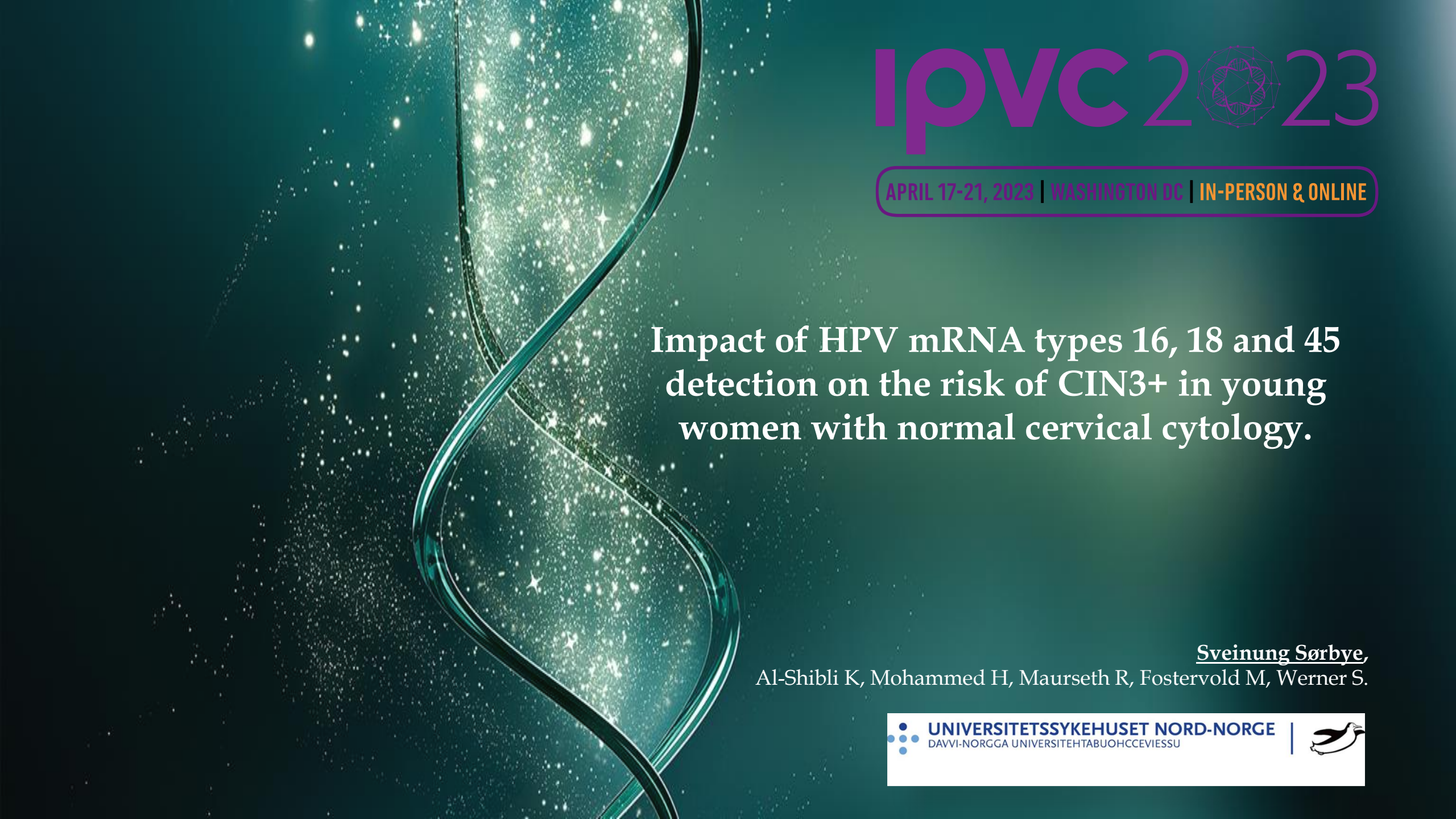

Impact of HPV mRNA types 16, 18 and 45 detection on the risk of CIN3+ in young women with normal cervical cytology.

