.[5] It is critical that patients are provided with accurate information regarding the efficacy and safety of treatment options, particularly when considering emerging technology. One component of this information is an accurate description of the FDA's clearance or approval terminology. Obstetrician–gynecologists have an ethical responsibility to provide accurate and current information to patients in order for them to be fully engaged in the informed decision-making process.

December 2018

Review › Neurourol Urodyn. 2019 Mar;38(3):1009-1023. doi: 10.1002/nau.23931. Epub 2019 Feb 11.

The clinical role of LASER for vulvar and vaginal treatments in gynecology and female urology: An ICS/ISSVD best practice consensus document

Mario Preti [1], Pedro Vieira-Baptista [2,3], Giuseppe Alessandro Digesu [4], Carol Emi Bretschneider [5], Margot Damaser [5,6,7], Oktay Demirkesen [8], Debra S Heller [9], Naside Mangir [10,11], Claudia Marchitelli [12], Sherif Mourad [13], Micheline Moyal-Barracco [14], Sol Peremateu [12], Visha Tailor [4], Tufan Tarcan [15], Elise J B De [16], Colleen K Stockdale [17]

Affiliations + expand

PMID: 30742321 DOI: 10.1002/nau.23931

Erratum in

Corrigendum.
[No authors listed]
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PMID: 32232995 No abstract available.

Abstract

Background: The clinical role of LASER for vulvar and vaginal treatments in gynecology and female urology is controversial.

Aims: In this best practice document, we propose recommendations for the use of LASER for gynecologic and urologic conditions such as vulvovaginal atrophy, urinary incontinence, vulvodynia, and lichen sclerosus based on a thorough literature review.

Materials & methods: This project was developed between January and September 2018. The development of this document followed the ICS White Paper Standard Operating Procedures.

Results: Most of the available studies are limited by their design: for example they lack a control group, patients are not randomized, follow up is short term, series are small, LASER is not compared with standard treatments, and studies are industry sponsored. Due to these limitations, the level of evidence for the use of LASER in the treatment of these conditions remains low and does not allow for definitive recommendations for its use in routine clinical practice. Histological evidence is commonly reported as proof of tissue regeneration following LASER treatment. However, the histological changes noted can also be consistent with reparative changes after a thermal injury rather than necessarily representing regeneration or restoration of function. The use of LASER in women with vulvodynia or lichen sclerosus should not be recommended in routine clinical practice. There is no biological plausibility or safety data on its use on this population of women.

Discussion: The available clinical studies do not present convincing data regarding the efficacy of LASER for the treatment of vaginal atrophy or urinary incontinence. Also, while short-term complications seem to be uncommon, data concerning long-term outcomes are lacking.

Conclusion: At this point, LASER is not recommended for routine treatment of the aforementioned conditions unless part of well-designed clinical trials or with special arrangements for clinical governance, consent, and audit.

Keywords: ICS; ISSVD; LASER; genitourinary syndrome of menopause; lichen sclerosus; urinary incontinence; vaginal laxity; vulvovaginal atrophy.

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Effectiviteit anno 2020

- 16 prospectieve studies (>10 cases)
- 7 retrospectieve studies (>20 cases)
- 4 RCTs
- 1 review & MA

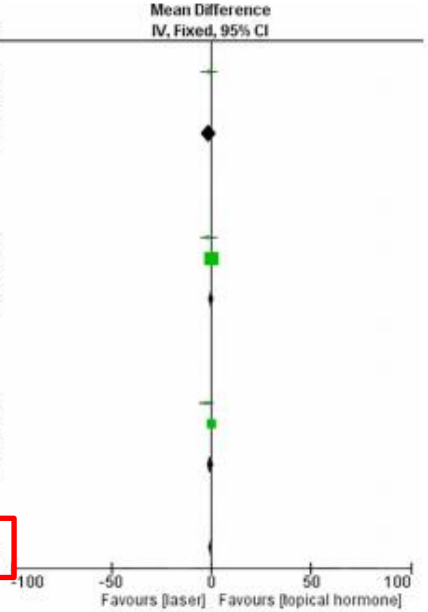
- Data van **2678** deelneemsters

(Li, Picard-Fortin et al. 2020)

Laser vs. “gouden standaard” (Oestrogenen topisch)

Visual Analog Sale score for dyspareunia, vaginal dryness, and vaginal burning. CI = confidence interval; IV = inverse variance; SD = standard deviation.

