# Transition Period Health and Reproduction: Preparing for a Successful Pregnancy

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# Transition health problems are common
# But healthy cows have good fertility

5719 cows in
7 US herds

**Table 2.** Impact of health problems in the first 60 d postpartum on pregnancy at first postpartum AI of dairy cows[1]

| Health status | Prevalence | Pregnant, % | Adjusted OR (95% CI)[2] | *P* |
|---|---|---|---|---|
| Health problem | | | | |
| Healthy | **56** | 51.4 | 1.00 | |
| 1 case of disease | **27** | 43.3 | 0.79 (0.69 – 0.91) | 0.001 |
| > 1 case of disease | **17** | 34.7 | 0.57 (0.48 – 0.69) | < 0.001 |
| Type of health problem[3] | | | | |
| Calving problem | **15** | 40.3 | 0.75 (0.63 – 0.88) | < 0.001 |
| Metritis | **16** | 37.8 | 0.66 (0.56 – 0.78) | < 0.001 |
| Clinical endometritis | **20** | 38.7 | 0.62 (0.52 – 0.74) | < 0.001 |
| Fever postpartum | **21** | 39.8 | 0.60 (0.48 – 0.65) | < 0.001 |
| Mastitis | **12** | 39.4 | 0.84 (0.64 – 1.10) | 0.20 |
| Clinical ketosis | **10** | 28.8 | 0.50 (0.36 – 0.68) | < 0.001 |
| Lameness | **7** | 33.3 | 0.57 (0.41 – 0.78) | < 0.001 |
| Pneumonia | **3** | 32.4 | 0.63 (0.32 – 1.27) | 0.20 |
| Digestive problem | **2** | 36.7 | 0.78 (0.46 – 1.34) | 0.38 |

Santos et al RepDomRum 2010

# Transition health problems are common



Brief report

## Economic burden of time lost due to injury in NHL hockey players

Laura Donaldson,[1,2] Bing Li,[3] Michael D Cusimano[1,2]

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/injuryprev-2013-041016).

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**ABSTRACT**

**Objective** To determine the economic burden of salary costs lost due to injury in the National Hockey League (NHL).

**Methods** All NHL players who engaged in at least one regular season game during the 2009–2010 to 2011–2012 seasons comprised the study population. We performed a retrospective cross-sectional analysis of publically available media sources to collect injury and salary data. Outcome measurements were games missed during regular season play due to hockey-related injury and lost salary.

**Results** A total of 50.9% of all NHL players missed at least one game within a season of play, and injuries represented a total salary cost of approximately US$218 million per year. Concussions alone amounted to a salary

### Data collection

Data sources

Full rosters and the number of games participated in by each player were obtained from the NHL website (http://www.nhl.com). Injury data were obtained from nhl.com, and official team injury reports. When more information was required, a variety of other publically available sources including The Sports Network (http://www.tsn.com), Yahoo Sports (http://sports.yahoo.com) and Rotoworld (http://www.rotoworld.com) were consulted. Annual player salaries (US$) were obtained from http://www.capgeek.com.

The increasing popularity of fantasy sports has resulted in a huge demand for information on the

Santos et al RepDomRum 2010

# Transition sets the stage for fertility

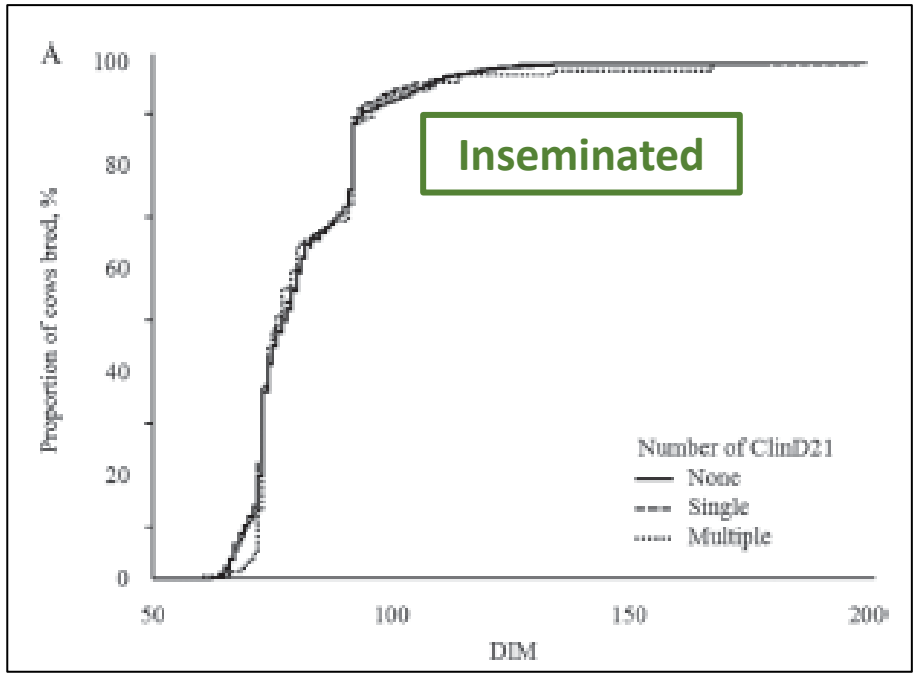
126 herds in Quebec, Canada

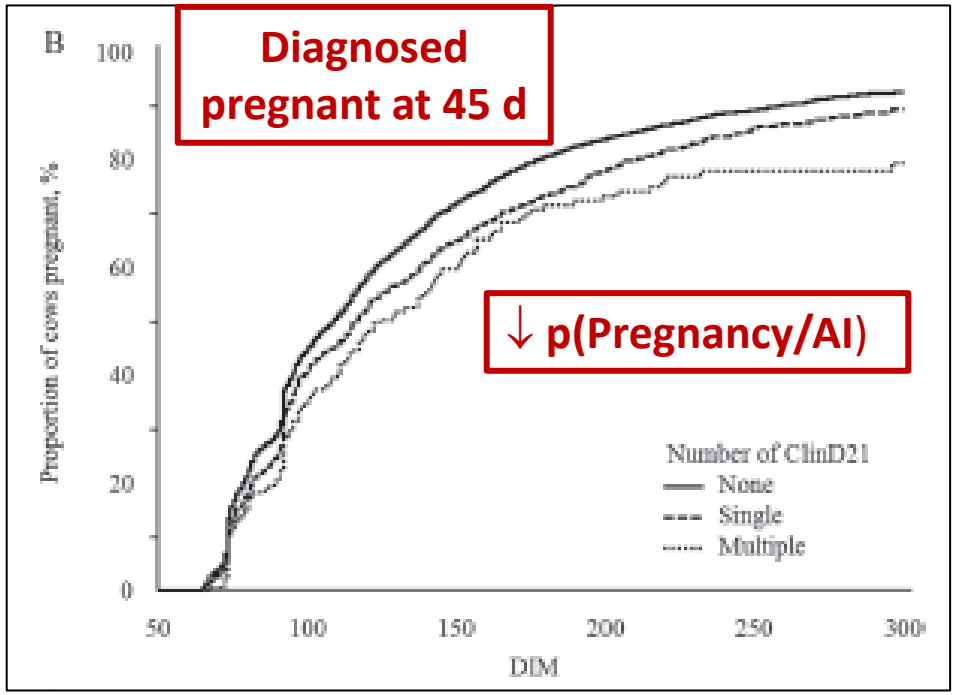
| Herd prevalence threshold (estimated from 20 cows) | Herd pregnancy at 1st AI < 40% | Herd pregnancy loss > 5% |
|---|---|---|
| RP | - | ≥ 5% |
| Ketosis (tested only once 1-14 DIM) | ≥ 12% | - |
| PVD | ≥ 5% | ≥ 5% |
| Endometritis (cytobrush) | ≥ 19% | - |
| Anovular (blood P4 30-44 and 44-57 DIM) | ≥ 21% | - |
| DA | ≥ 4 % | - |

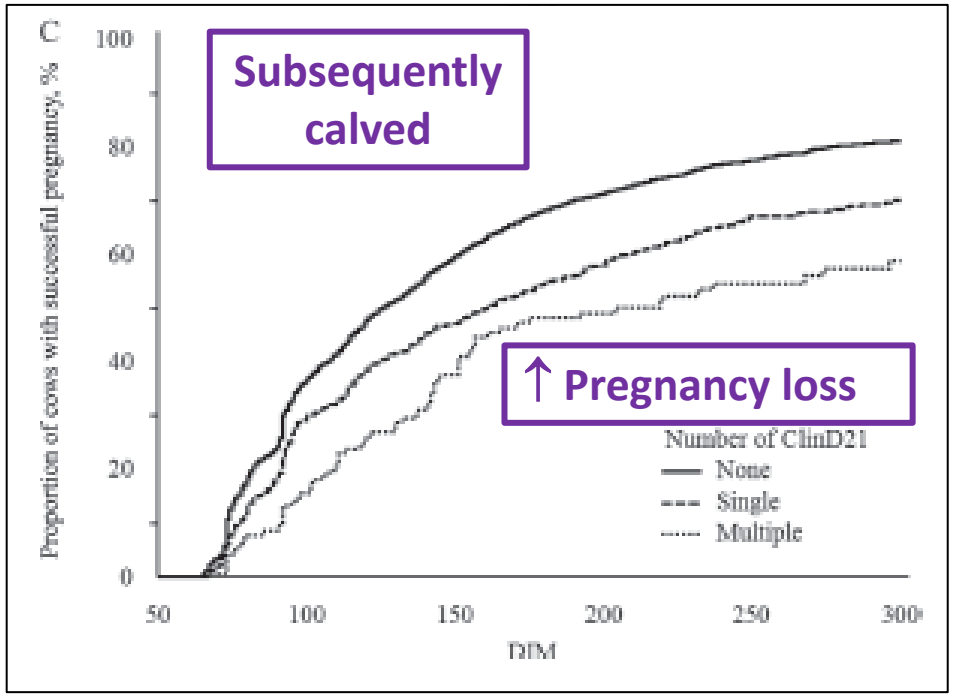
Dubuc & Denis-Robichaud JDS 2017

# Effect of disease in early lactation on reproduction

- Data from 1 freestall herd in Florida
- All cows that calved in 2012 (data on n = 4333)



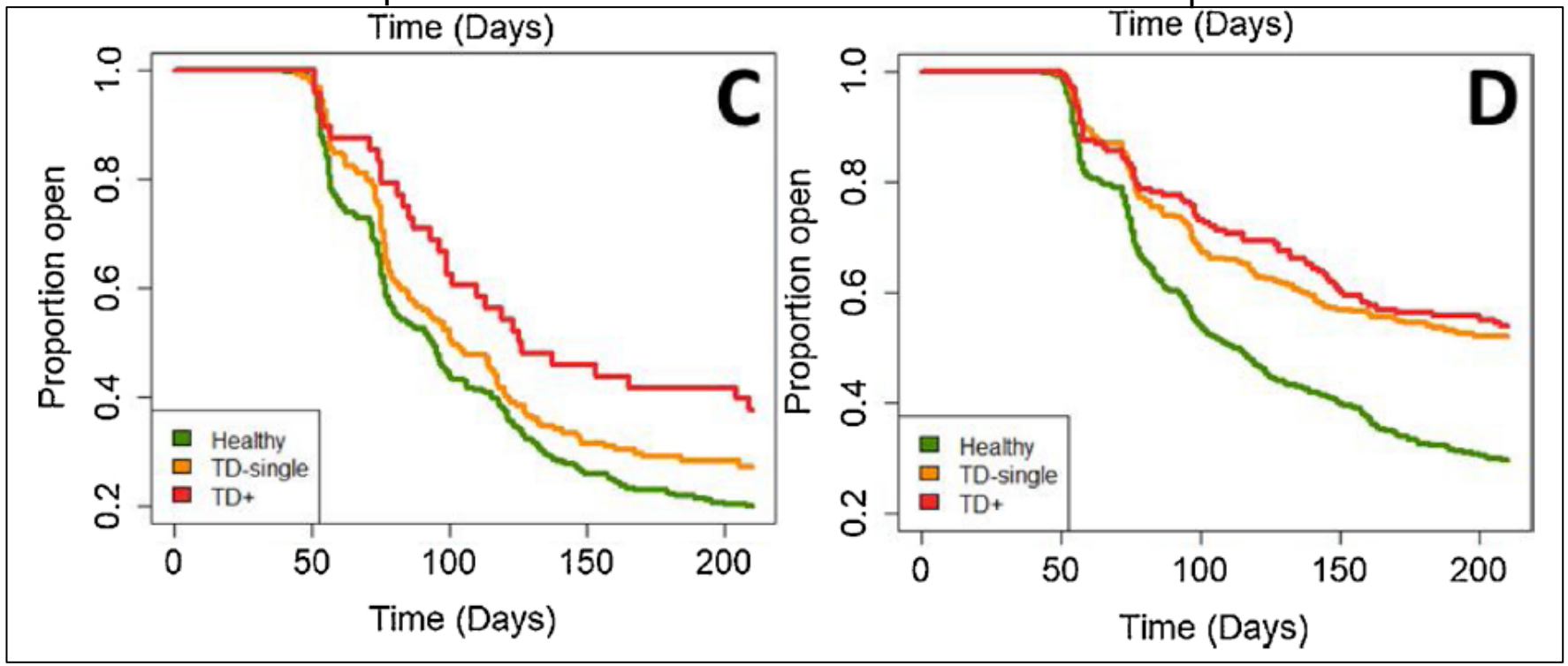




Carvalho et al 2019

# Effect of transition disease on reproduction

- 1 year cohort of 1946 calvings from 1 farm in Germany
- Survival analysis and machine learning on same data
- Greater effects of disease in multiparous cows: all reduced pregnancy rate