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Disclosures

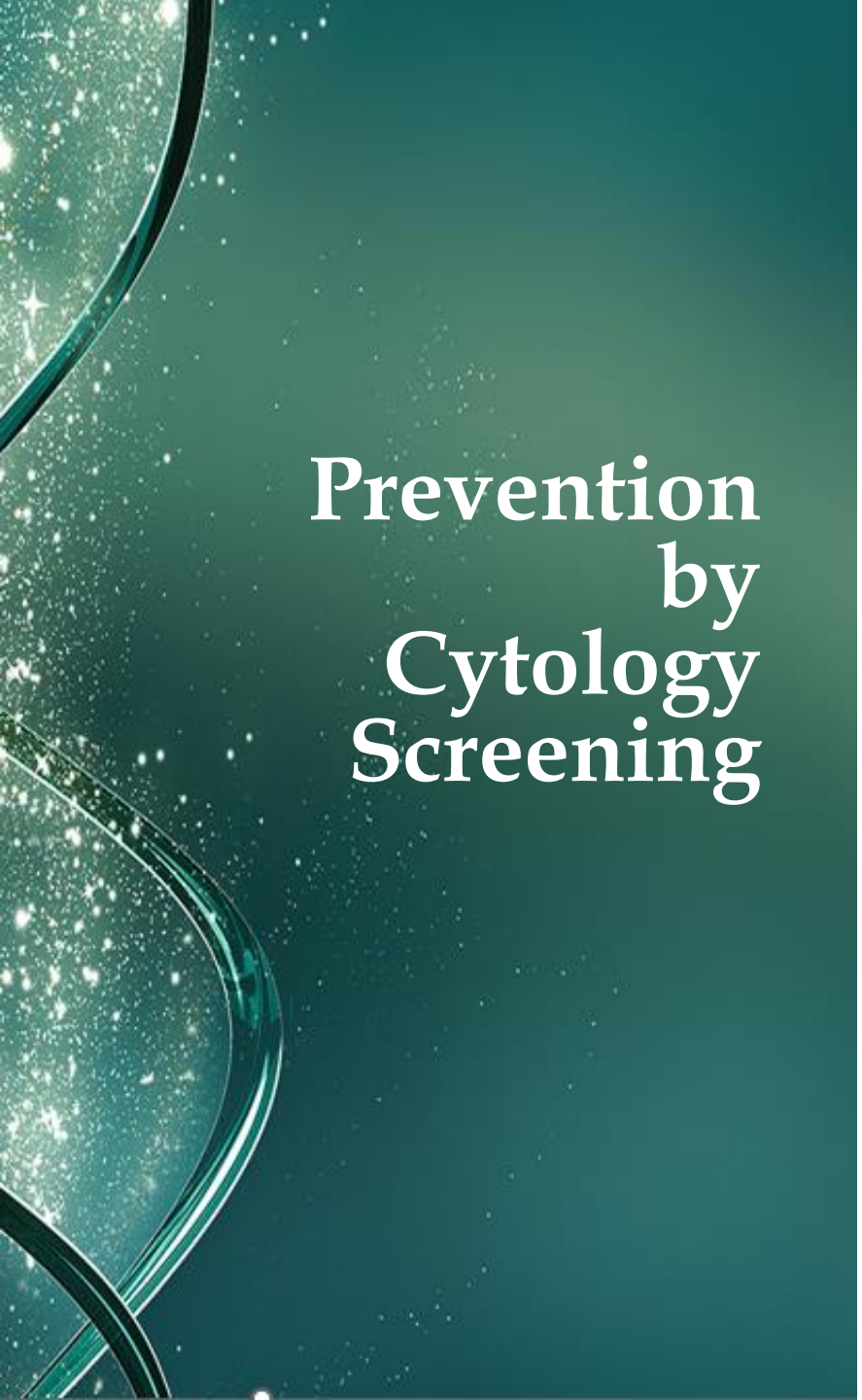
I have nothing to declare

Cervical Cancer Screening

- Today, HPV-based screening is the preferred strategy for cervical cancer prevention, commonly recommended for women > 30 years of age

