IUI: State of art

Review literatuur

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Radboudumc

De spreker heeft:
Geen financiële banden met de IVD industrie
Geen sponsoring door belanghebbende industrie
Geen honoraria van belanghebbende industrie
Geen aandeelhouder van belanghebbende industrie
Geen andere relaties met belanghebbende industrie die gezien kunnen worden als belangenverstrengeling

Introduction

- Female age
- Duration of infertility
- Underlying diagnosis

(…)

Pregnancy rates of IUI

Ongoing discussion: when to apply IUI or IVF/ICSI (NICE 2013)

- Evidence factors: clinical and financial

Introduction

Impact technical aspects of IUI: more or less unclear

Laboratory manuals:

- WHO
- ESHRE
- NICE

Lack of standardization:

- Limited willingness
- Impractical recommendations

Review

Semen collection

- Ejaculatory abstinence
- Semen collection place
- Time interval: semen production - processing
- IUI devices

Semen processing

- Semen separation method
- Centrifugation medium
- Centrifugation temperature
- Storage temperature
- Time interval: semen processing - insemination
- IUI devices

Insemination (IUI)

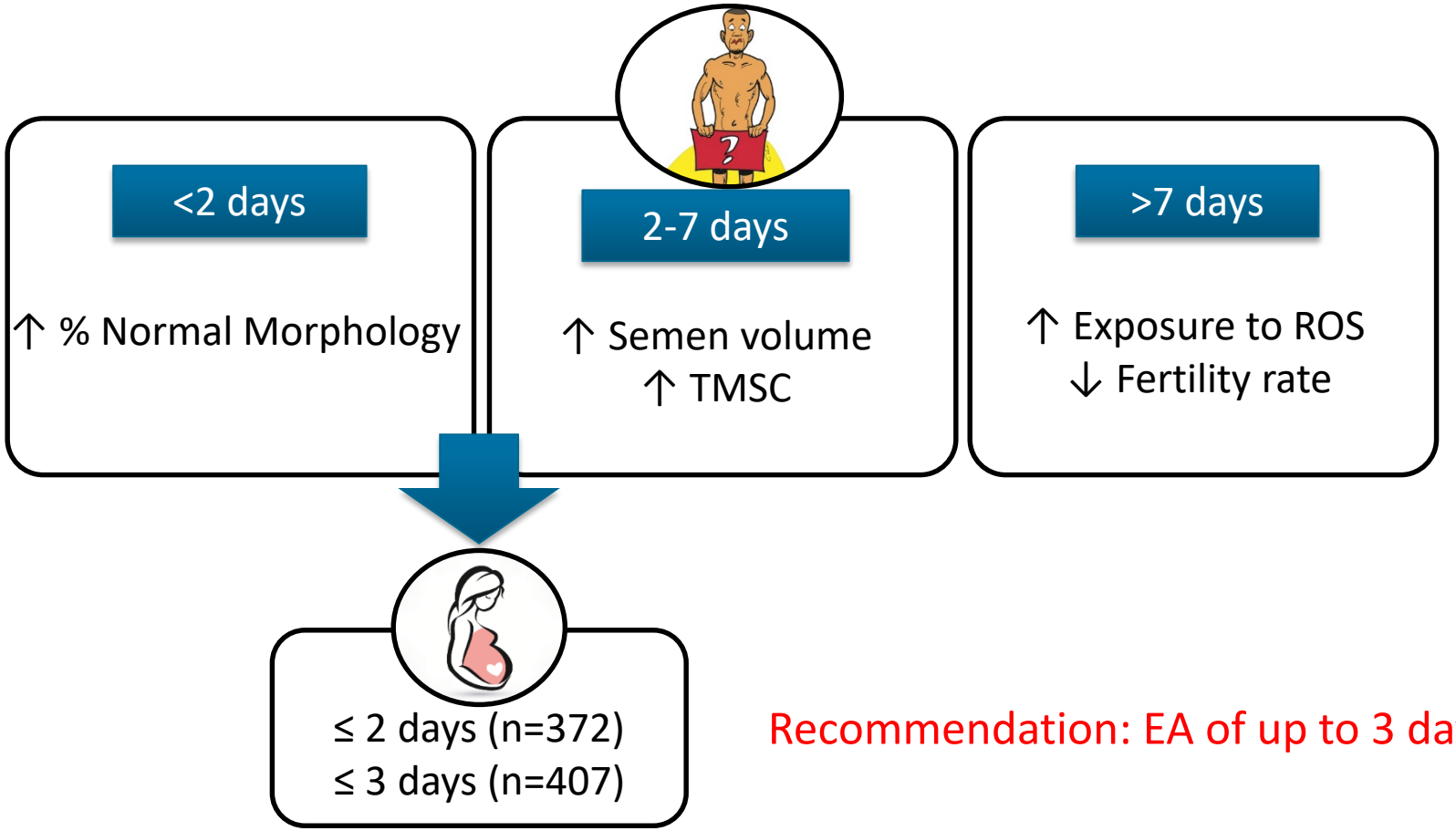
- Timing method of IUI
- Time between ovulation and insemination
- Time interval: semen production – insemination
- Bed rest after IUI
- IUI devices