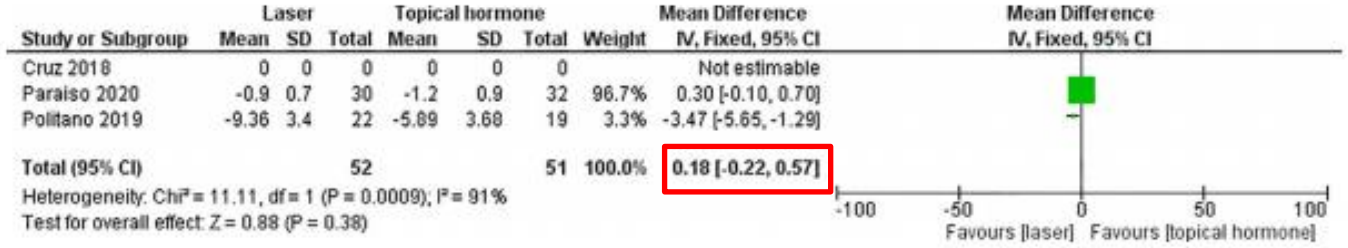
Study or Subgroup	Laser Mean	Laser SD	Laser Total	Topical hormone Mean	Topical hormone SD	Topical hormone Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Dyspareunia								
Cruz 2018	-4.2	5.4644	15	-3	5.6277	15	5.5%	-1.20 [-5.17, 2.77]
Paraiso 2020	0	0	0	0	0	0		Not estimable
Politano 2019	0	0	0	0	0	0		Not estimable
Subtotal (95% CI)			15			15	5.5%	**-1.20 [-5.17, 2.77]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.59 (P = 0.55)								
1.1.2 Vaginal dryness								
Cruz 2018	-6.6	6.1736	15	-5.1	4.7705	15	5.6%	-1.50 [-5.45, 2.45]
Paraiso 2020	-5.48	2.68	30	-5.76	2.48	32	52.5%	0.28 [-1.01, 1.57]
Politano 2019	0	0	0	0	0	0		Not estimable
Subtotal (95% CI)			45			47	58.1%	**0.11 [-1.12, 1.33]**
Heterogeneity: Chi² = 0.71, df = 1 (P = 0.40); I² = 0%								
Test for overall effect: Z = 0.17 (P = 0.86)								
1.1.3 Vaginal burning								
Cruz 2018	-3.4	5.0174	15	-0.8	4.5828	15	7.4%	-2.60 [-6.04, 0.84]
Paraiso 2020	-3.29	3.73	30	-3.49	3.19	32	29.0%	0.20 [-1.53, 1.93]
Politano 2019	0	0	0	0	0	0		Not estimable
Subtotal (95% CI)			45			47	36.4%	**-0.37 [-1.91, 1.18]**
Heterogeneity: Chi² = 2.03, df = 1 (P = 0.15); I² = 51%								
Test for overall effect: Z = 0.46 (P = 0.64)								
Total (95% CI)			105			109	100.0%	**-0.14 [-1.07, 0.80]**
Heterogeneity: Chi² = 3.25, df = 4 (P = 0.52); I² = 0%								
Test for overall effect: Z = 0.29 (P = 0.77)								
Test for subgroup differences: Chi² = 0.52, df = 2 (P = 0.77), I² = 0%								



(Li, Picard-Fortin et al. 2020)

Laser vs. “gouden standaard” (Oestrogenen topisch)

Vaginal Health Index score. CI = confidence interval; IV = inverse variance; SD = standard deviation.