- Yet, it is still debated how to best screen young women below 30 years of age:
  - high prevalence of HPV-infections (30%< 30 yrs.)
  - high prevalence of CIN2, most cases regress
  - need to minimize the harms of overdiagnosis

- Several countries still recommend cytology as the preferred technology for this subgroup



Prevention by Cytology Screening

- Age-dependent sensitivity for cervical cancer
  - Only 20 – 50% for women below 40 years of age
- Limited reproducibility, naked eye evaluation
- More than 50% of cervical cancers might be missed by cytology
  - Increased incidence of adenocarcinomas - not diagnosed by cytology
- Research on how to further improve cytology readings seem quite limited

Norwegian failure rates in screening 2011-2021

- Despite a well-established cervical cancer (CC) screening program, the incidence of CC in young women is increasing, peaking at 35 years of age
- 25% of all women diagnosed with CC had normal cytology readings within 3 years prior to their diagnosis
- The need to further improve screening to reduce cancer missed by cytology is paramount
- Co-testing cytology normal women with a 3-type HPV mRNA (16-18-45) test might be an alternative to improve safety, balancing benefits and harms of HPV-testing young women

Impact of HPV 16, 18, 45

- Not all HPV types carry equal risk of cervical disease
- HPV 16, 18 and 45 are aggressive types known to cause a more rapid development of severe lesions, even if cytology is negative at baseline
- HPV 16, 18 and 45 are associated with
  - > 75% of all cervical cancer cases worldwide
  - > 90% of all cases in young women < 40 yrs.
- HPV 16, 18 and 45 are strongly linked to adenocarcinomas (> 94%), a known challenge for cytology readings
- mRNA detection reveals ongoing oncogene activity, not just viral presence, reducing detection of transient HPV-infections

STUDY: Impact of HPV mRNA types 16, 18 and 45 detection on the risk of CIN3+ in young women with normal cervical cytology*

Primary Cytology Screening (**Control**)

- ❑ Women 25-39 years of age attending routine cytology screening (2014-2017) at Nordlandssykehuset, North Norway

HPV mRNA testing (**Intervention**)

- ❑ Women 25-39 yrs. with **NILM** cytology & **HPV mRNA test** (PreTect SEE; 16, 18, 45)
- ❑ Rescreening of index cyt. for all mRNA+ cases

Study endpoint

- ❑ Histologically confirmed CIN3+
- ❑ Follow-up: December 2021 (5 - 7 yrs.)

*Data published

- ❑ Nov.2022. PLoS ONE 17(11): e0275858. https://doi.org/10.1371/journal.pone.0275858