Pascottini et al 2020
https://doi.org/10.1016/j.prevetmed.2020.104908

# Impacts of ketosis - Reproduction

**Subclinical ketosis (serum BHB > 1.0 – 1.4 mmol/L) in early lactation is associated with:**

- 3 X Increased risk of metritis (not in all studies)

  Hammon et al 2006; Duffield et al 2009

- 1.4 X greater odds of endometritis (uterine inflammation based on cytology) at 35 DIM

  Dubuc et al 2011

- 1.5 X increased odds of being anovular (not cyclic) at 63 DIM (19% vs. 13% of cows)

  Walsh et al 2007; Dubuc et al 2012

- Decrease in pregnancy at first AI

  Walsh et al, 2007

- Point prevalence (20 cows, 1 test, BHB ≥ 1.4 mmol/L) ≥ 20% associated with herd annual pregnancy at 1$^{st}$ AI < 40%

  Dubuc & Denis-Robichaud, 2017

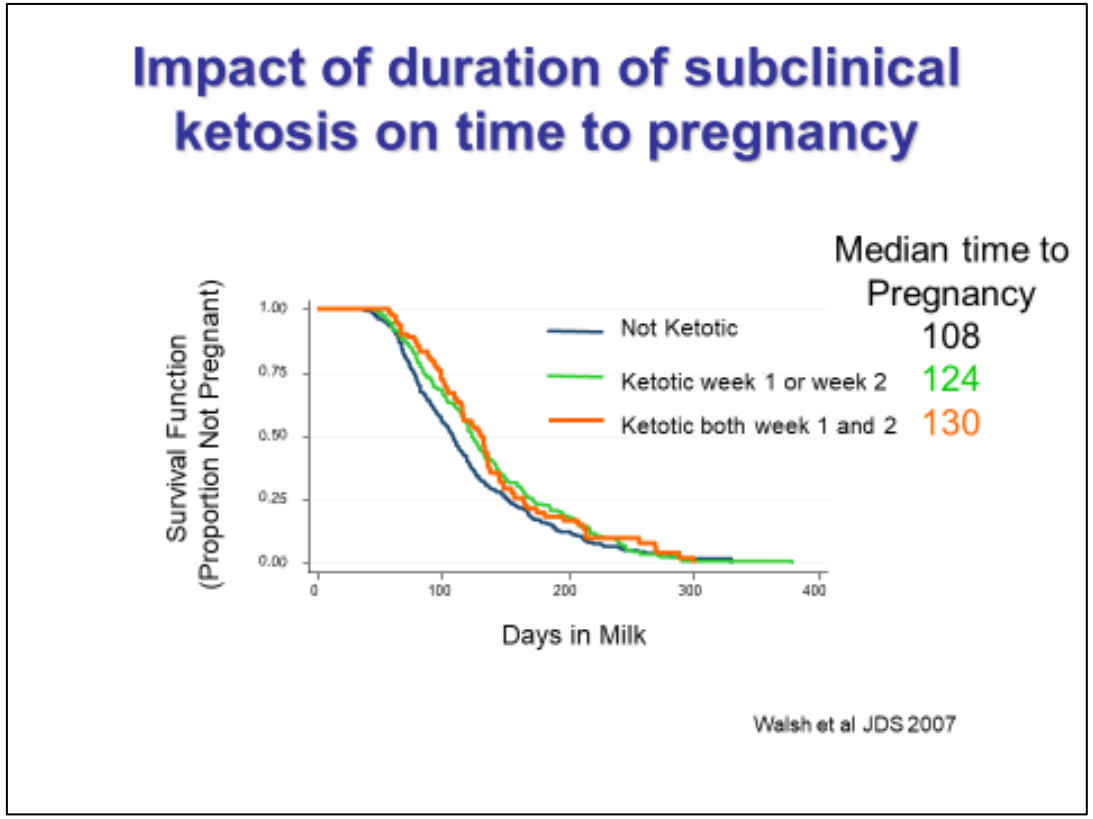
- BHB > 1.2 mmol/L in any of 1$^{st}$ 5 weeks postpartum associated with lower 6-week in-calf in pasture system (78 vs. 85%)

  Compton et al 2015

# Impacts of ketosis Reproduction

Ketosis in week 1 or 2 decreased pregnancy rate (Walsh et al 2007)

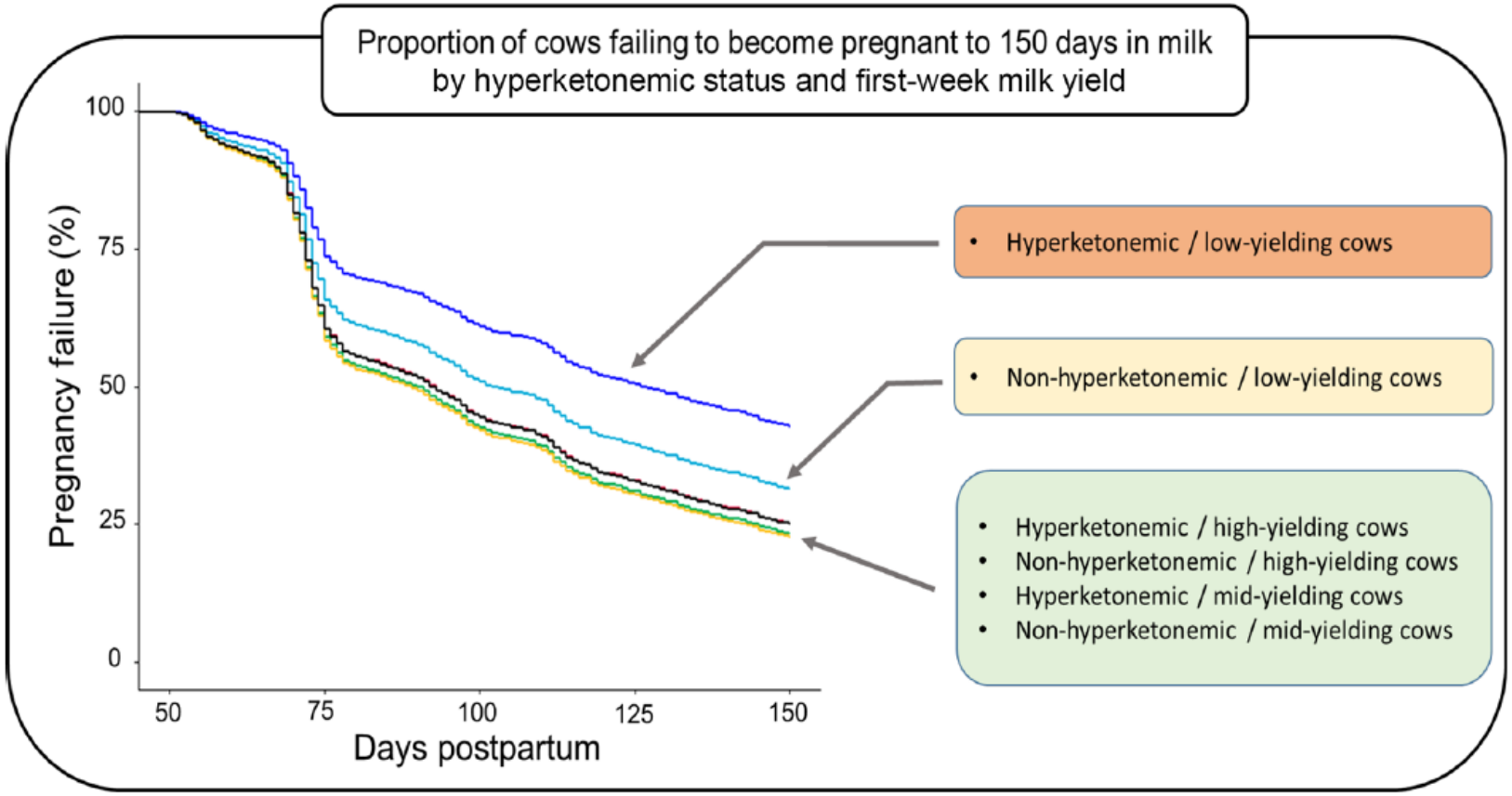
| | CR at 1st AI |
|---|---|
| No ketosis | 42% |
| Ketosis in 1 week | 36% |
| Ketosis for 2 weeks | 28% |




Reduced pregnancy rate until 165 DIM

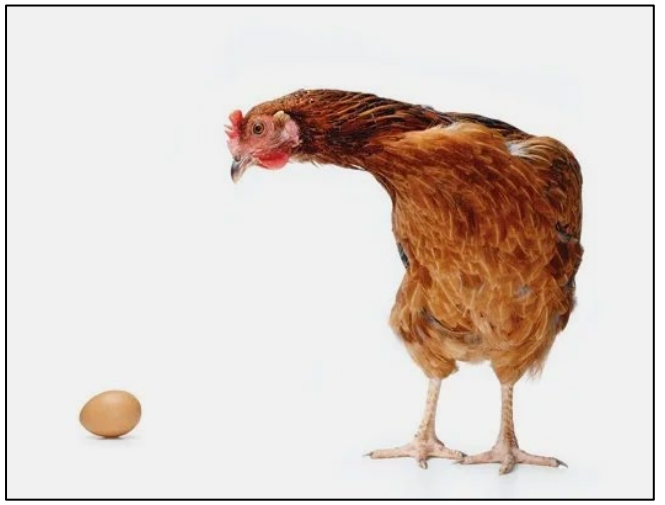
# Effects of ketosis depend on milk yield (or vice versa)

2091 cows from 5 herds in Minnesota 13,00 – 15,000 kg 305ME milk
Blood BHB tested twice 3-10 DIM. HYK ≥ 1.2 mmol/L
14% cumulative incidence (4 to 22% among herds)
Week 1 milk ranked < 25$^{th}$, 25-75$^{th}$ or > 75$^{th}$ percentile by parity within herd
4 herds Double Ovsynch for 1$^{st}$ AI; other PreSynch with HD, then TAI; then HD followed by Ovsynch




Rodriguez et al JDSC 2021

# Effects of ketosis depend on milk yield (or vice versa)



Performance of cows with HYK relative to cows without

| | | Estimates (95% CI) | | | |
|---|---|---|---|---|---|
| Events | | Overall[1] | Low milk yield[2] | Mid milk yield[2] | High milk yield[2] |
| Pregnancy to first AI[3] | **RR** | 0.86 (0.70, 1.06) | 0.62 (0.39, 0.98) | 0.96 (0.73, 1.28) | 0.93 (0.64, 1.35) |
| Pregnancy by 150 DIM[4] | **HR** | 0.83 (0.71, 0.97) | 0.70 (0.51, 0.96) | 0.90 (0.72, 1.13) | 0.87 (0.64, 1.17) |
| Calving-to-conception interval[5] | **Mean diff, d** | 7.77 (3.34, 12.2) | 13.03 (5.12, 20.9) | 3.36 (−3.35, 10.10) | 4.68 (−4.06, 13.40) |