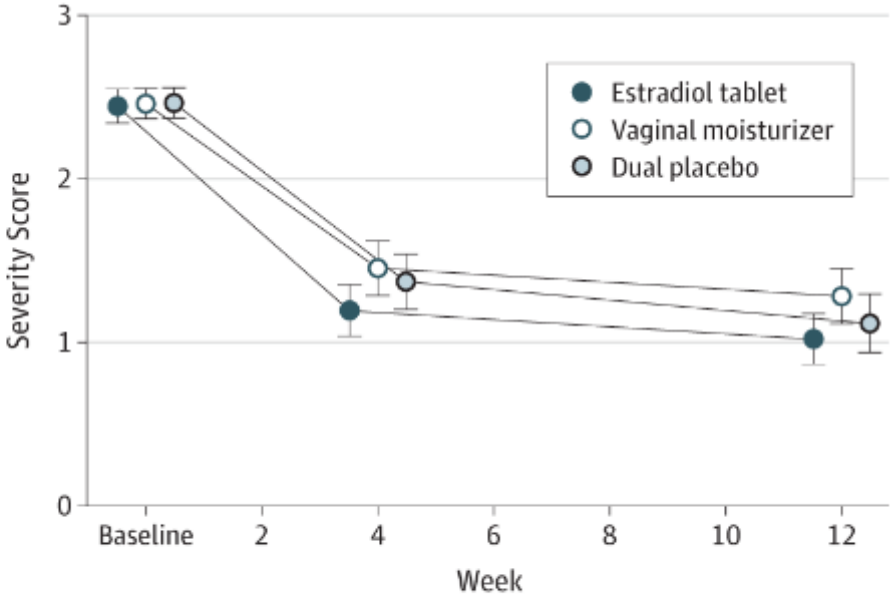


(Li, Picard-Fortin et al. 2020)

Oestrogenen vs. placebo:

No significant difference in the change from baseline in severity scores between treatment groups at 4 or 12 weeks (estradiol vs dual placebo, *P* = .25; moisturizer vs dual placebo, *P* = .31).

(Mitchell, Reed et al. 2018)



No. at risk			
Estradiol tablet	99	97	96
Vaginal moisturizer	100	97	99
Dual placebo	99	97	95

Laser vs. Placebo:

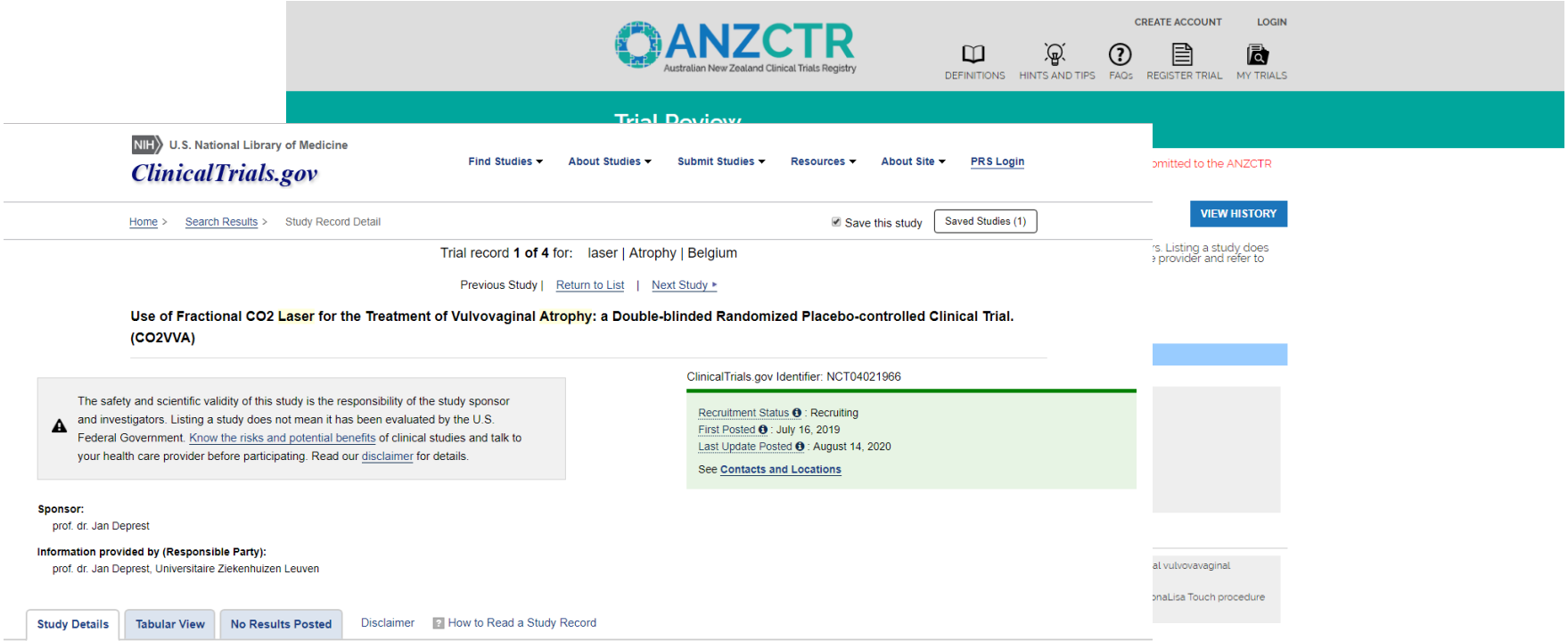
	Laser group ($n = 39$) N (%)	Sham group ($n = 38$) N (%)	P
Very satisfied or satisfied	31 (79.5%)	17 (44.7%)	
Neither satisfied nor dissatisfied or lower	8 (20.5%)	21 (55.3%)	0.002[a]