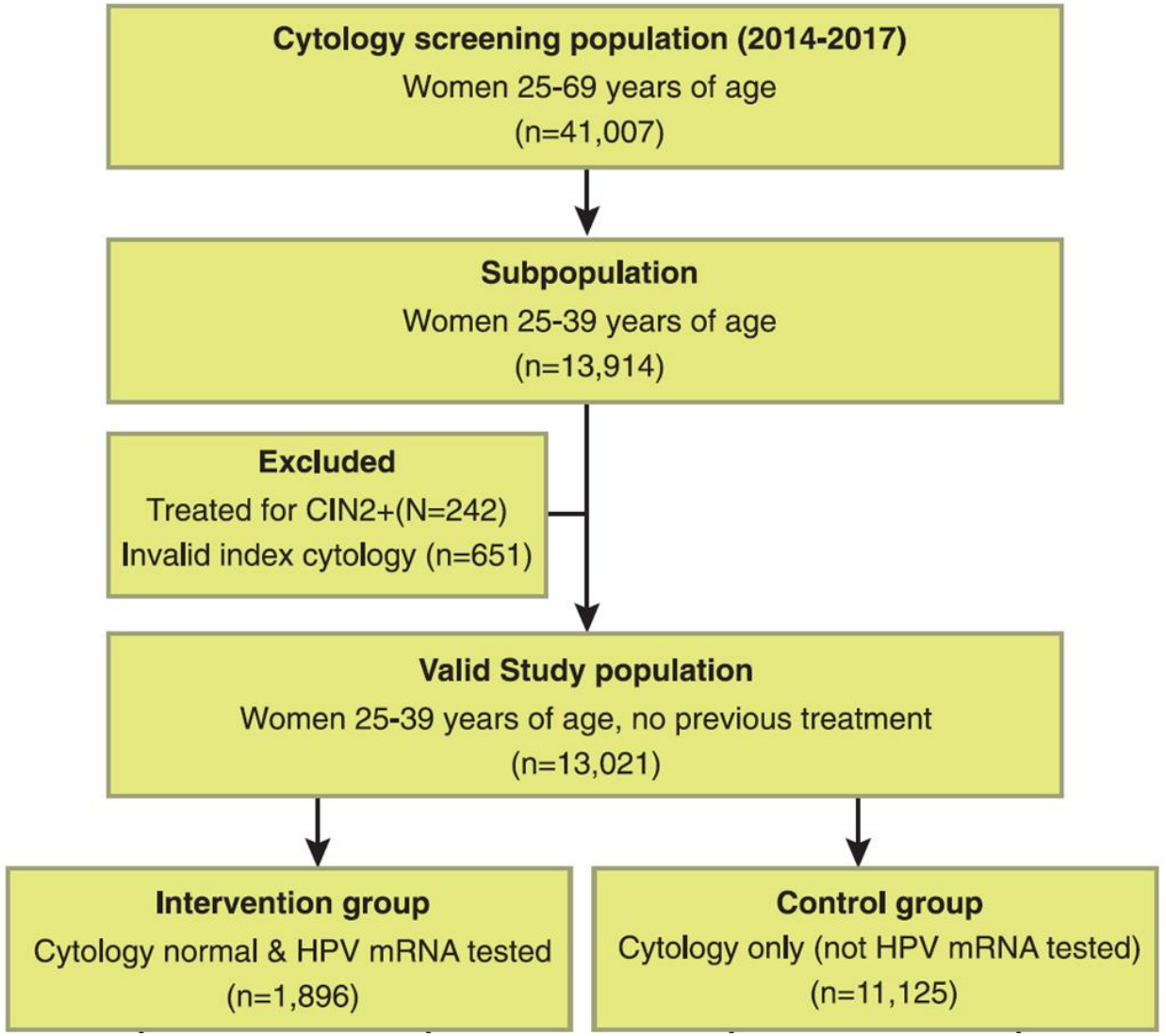
NORDLANDSSYKEHUSET
NORDLÁNDA SKIPPIJVIESSO

Study Objectives

- Investigate the detection rate of CIN3+ in women 25-39 yrs. attending routine cytology screening
  - **Control group**: Women screened by cytology only
  - **Intervention group**: Women screened with normal cytology & tested with a 3-type HPV mRNA test
- Evaluate the impact of HPV mRNA 16, 18, 45 expression in cytology negative women on the 5-year risk of CIN3+