Rodriquez et al JDSC 2021

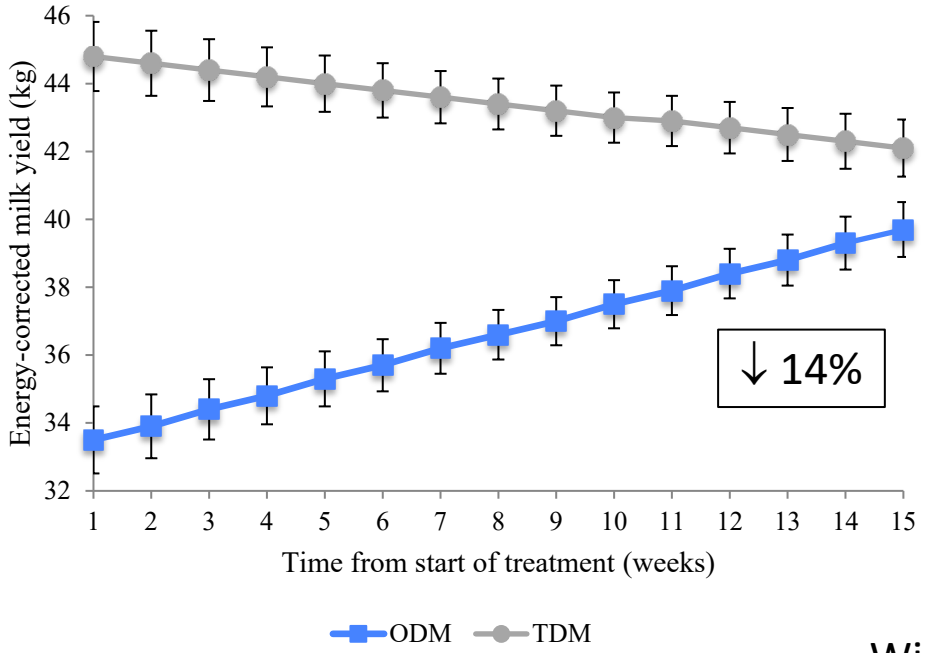
# Ketosis treatment summary

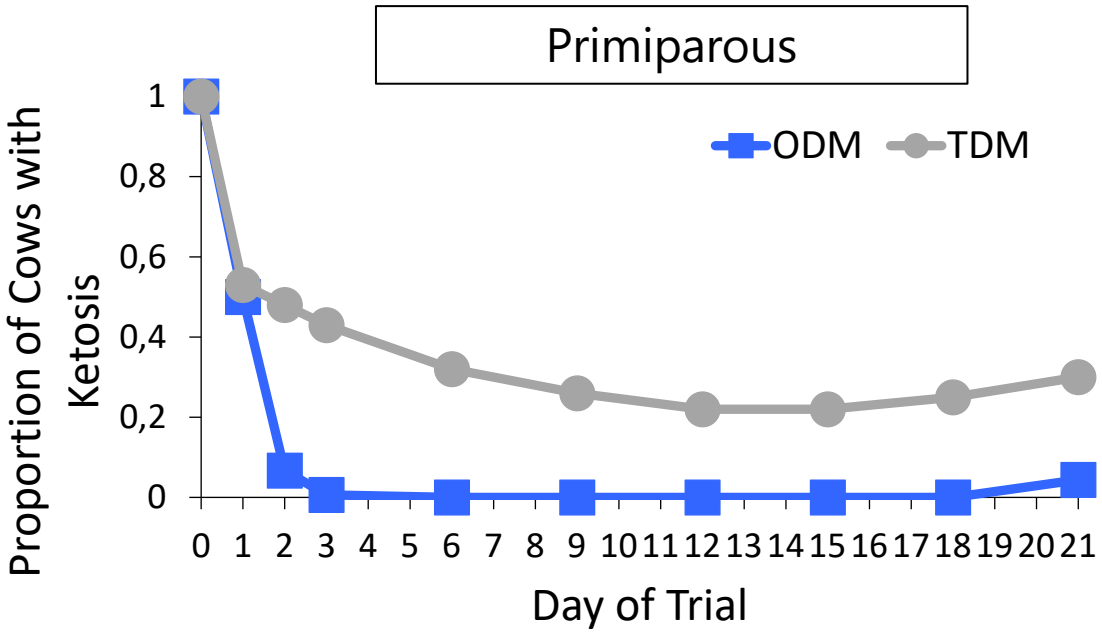
## Gordon et al JDS 2017a,b

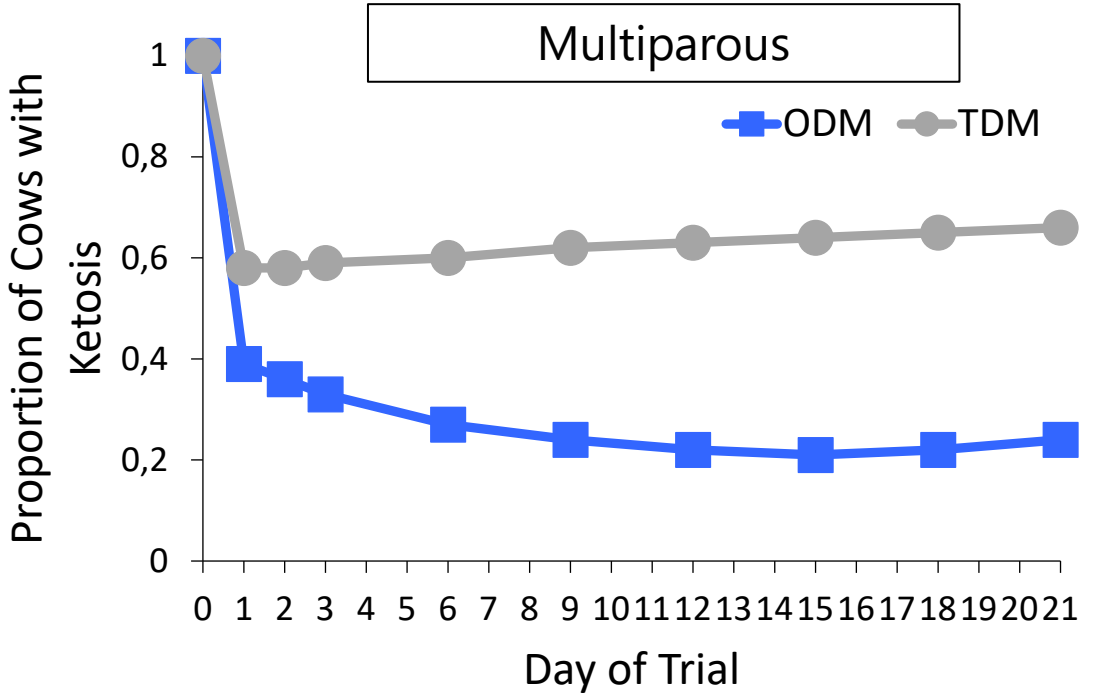
- Based on ketosis cure +1 and +2 weeks and milk yield to 30 DIM
- Blood BHB ≥ 1.2 but < 2.4 mmol/L (or KetoTest = 100)
    - **Treat with 3 d glycol 300g 1X/day**
- Blood BHB > 2.4 mmol/L (KetoTest ≥ 200)
    - **Treat with 5 d glycol**
- If BHB > 1.2 mmol/L and glucose < 2.2 mmol/L (38% of cases)
    - **Add treatment with Catosal or B12 (1.25 mg) for 3 d**
    - Re-test at end of treatment
- Addition of dexamethasone not recommended (Tatone et al 2016)

# Once-daily milking (ODM) as treatment for ketosis

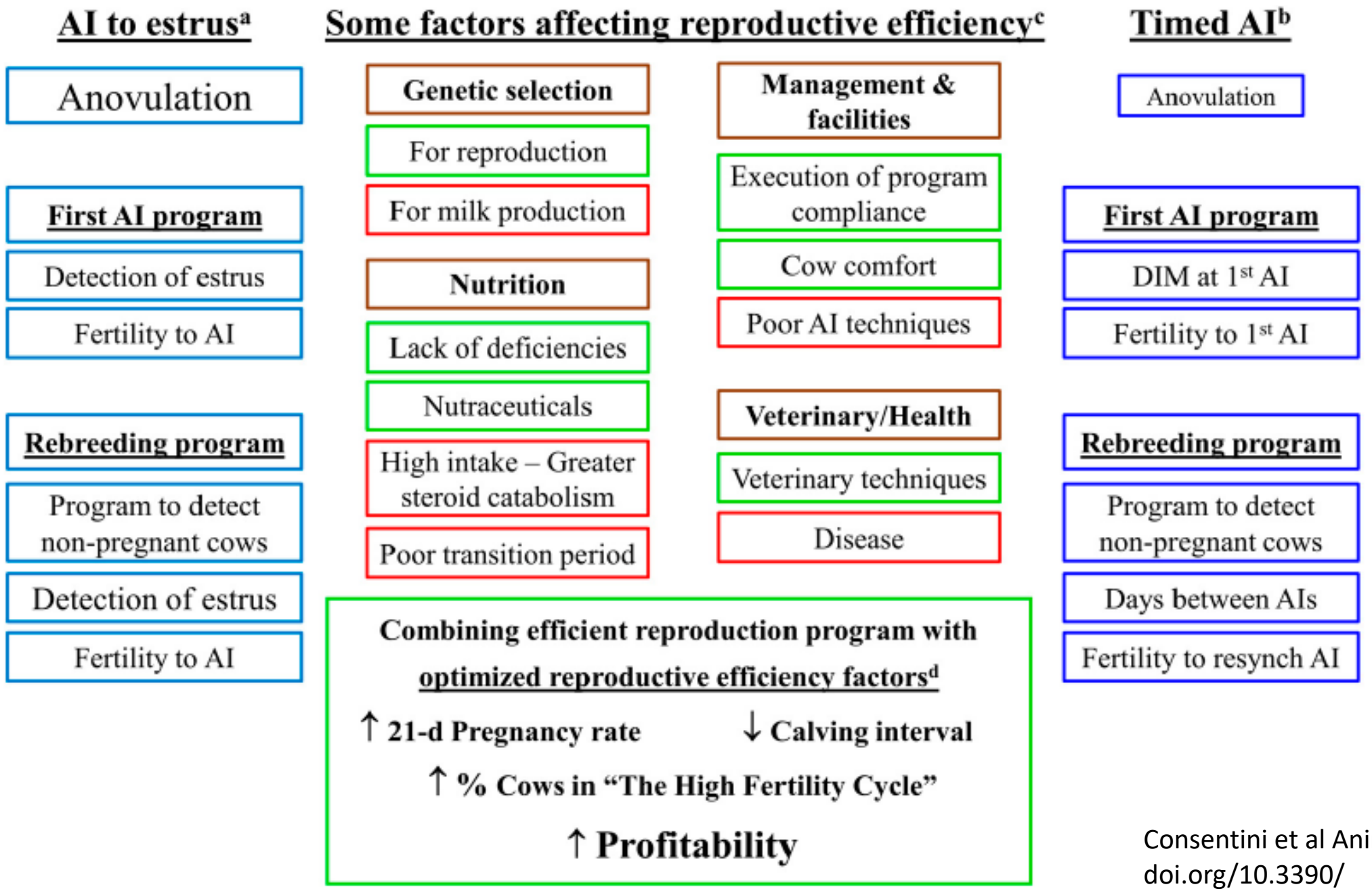
**103 cows with blood BHB ≥ 1.2 mmol/L**
**All got 5 d 300 g/d glycol, repeated up to 3X**
**Assigned to 1X or 2X milking on AMS**
**No difference in DMI**
**Pregnancy at 1st AI (~85 DIM)**
**ODM 45%  TDM 30%**




Williamson JDS 2022




Consentini et al Animals 2021
doi.org/10.3390/
ani11020301

# Production and BCS associations with cyclicity and pregnancy

- 6396 cows in 4 herds in California; all on PreSynch with estrus detection
- Average milk to 90 DIM
  - Lact 1 = 34 k g/d  Lact ≥ 2 = 48 kg/d
- Mean BCS(calving) = 3.25; AI = 2.75-3.0
- P4 at 51 and 63-65 DIM
- Pregnancy diagnosis at 30 and 58 d

Santos et al ARS 2009

# Production and BCS associations with cyclicity and pregnancy

Ovulatory at 65 DIM

- Accounting for farm, parity, season
  - BCS < 3 at calving or AI, or loss > 1 point associated with ↓ probability of cyclicity

Milk yield

- Q1 32 kg/d 73% ovulatory (P < .05)
- Q2 39 kg/d 78%
- Q3 44 kg/d 78%
- Q4 50 kg/d 75%

Santos et al ARS 2009

# Production and BCS associations with cyclicity and pregnancy

Probability of pregnancy at first AI (30 d or 58 d)

- Accounting for farm, parity, cyclic @65 DIM, HD vs. TAI, season
- No association of milk yield (~ 38%)
- BCS < 3 at calving or AI, or loss > 1 point associated with ↓ pregnancy