Recommendations by:

- WHO

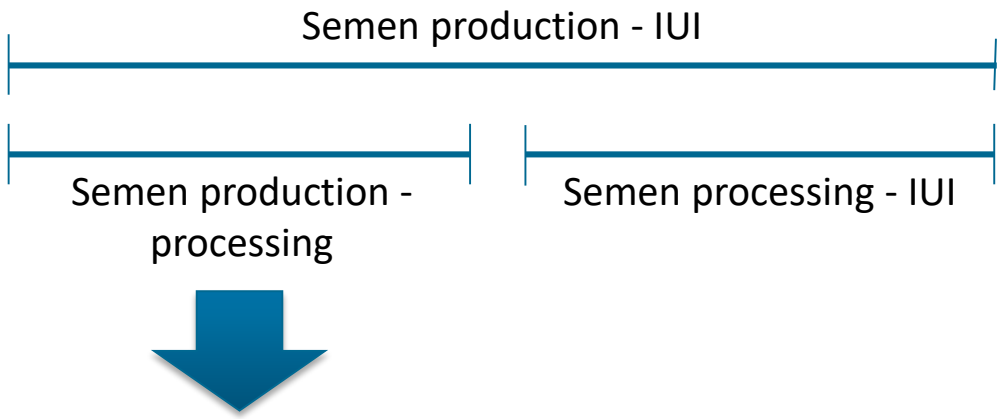
Ejaculatory abstinence

WHO: EA of 2-7 days