PLoS ONE 17(11): e0275858.
https://doi.org/10.1371/journal.pone.0275858

Selection Study population



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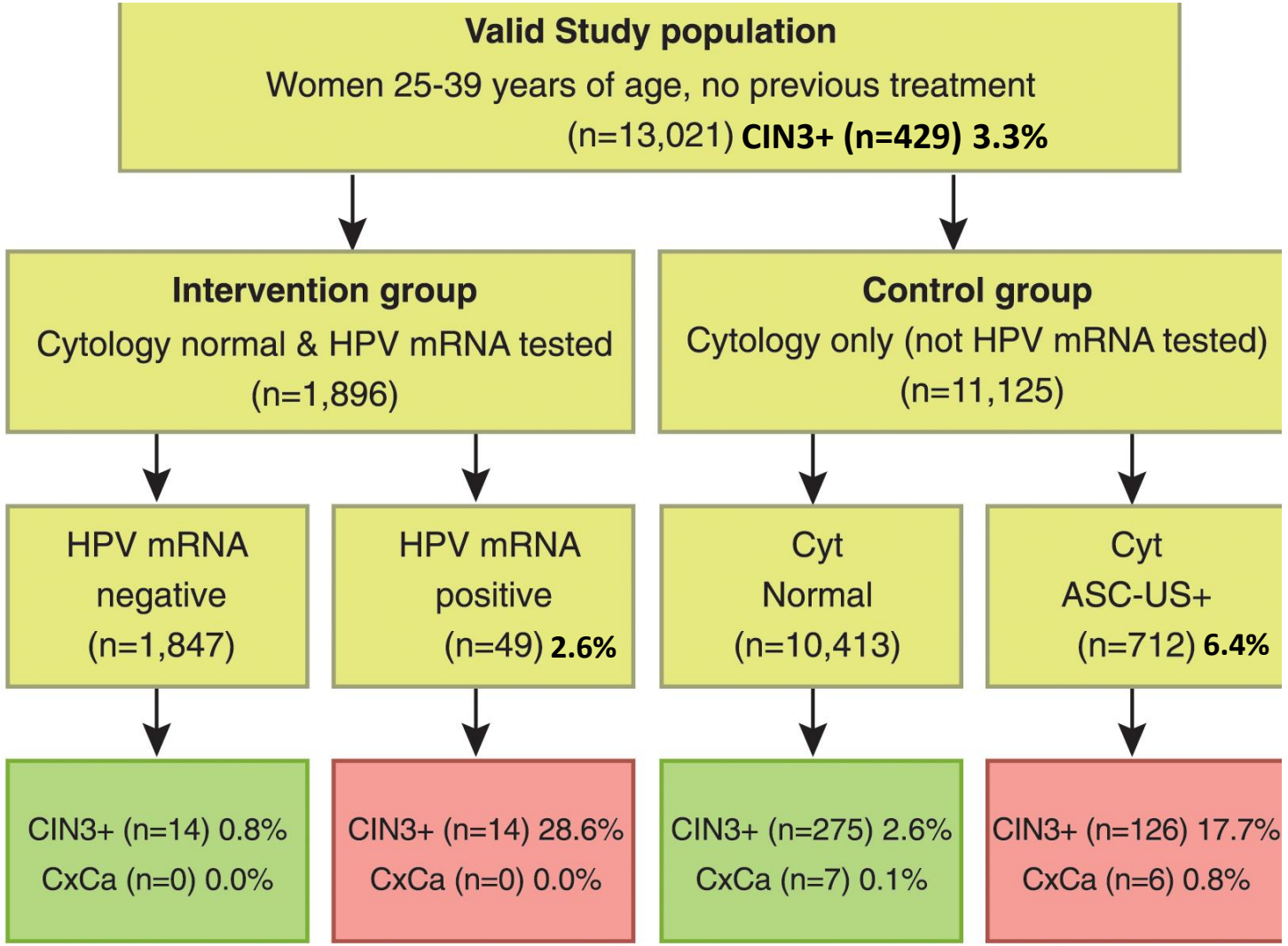
RESULTS

Al-Shibli K, Mohammed HAL, Maurseth R, Fostervold M, Werner S, **Sørbye SW** (2022). Impact of HPV mRNA types 16, 18, 45 detection on the risk of CIN3+ in young women with normal cervical cytology. PLoS ONE 17(11): e0275858. https://doi.org/10.1371/journal.pone.0275858