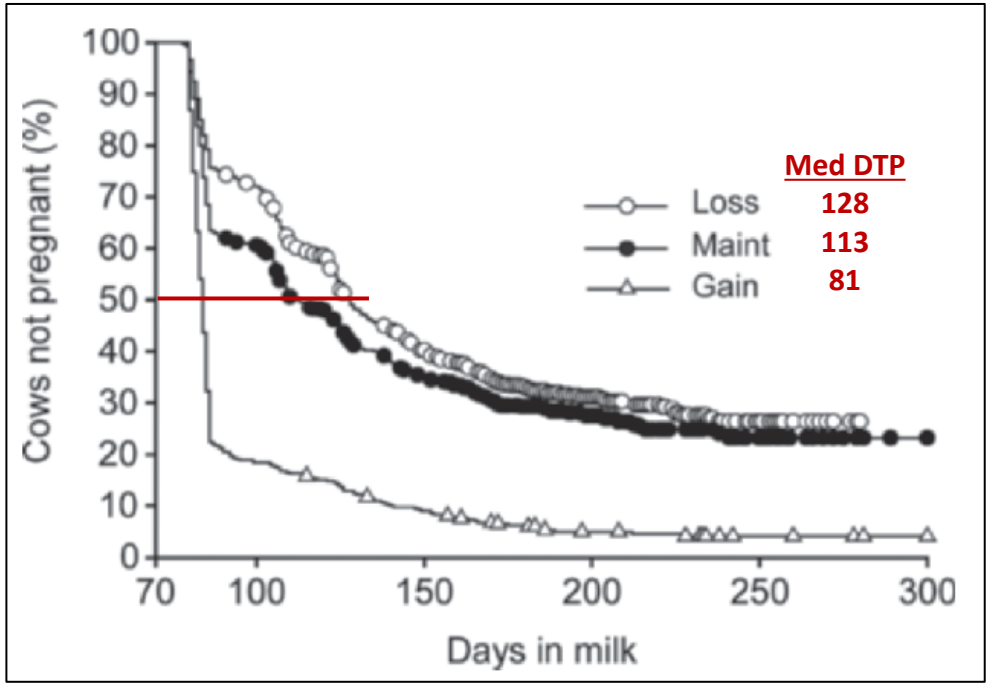
Pregnancy loss 30 to 58 d

- Accounting for farm, parity, cyclic @65 DIM, HD vs. TAI, season
- No association of milk yield (~ 12%)
- Increasing loss with lower BCS at calving or AI and especially BCS loss

Santos et al ARS 2009

# Association of BCS change from week 1 to week 3 in lean cows

**2 herds in Wisconsin – Double Ovysnch for 1st AI for all cows**
**NB similar directions but large between-farm differences**
**Carvalho et al JDS 2014** doi.org/ 10.3168/jds.2013-7809
**Confounding effects of health?**




| Item | BCS change[1] Lost | Maintained | Gained | BCS change |
|---|---|---|---|---|
| All cows | | | | |
| % of cows (n/total no.) | 41.8 (789/1,887) | 35.8 (675/1,887) | 22.4 (423/1,887) | |
| P/AI at 40 d [% (no./total no.)] | 25.1 (198/789)$^{c}$ | 38.2 (258/675)$^{b}$ | 83.5 (353/423)$^{a}$ | <0.001 |
| P/AI at 70 d [% (no./total no.)] | 22.8 (180/789)$^{c}$ | 36.0 (243/675)$^{b}$ | 78.3 (331/423)$^{a}$ | <0.001 |
| Pregnancy loss [% (no./total no.)] | 9.1 (18/198) | 5.8 (15/258) | 6.2 (22/353) | 0.34 |
| BCS at parturition | 2.93 ± 0.01$^{a}$ | 2.89 ± 0.02$^{b}$ | 2.85 ± 0.02$^{b}$ | 0.005 |
| BCS at 21 DIM | 2.64 ± 0.01$^{c}$ | 2.89 ± 0.02$^{b}$ | 3.10 ± 0.02$^{a}$ | <0.001 |
| ECM[2] (kg/d) | 30.9 ± 0.4 | 31.5 ± 0.4 | 28.7 ± 0.4 | 0.30 |

# Which cows lose condition?

- BCS ≥ 3.25 at calving very likely to lose condition
- BCS ≤ 3.0 at calving ~ 60% maintained or gained condition
- BCS loss associated with health problems
- More data needed to distinguish time order and causality
- (n = 245 cows, 1 farm, Brazil Barletta et al Therio 2017)

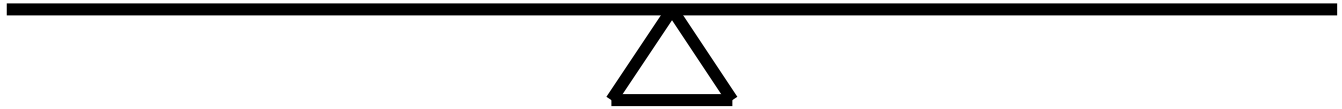
# Risk factors for uterine disease

- Species of bacteria
  - Virulence factors
  - Strain
- Level of contamination
  - Diversity of the uterine microbiome

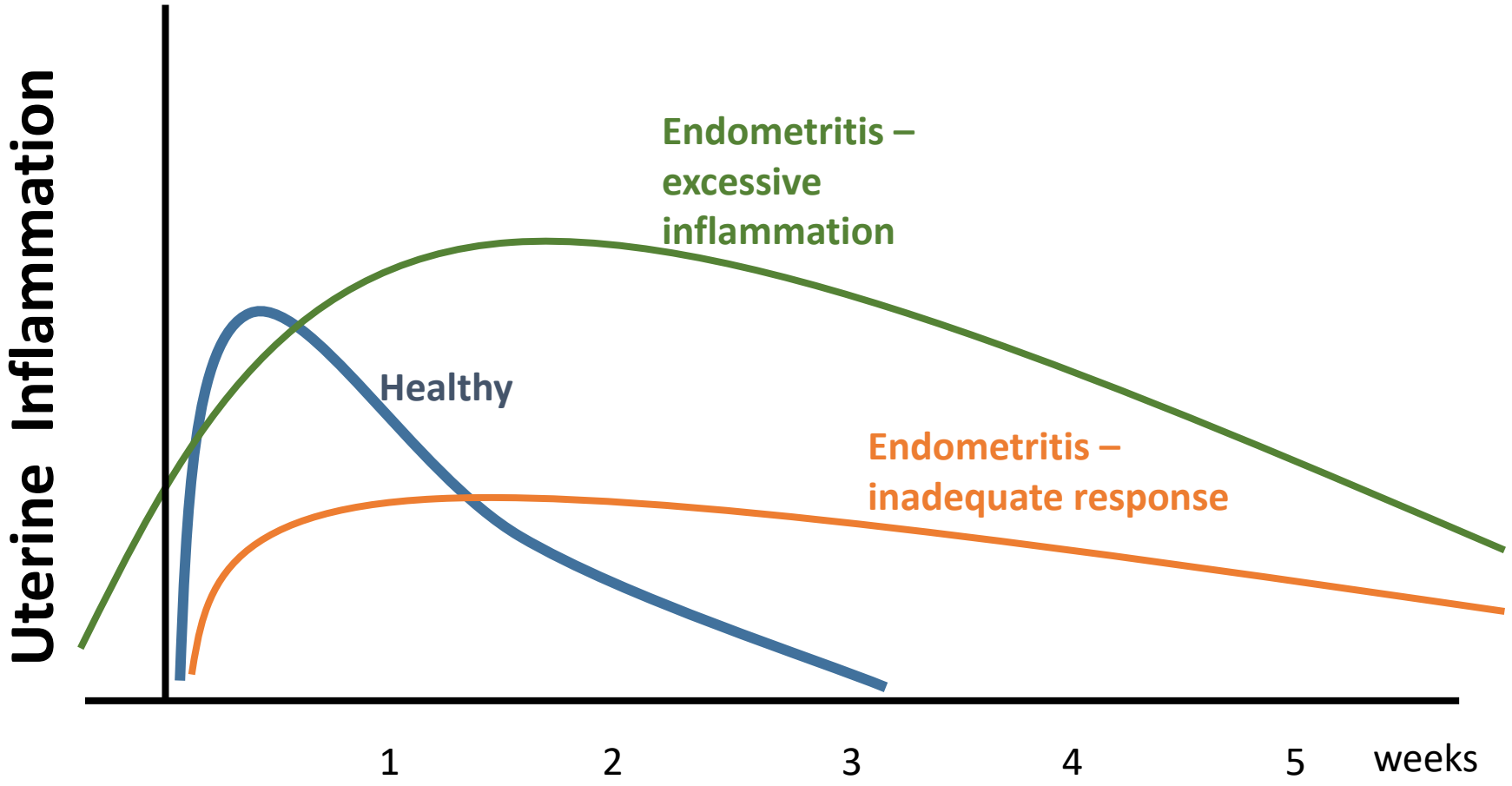
- Dry matter intake
- Energy and lipid metabolic health
- Stressors & hormonal changes
- Hypocalcemia

**Bacteria**

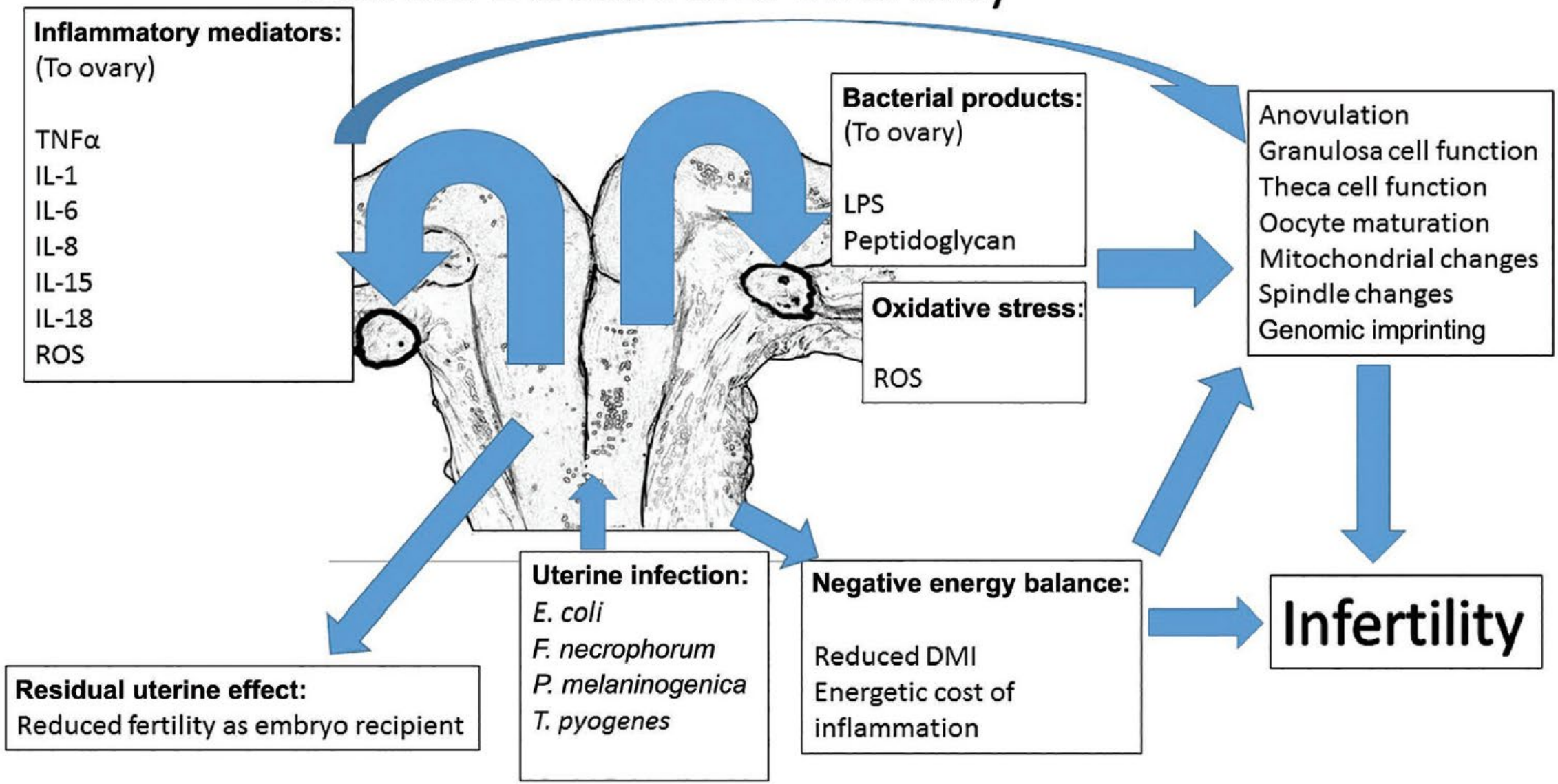
**Immune response**
**Regulation of inflammation**