[a] P value for chi-square test.

(Ruanphoo and Bunyavejchevin 2020)



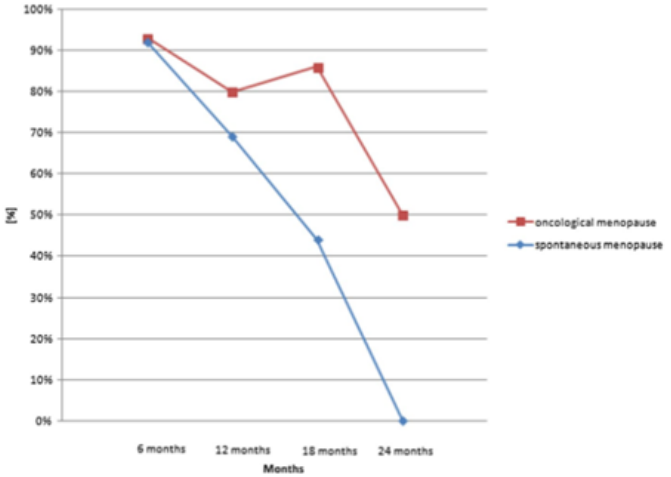
Laser vs. Placebo:



Duurzaamheid

- **Quid onderhoudsbehandeling?**

Fig. 3 Patients' satisfaction rate during follow-up period in two groups: spontaneous and oncological menopause



(Pieralli, Bianchi et al. 2017)

Veiligheid

- **Enkel mineure complicaties**
- **Geen ernstige bijwerkingen**

- **Meest frequente bijwerkingen na applicatie (2%-55%)**
    - Vaginaal bloedverlies, spotting, fluor
    - Vulvovaginale pijn / discomfort
    - Oedeem

(Li, Picard-Fortin et al. 2020)

Veiligheid

- 7 gevallen van ernstige complicaties (case series):

  - Postcoïtale laceratie vaginale wand
  - Toename dyspareunie
  - Toename verlittekening en rigiditeit van de vaginale mucosa

  (Al-Badr and Alkhamis 2019)(Gordon, Gonzales et al. 2019)

“Key Questions” voor klinische implementatie

- **Effectiviteit?**
- **Duurzaamheid?**
- **Veiligheid?**

- **Kostprijs?**
- **Specifieke populatie?**

Besluit:

Laserbehandeling van vaginale atrofie in de menopauze

Veelbelovend,

maar te vroeg voor routinematige implementatie in de klinische praktijk.