Results 1. Positivity rates & CIN3+ prevalence



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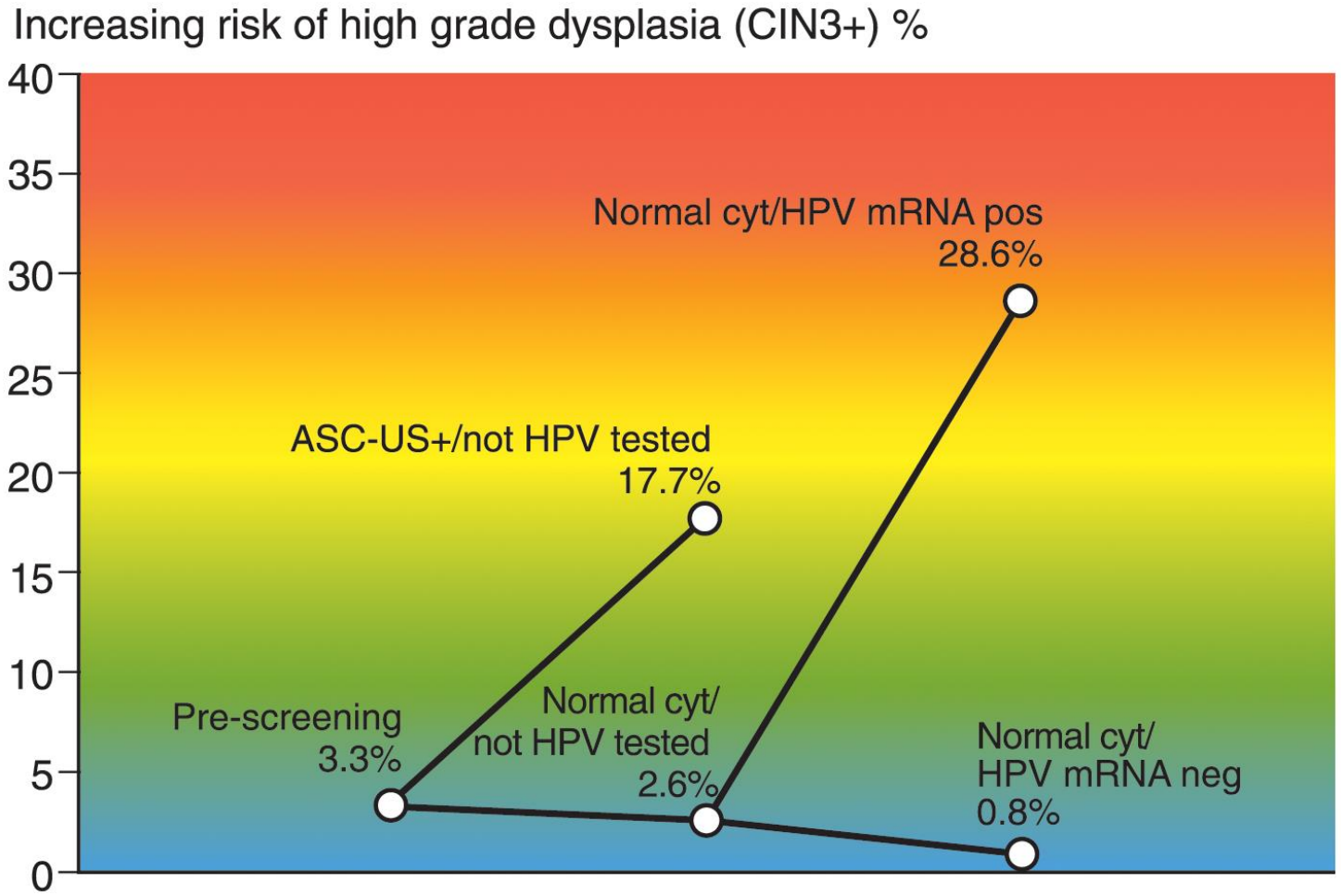
Results 2. Risk of CIN3+ In Control-versus Intervention group