# Concepts of inflammatory response

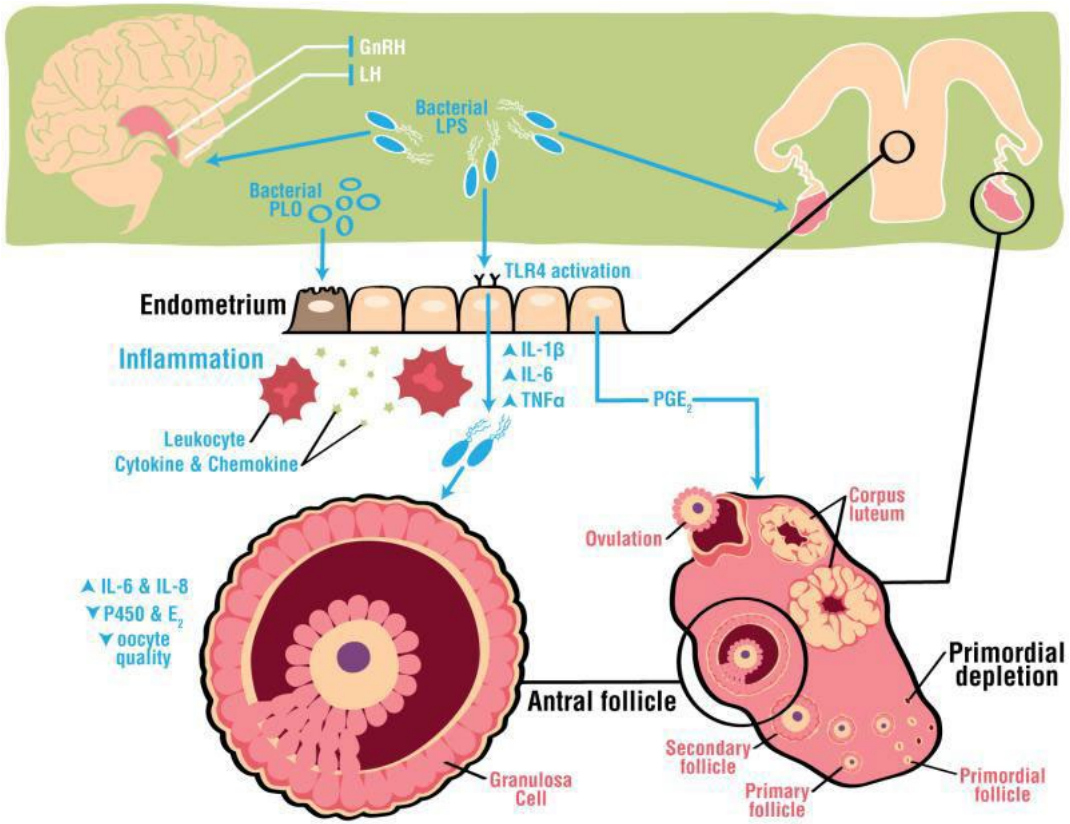


# Uterine Disease and Infertility

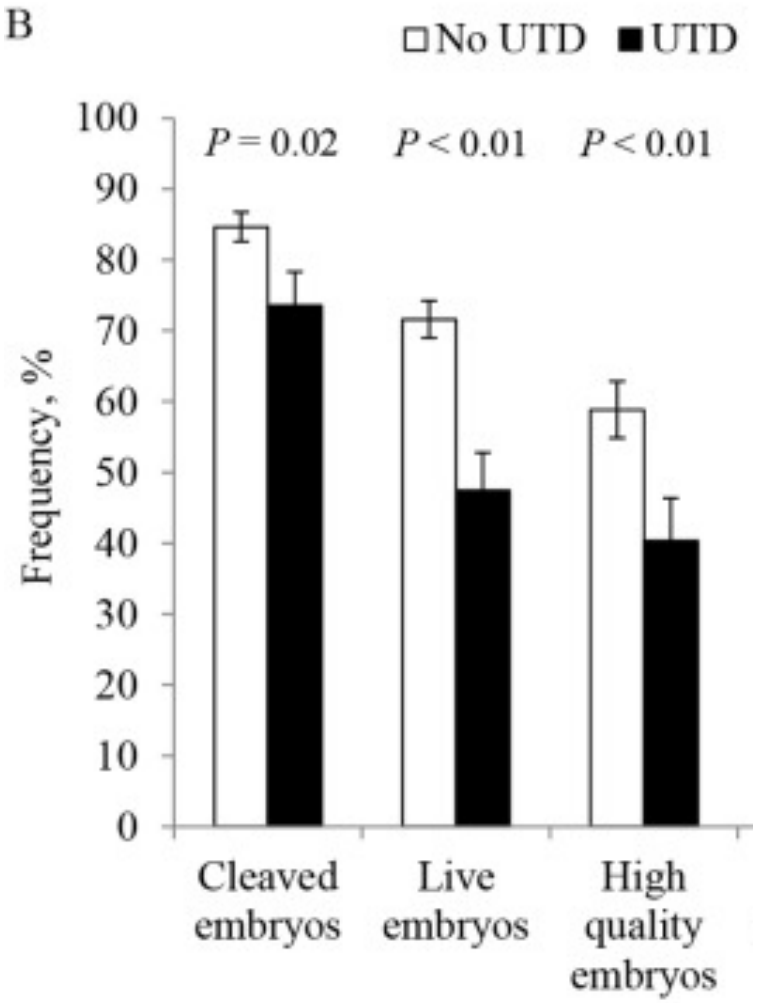



Gilbert JDS 2019

# Mechanisms of uterine disease effects on fertility

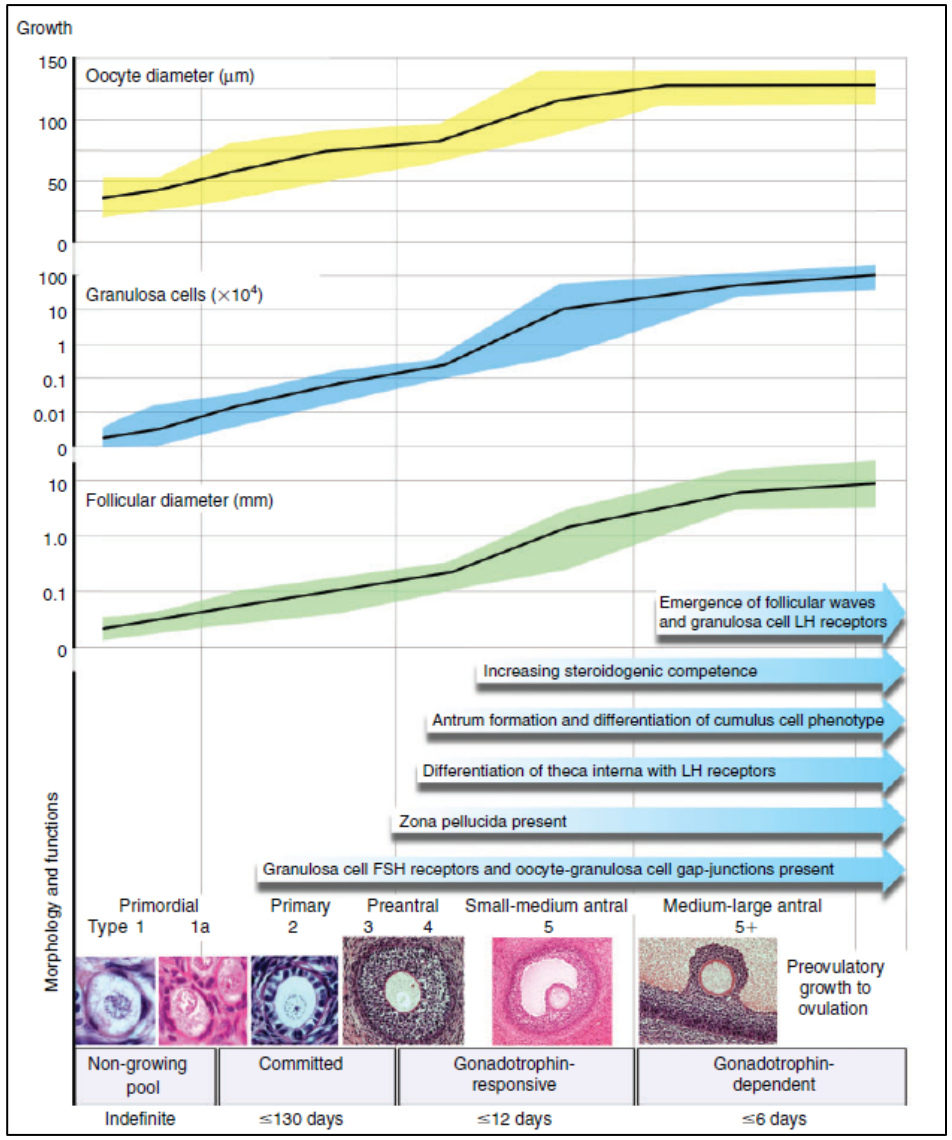



Bromfield et al., 2015



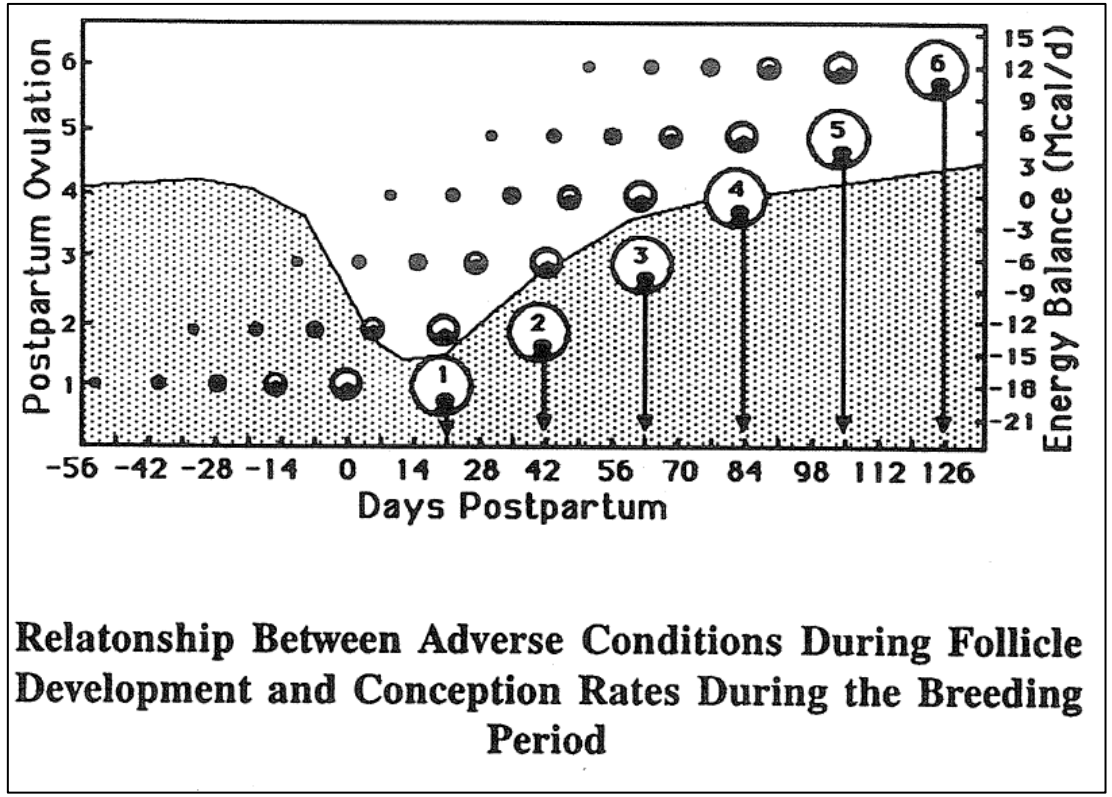

Ribeiro et al., 2016

# Follicular development occurs over 2 to > 4 months



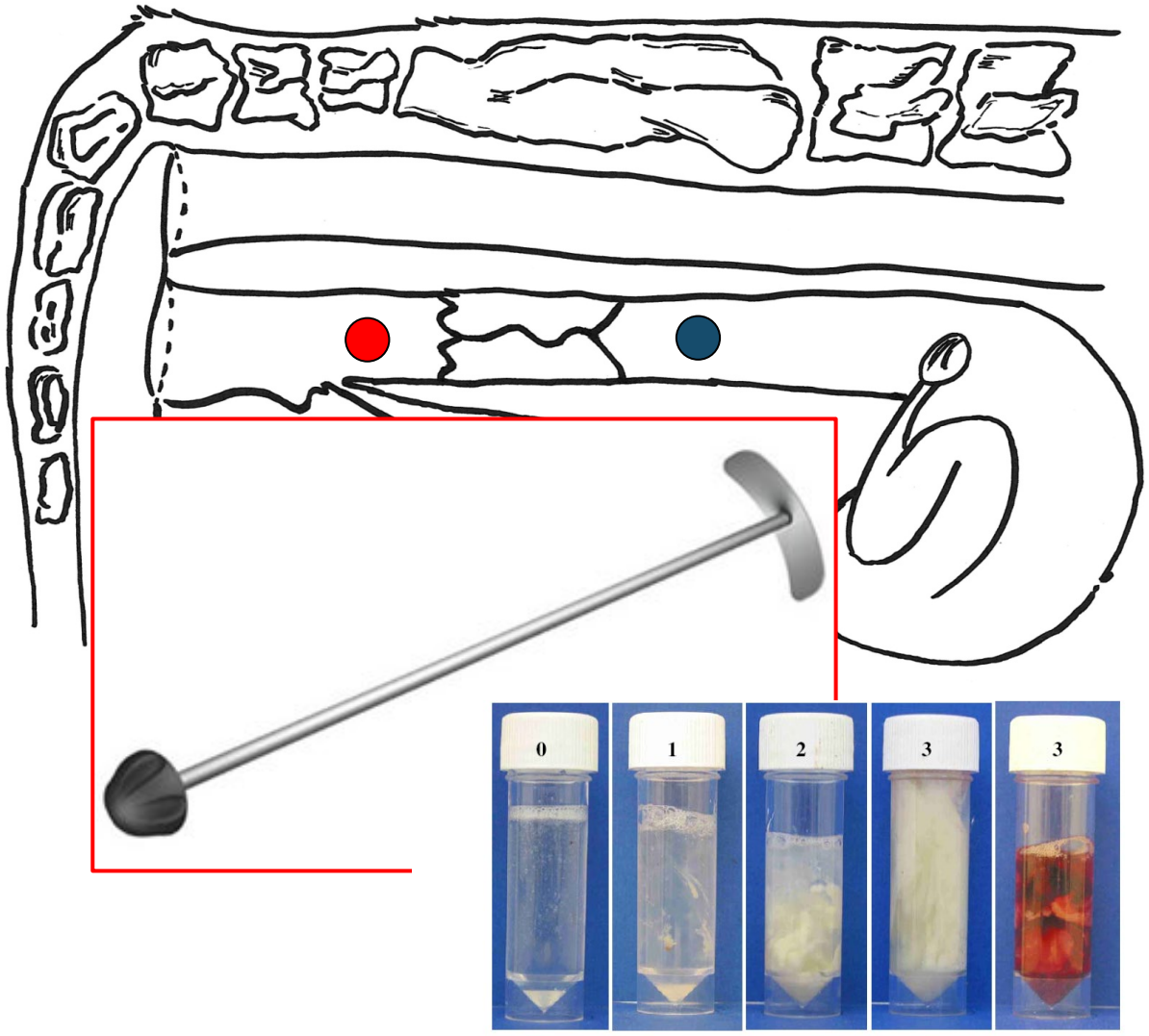

Ewe model - Scaramuzzi et al RFD 2011

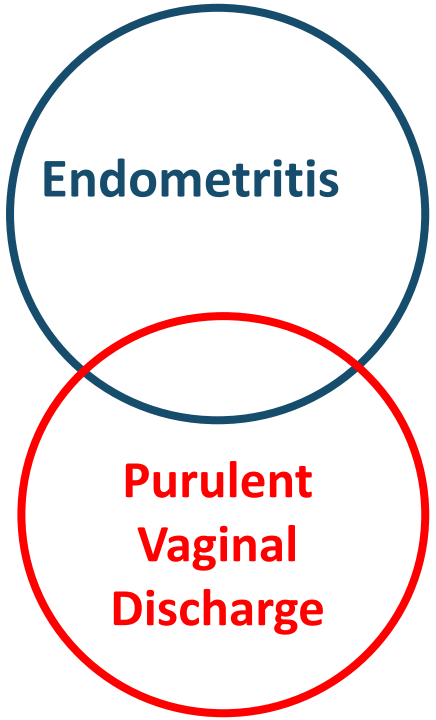
## Britt hypothesis (1992)




**Relatonship Between Adverse Conditions During Follicle Development and Conception Rates During the Breeding Period**

# Reproductive tract infection and inflammation




Each affects 15 – 20% of cows

# Reproductive tract inflammatory disease

- PVD ≠ endometritis