Recommendation: EA of up to 3 days

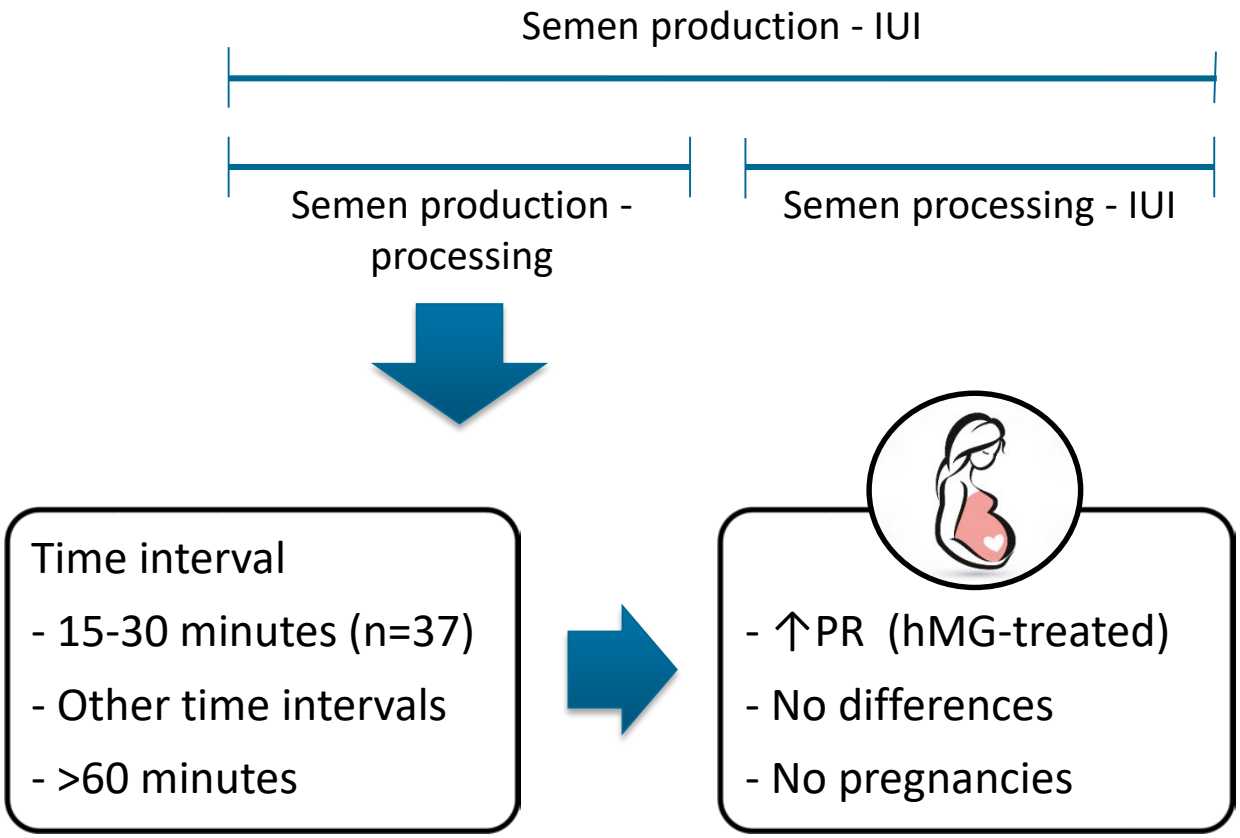
Time intervals



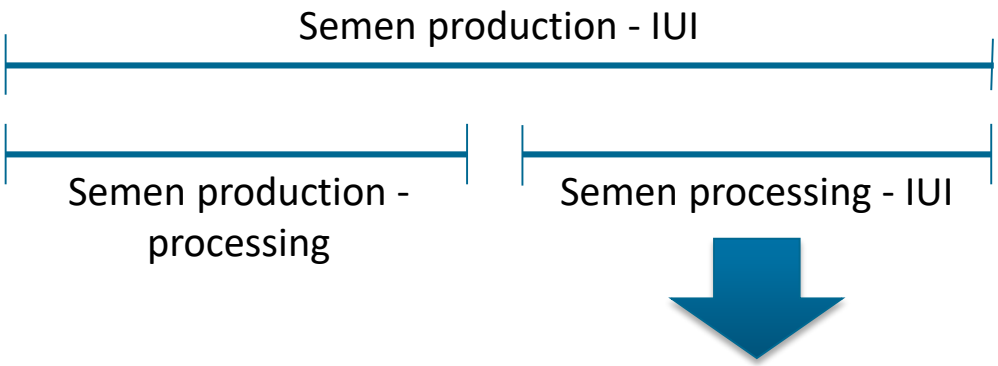
WHO:

- private room near laboratory
- collection at home: delivery within 1 hour

Time intervals



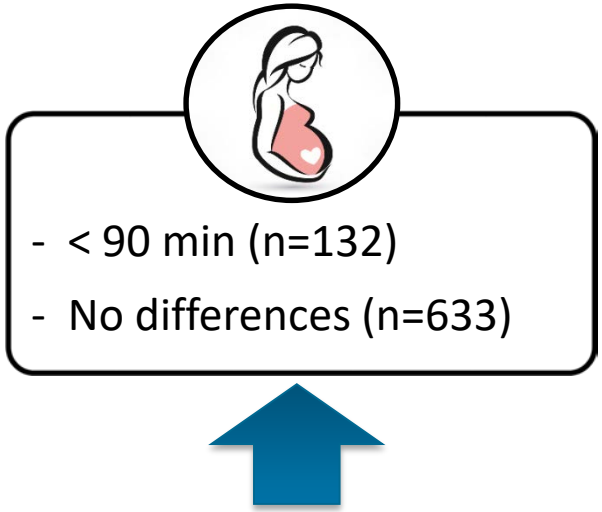
Time intervals

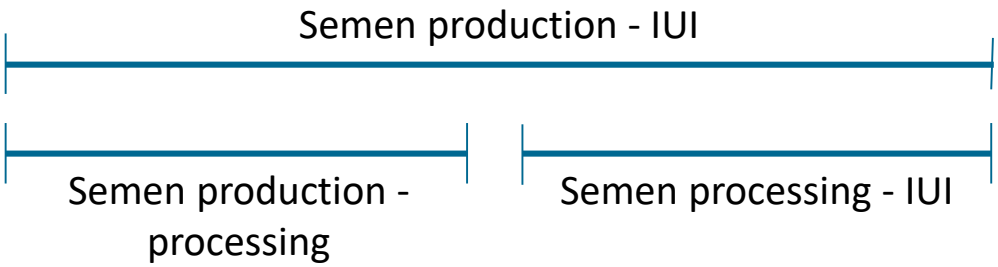


Shorter interval: less DNA damage

- < 30 min and 31-60 min (n=37)
- 40-80 min (n=862)
- >30 min (n=1125)
- No differences (n=633 / 2154)

Time intervals





Recommendation: sample delivery <1 hour, avoid long time intervals

Semen separation method

Wide variance of products and methods

WHO: selection based on nature of semen sample

Pregnancy rates:
- 10 RCTs in total
- 6 RCTs in systematic review (Boomsma et al.)

- Density gradient
- Swim-up
- Wash-only

Meta-analysis: no difference in pregnancy rates
Contradicting results

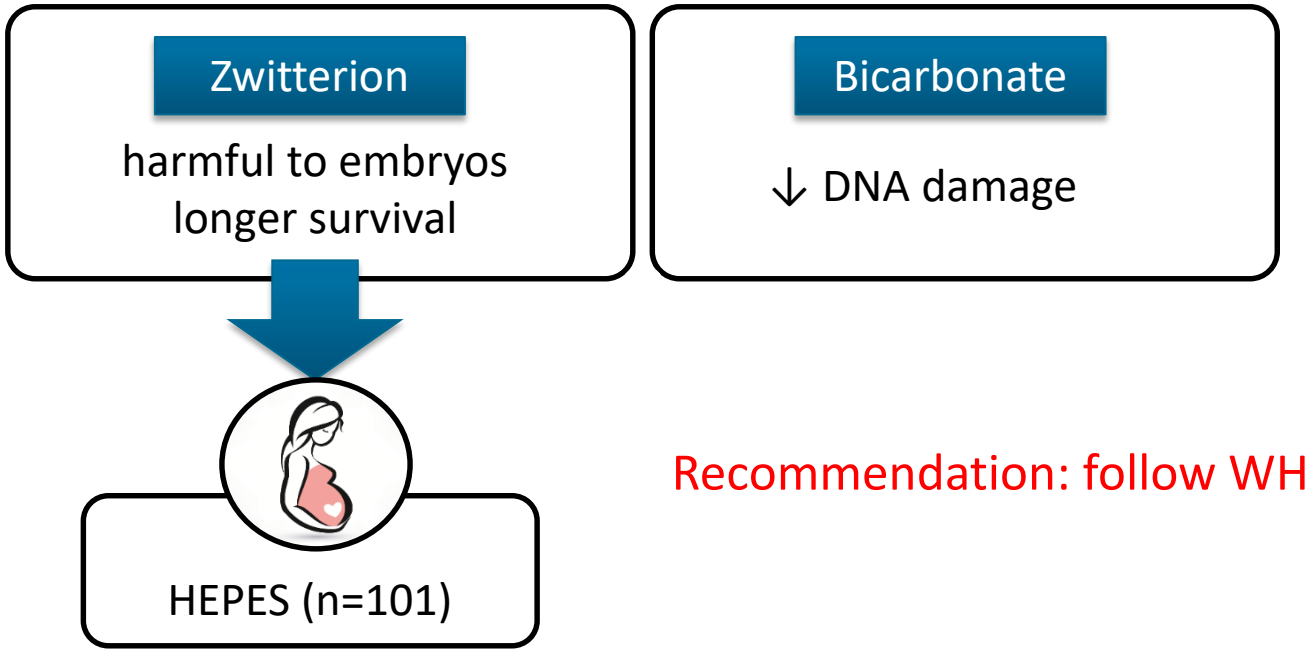
Difference in study designs:
- population
- methods of separation