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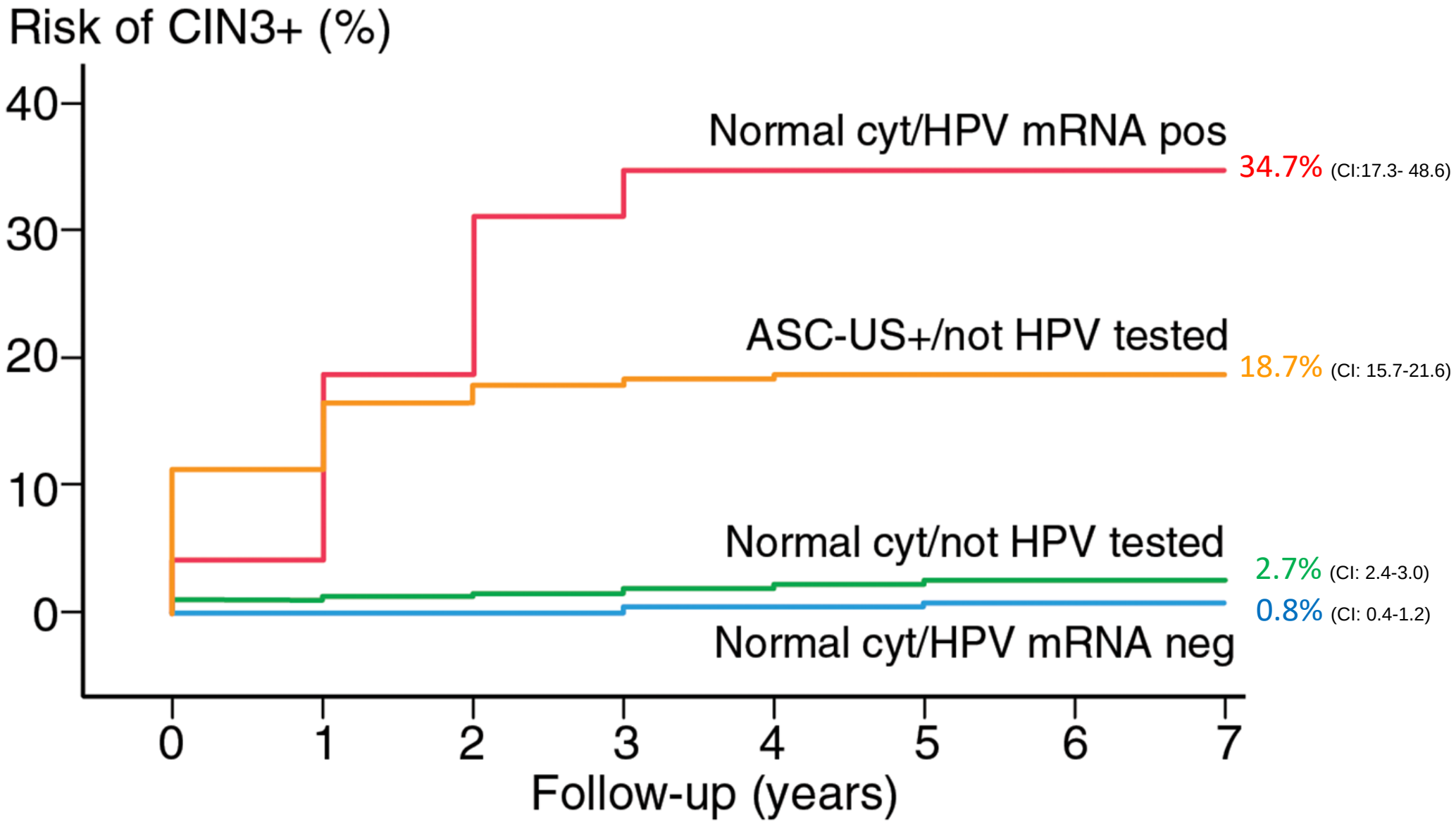
Results 3. Cumulative incidence ratios (CIR) for CIN3+ in 5-7 years follow-up



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Results 4. Cervical Cancer characteristics

- The risk of cervical cancer in women 25-39 years old screened by cytology
  - 14.3 per 100,000 women per year
- The risk of cervical cancer in women 25-39 yrs. with normal cytology at baseline
  - 9.6 per 100,000 women per year

Control group:

- 13 cases of invasive cervical cancer
- 7 cases had normal cytology at baseline
  - 5/7 adenocarcinoma (ADC)
  - 2/7 squamous cell carcinoma (SCC)
- 6 cases had abnormal cytology at baseline
  - 6/6 squamous cell carcinoma (SCC)

Intervention group:

- None of the women developed cervical cancer within 5-years follow-up

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Study Conclusions

- Cytology screening of young women has limitations and miss lesions that need to be treated
- Rescreening only 2.6% of the cytology normal smears for **HPV mRNA+** women, revealed missed abnormalities in 53.1% of the cases
- HPV mRNA 16, 18, 45 positive women have high 5-year CIN3+ risk (34.7%), despite normal cytology
- Co-test negative women (Cyt-/HPV mRNA-) have very low risk of CIN3+ (0.8%)
- A 3-type mRNA test might be a highly relevant biomarker for the identification of women at higher risk, improving safety for young women screened by cytology

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Thank you for your attention!

Kjerringøy-Bodø, Norway