  - Poor agreement (42% of cows with PVD had concurrent endometritis; Dubuc et al 2010a)
  - Different risk factors (Dubuc et al 2010b)
  - Additive effects on reproduction and pregnancy loss (Dubuc et al 2010; Lima et al 2013)
  - Cervicitis is a co- or independent factor in many cases

**PVD**

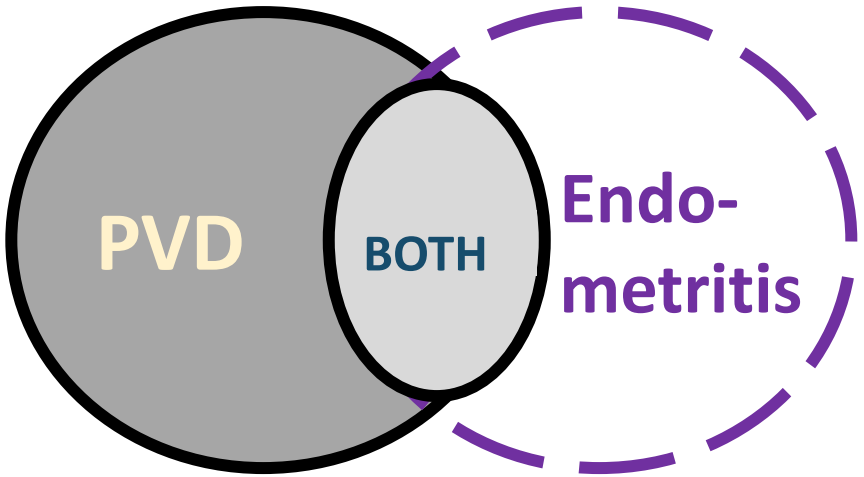
Metricheck

Associated with:

*Trueperella pyogenes*

Endometrial trauma

Treatment = Cephapirin IU




**Endometritis**

Cytology

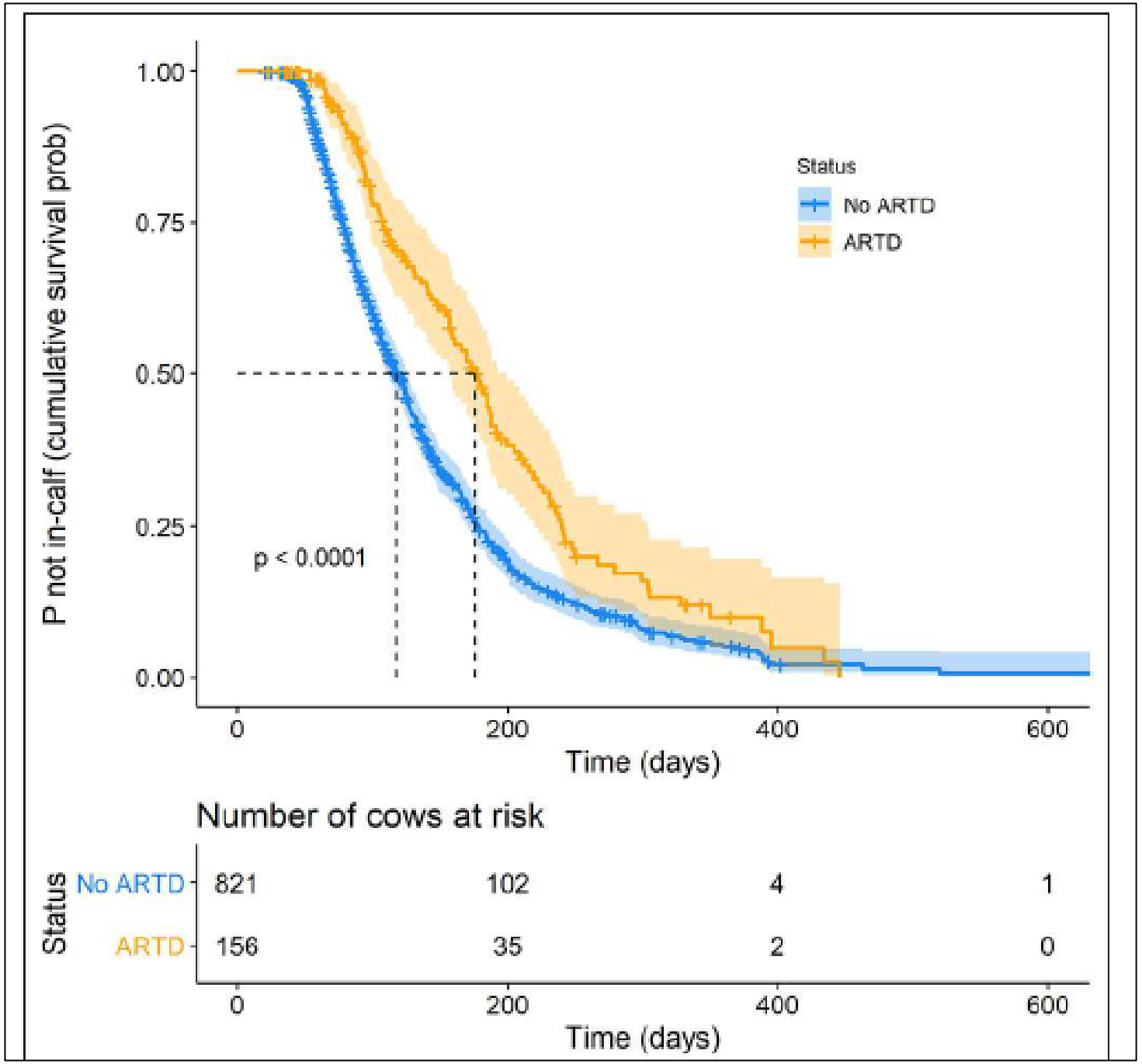
Not associated with concurrent bacterial infection

Hypothesis: dysregulation of postpartum inflammation

Treatment = ??

# Effect of PVD

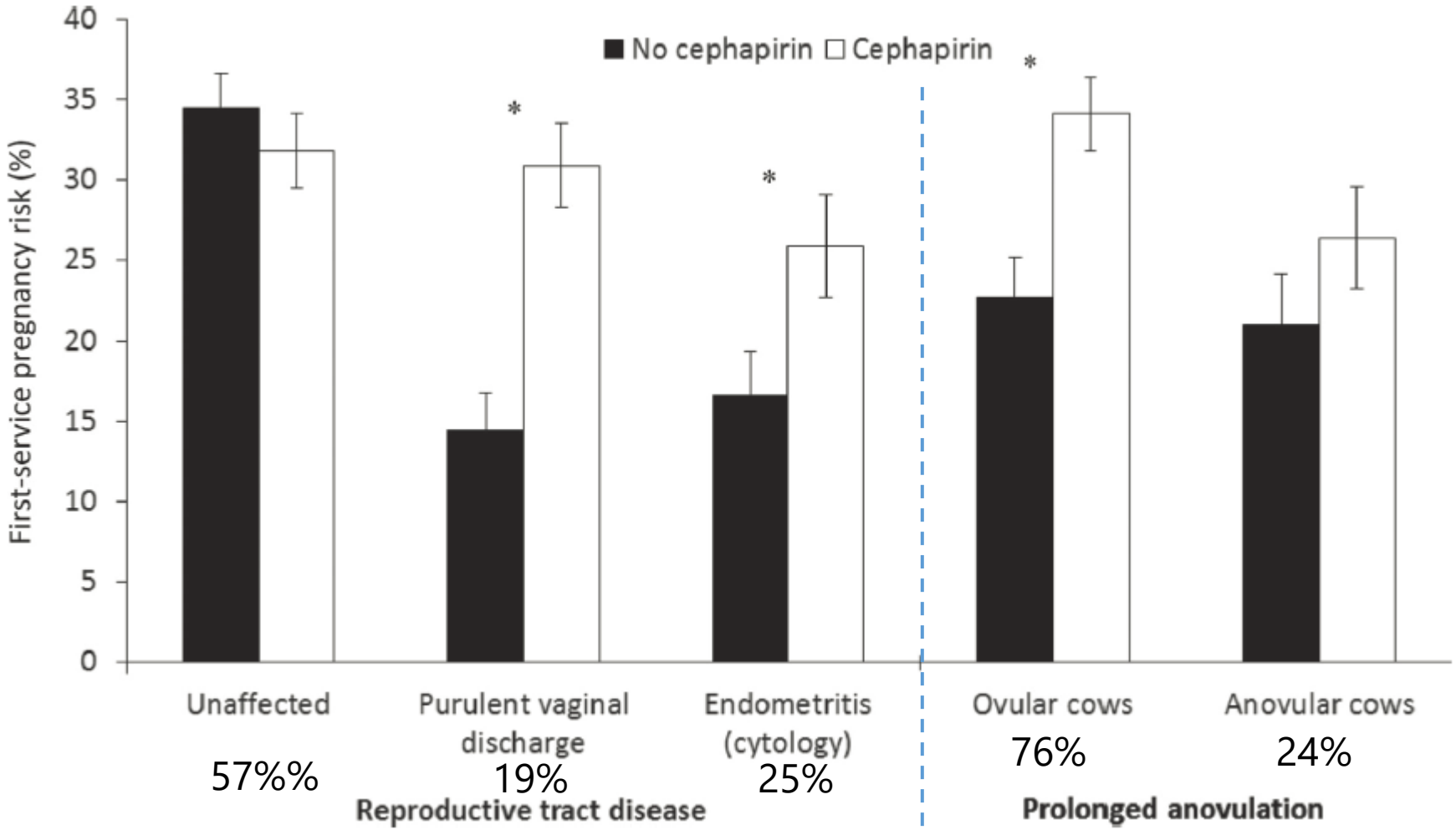
- Observational study, 3 herds in Australia
- Diagnosis at ~35 DIM
- Despite treatment with PGF (repeated at ~ 55 DIM if still clinical)