Recommendation: selection of method based on semen sample

Centrifugation medium

WHO: based on used incubator

- atmospheric air: zwitterion-buffered
- atmosphere of 5% CO2: bicarbonate-buffered



Recommendation: follow WHO

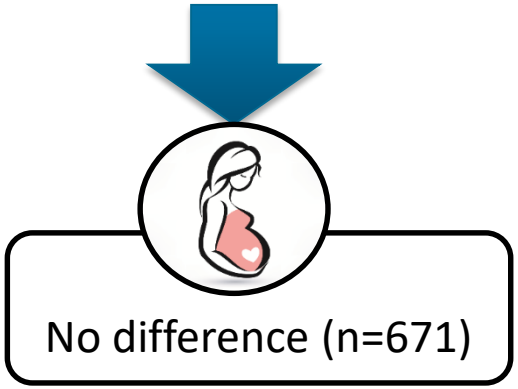
Temperature during centrifugation

No recommendations

Room temperature commonly used

Body/testis vs. room temperature:

- no difference DNA damage (n=50)
- ↑ % motile sperm cells (n=10)

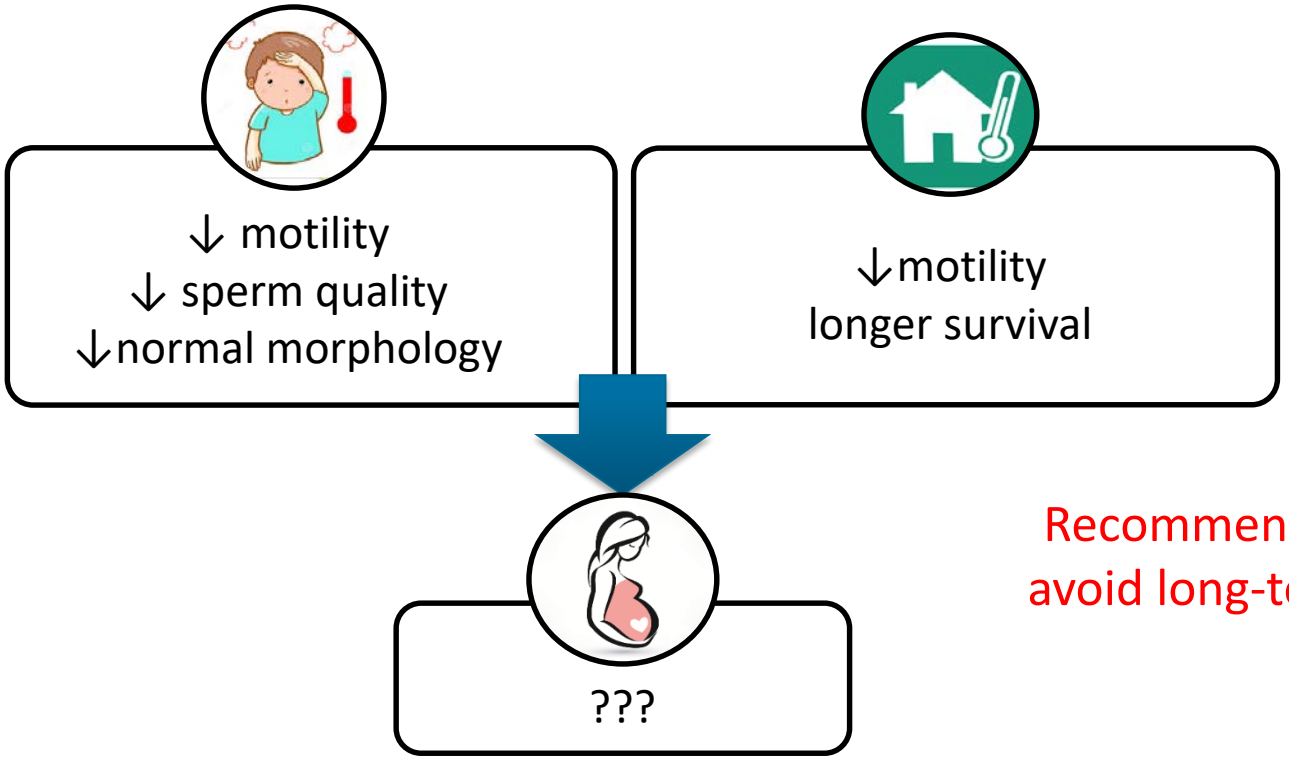


Recommendation: room temperature

Temperature during storage

No recommendations

Usually at body temperature
- long-term storage?