Hay et al 2019 FrontVetSci 2019

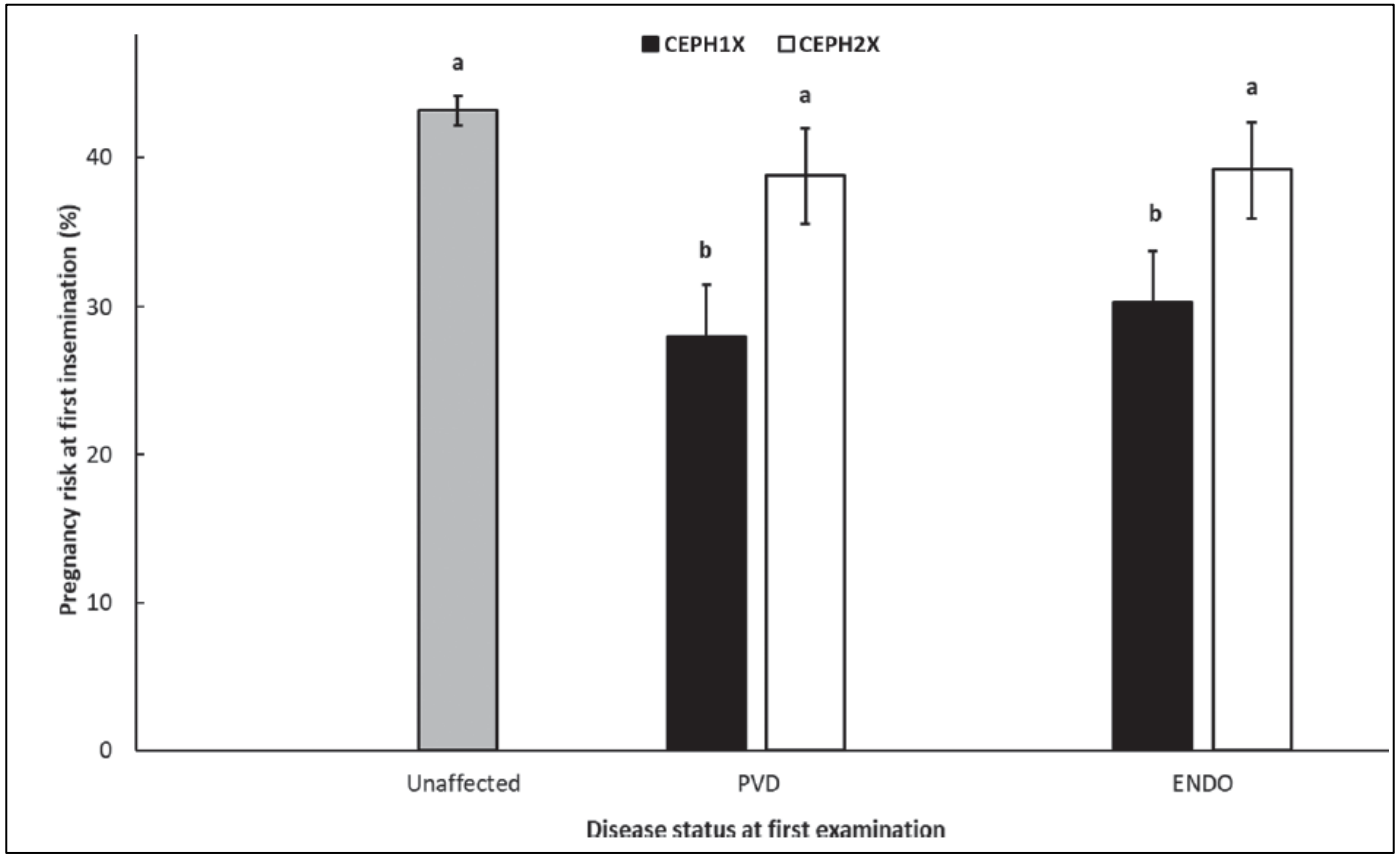
# Treatment of PVD or endometritis with IU cephapirin

2259 cows Examined at 35 ± 7 DIM by Metricheck and cytobrush




Denis-Robichaud & Dubuc, 2015

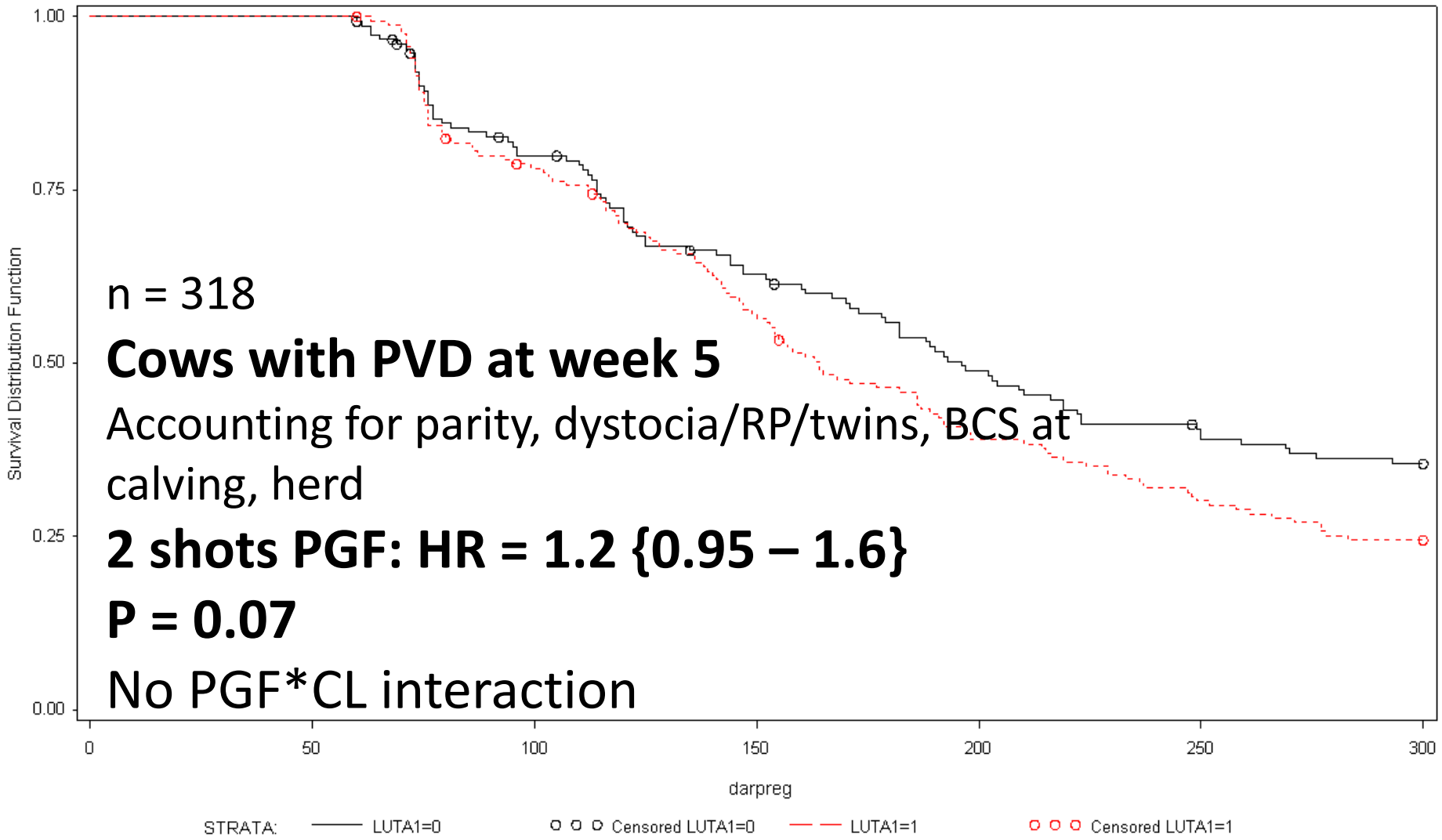
# 1 vs 2 IU treatments for PVD or endometritis




Dubuc et al JDS 2021 doi.org/10.3168/jds.2020-19537

| | | Category | | | | | |
|---|---|---|---|---|---|---|---|
| | | Overall | | Purulent vaginal discharge | | Endometritis | |
| Item | Unaffected | CEPH1X | CEPH2X | CEPH1X | CEPH2X | CEPH1X | CEPH2X |
| N | 1,946 | 1,294 | 1,301 | 522 | 516 | 772 | 785 |

# PGF treatment of PVD




n = 318

**Cows with PVD at week 5**

Accounting for parity, dystocia/RP/twins, BCS at calving, herd

**2 shots PGF: HR = 1.2 {0.95 – 1.6}**

**P = 0.07**

No PGF*CL interaction

# Treatment of PVD with PGF

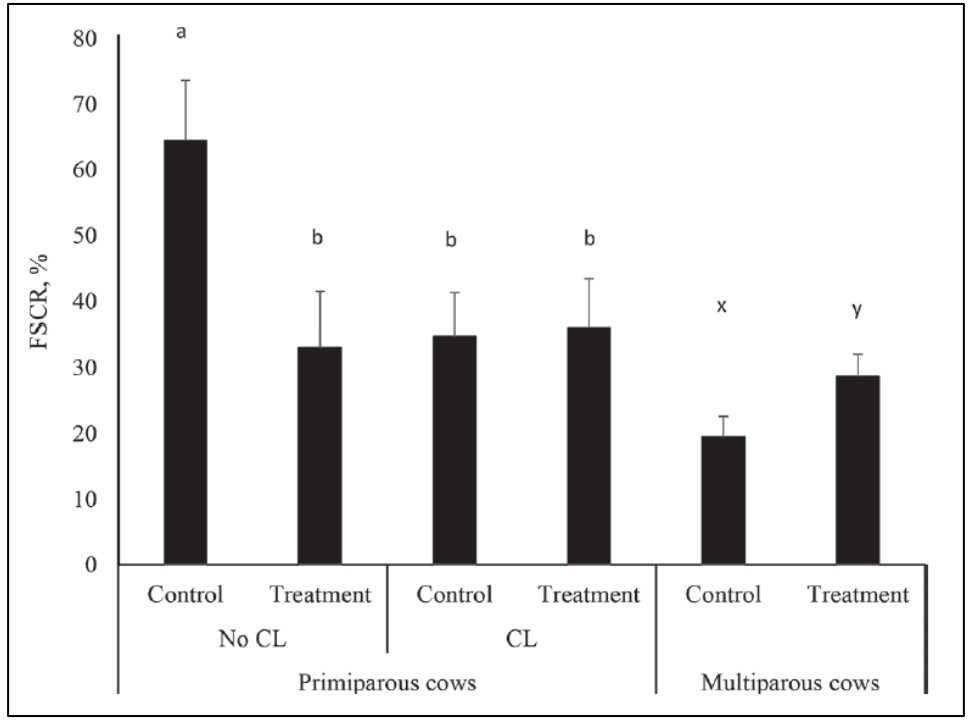
- 2473 cows from 1 farm in Germany screened weekly with Metricheck at 32 DIM
- No effect on time to 1st AI