Recommendation: ???
avoid long-term storage

Method of timing IUI

- LH detection
- hCG administration
- body temperature charts
- ultrasound detection
- combination

No recommendations

Pregnancy rates: 18 RCTs in systematic review (catineau et al.)

- hCG vs. LH detection: no differences
- other comparisons: no differences
- low/ very low evidence

Time interval: ovulation induction – insemination

- 24-48 hours
- no differences in PRs

Recommendation: method own preferences

Bed rest after IUI

NICE: bed rest >20 minutes does not improve IVF outcome

- immediate mobilization
- bed rest (10 / 15 minutes)

Bed rest:

- 10 minutes
- 15 minutes

- ↑ PRs (n= 95)
- ↑ PR (n= 391)
- No impact (n=479)

Recommendation: bed rest of 10-15 min or direct mobilization

Discussion

Technical aspects of IUI:

- lack of evidence
- contradictory findings
- low degree of standardization

Variable	Level of evidence	Number of studies	Main conclusions in literature; reported procedure with highest PRs	Recommendations based on literature and WHO guideline	Next steps in research
Ejaculatory abstinence	3	2	EA up to 2 // 3 days	EA ≤ 3 days	Evaluation in RCTs, with stratification for oligo- and normozoospermic men
Collection place (clinic versus at home)	3#	2	Collection in the clinic // no difference	Either in the clinic or at home	Evaluation in RCTs, with stratification for oligo- and normozoospermic men
Time intervals	3#	4	Avoid short and long TIs // no impact	Sample delivered within 1 h after collection, avoid long TIs between semen collection-insemination and semen processing-insemination	In first instance in multi-center retrospective studies, separately for oligo- and normozoospermic men
Semen preparation technique	Ia#	6 †@	No superior method	Method selection should be based on semen sample	Identification of methodologies with best IUI results in retrospective studies (e.g. number of layers, volume of medium)
Buffer of wash medium	Ib	1	HEPES buffer better than bicarbonate buffer	Selection of the medium buffer should be based on used incubator	Additional evaluation in RCTs, with stratification for oligo-and normozoospermic men
Centrifugation temperature	Ib	1	No difference between body // testis and room temperature	Non-controlled centrifugation temperature, for reasons of ease	None
Storage temperature	2*	4	Storage at room temperature better than body temperature*	Avoid body temperature, especially during long-term storage	Evaluation of impact on PRs in RCTs, with stratification for oligo- and normozoospermic men
Method of timing IUI	Ia	18 †	No superior method	No recommendable method	Evaluation in RCTs with standardized methods
Time between ovulation and insemination	Ib	7	No superior time interval	Insemination 24–48 h after ovulation induction	Evaluation in RCTs with standardized methods, including insemination <24 h after ovulation induction. With stratification for oligo-and normozoospermic men
IUI devices	–	–	Some devices were reported as cytotoxic	Avoid the use of IUI devices that cause reprotoxicity	Development of well-described tests to identify safe and effective devices
Bed rest after IUI	Ib	3	Bed rest of 10 // 15 min // no difference between bed rest and immediate mobilization	Either bed rest of 10–15 min or direct mobilization	Additional evaluation in RCTs, with stratification for oligo-and normozoospermic men

Discussion

Technical aspects of IUI:

- lack of evidence
- contradictory findings
- low degree of standardization

Recommendations introduced for:

- standardization
- ease / costs
- quality control

Further research is needed!

Conclusion

Further research: RCTs

- Wash medium buffer
- Storage temperature
- Timing of insemination
- Bed rest

Guidelines updated

Implementation strategies