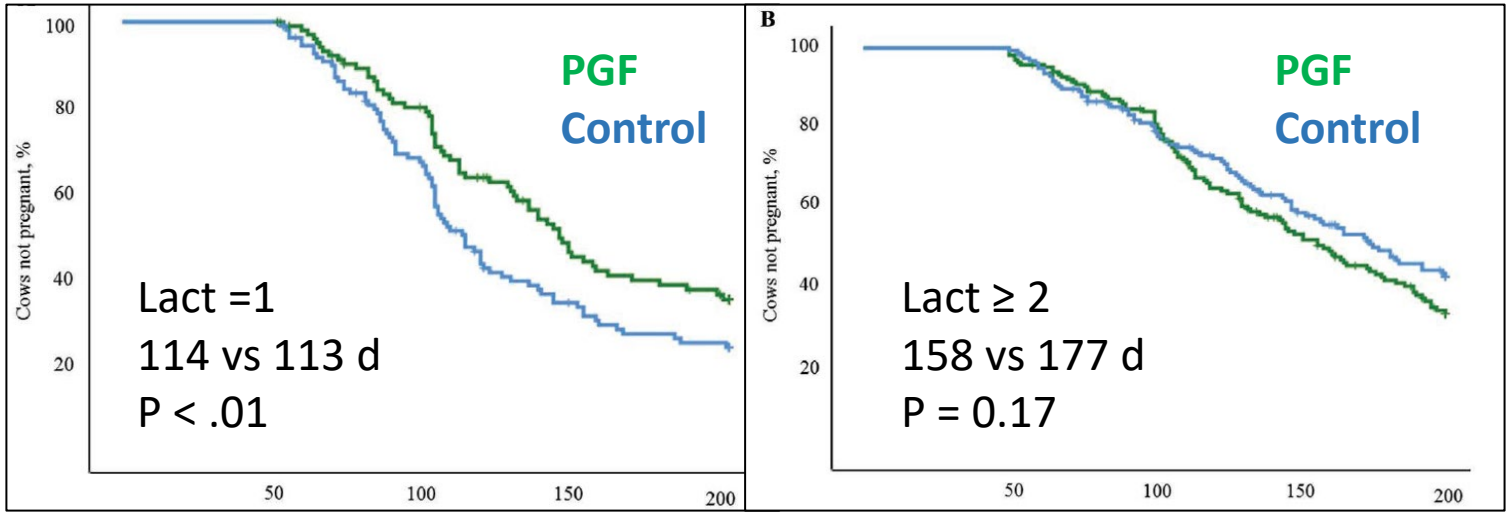
Lact=1

- No benefit, some harm for pregnancy at 1st AI
- Longer time to pregnancy

Lact ≥ 2

- Increased pregnancy at 1st AI
- No difference in time to pregnancy

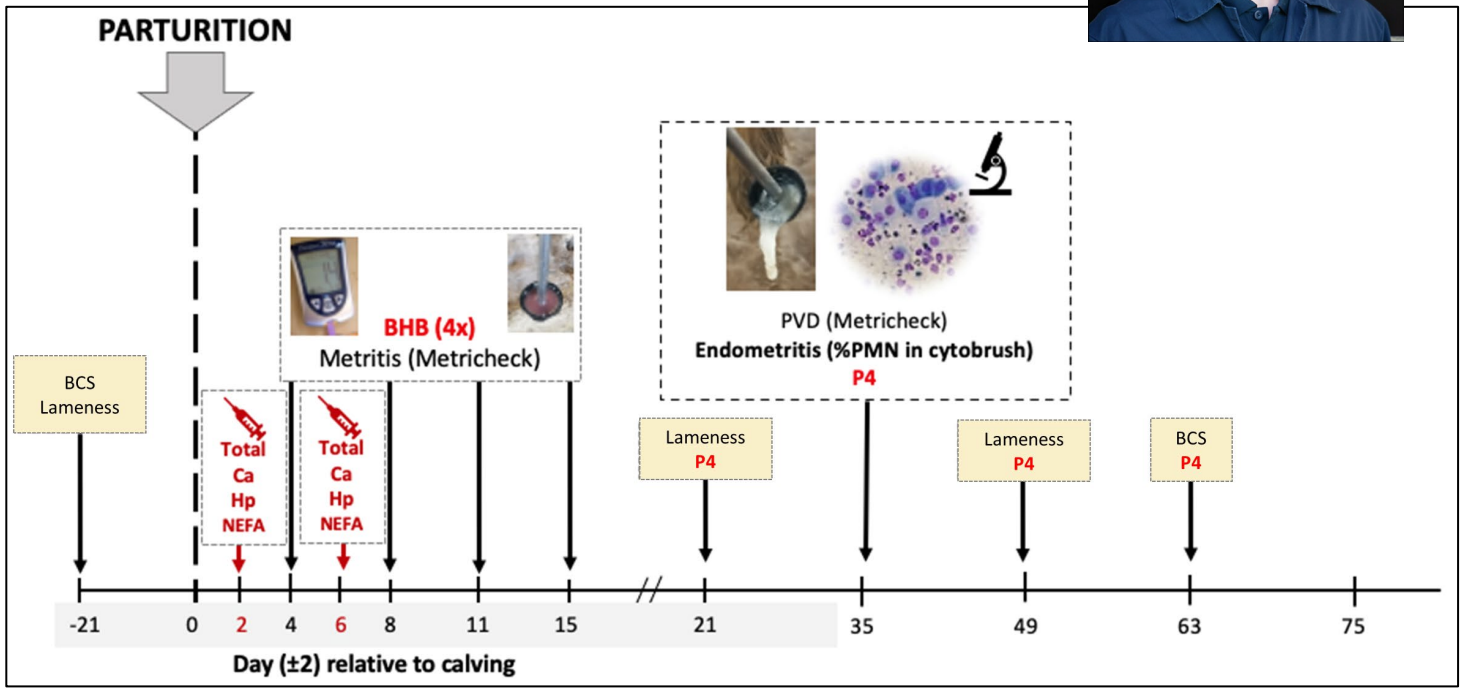



Borchart et al JDS 2018

# Transition health and estrus detection

- Prospective observational study in 2 commercial dairy herds in Ontario, Canada (~450 lactating cows each) from May 2019 to April 2021
- Prepartum Holstein cows (n = 1,357) were enrolled and examined
- **1st AI primarily based on detection of estrus** by AAM from 50 to 75 d, or timed AI thereafter




| Prevalence of risk factors | | | |
|---|---|---|---|
| Retained placenta (RP) | **10%** | Lameness (49 d) | **14%** |
| Haptoglobin at d6 (≥ 0.5 g/L) | **48%** | Acyclic by 49 d | **15%** |
| Hyperketonemia (≥ 0.7 m*M*) | **50-55%** | BCS Loss (≥ 0.50 point by 63 d) | **53%** |
| Endometritis (≥ 2.4% PMN) | **44%** | One clinical disease | **29%** |
| Purulent vaginal discharge (PVD) | **21%** | Multiple clinical diseases | **18%** |

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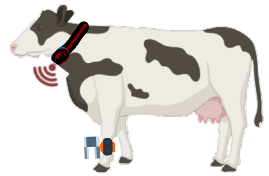
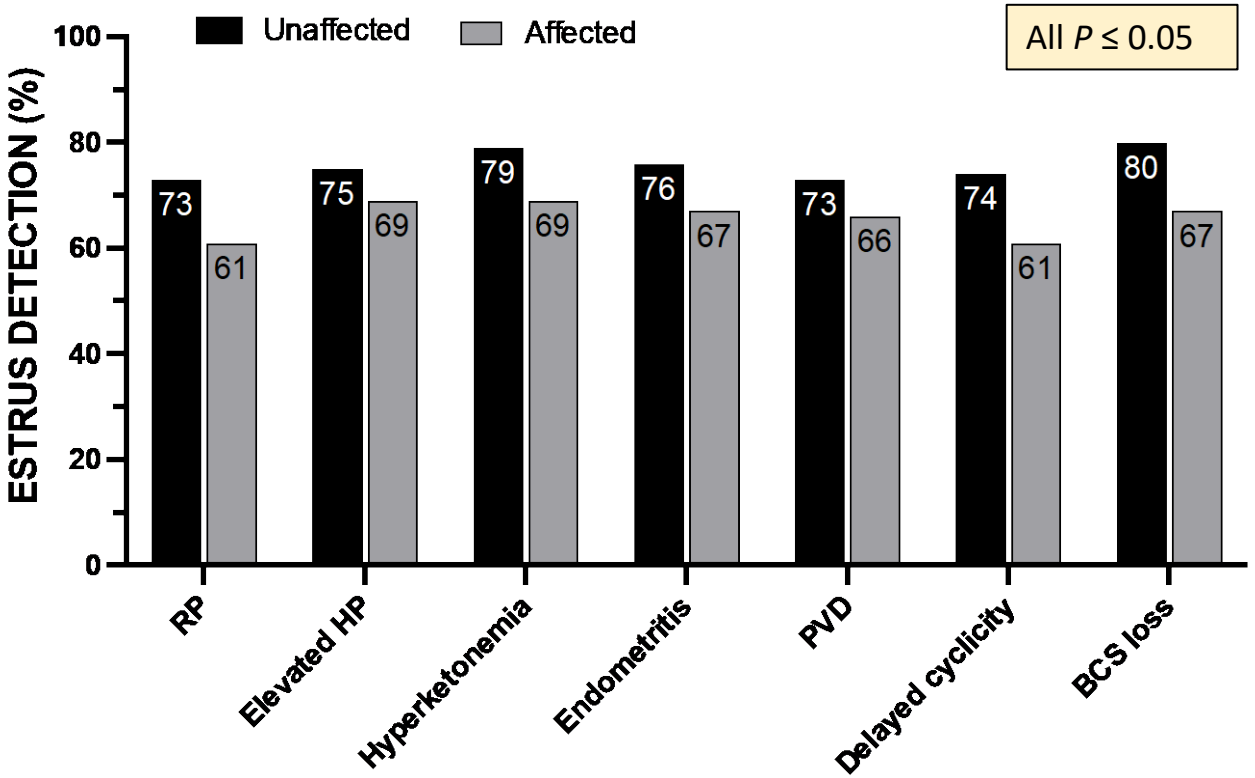
# Transition health associations with estrus

n = 1,210

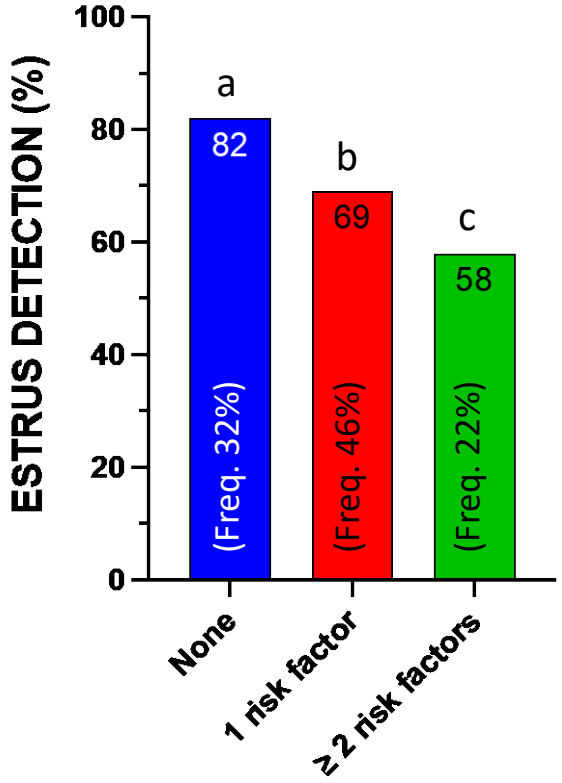


**70%** of cows detected in estrus by 75 DIM



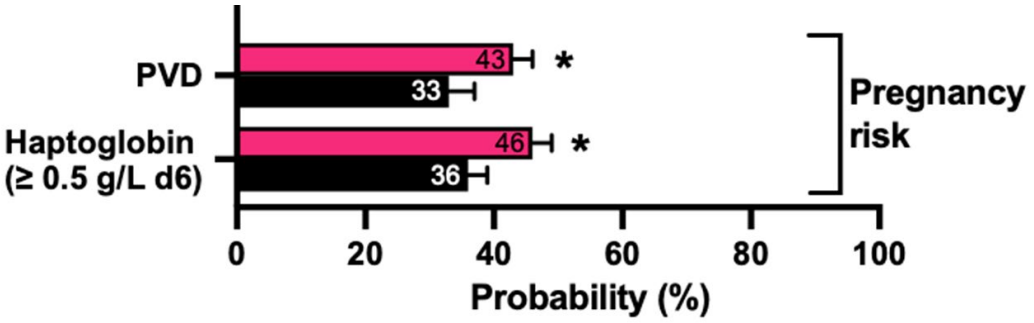

**ONLY RISK FACTORS DIAGNOSED ON FARM**

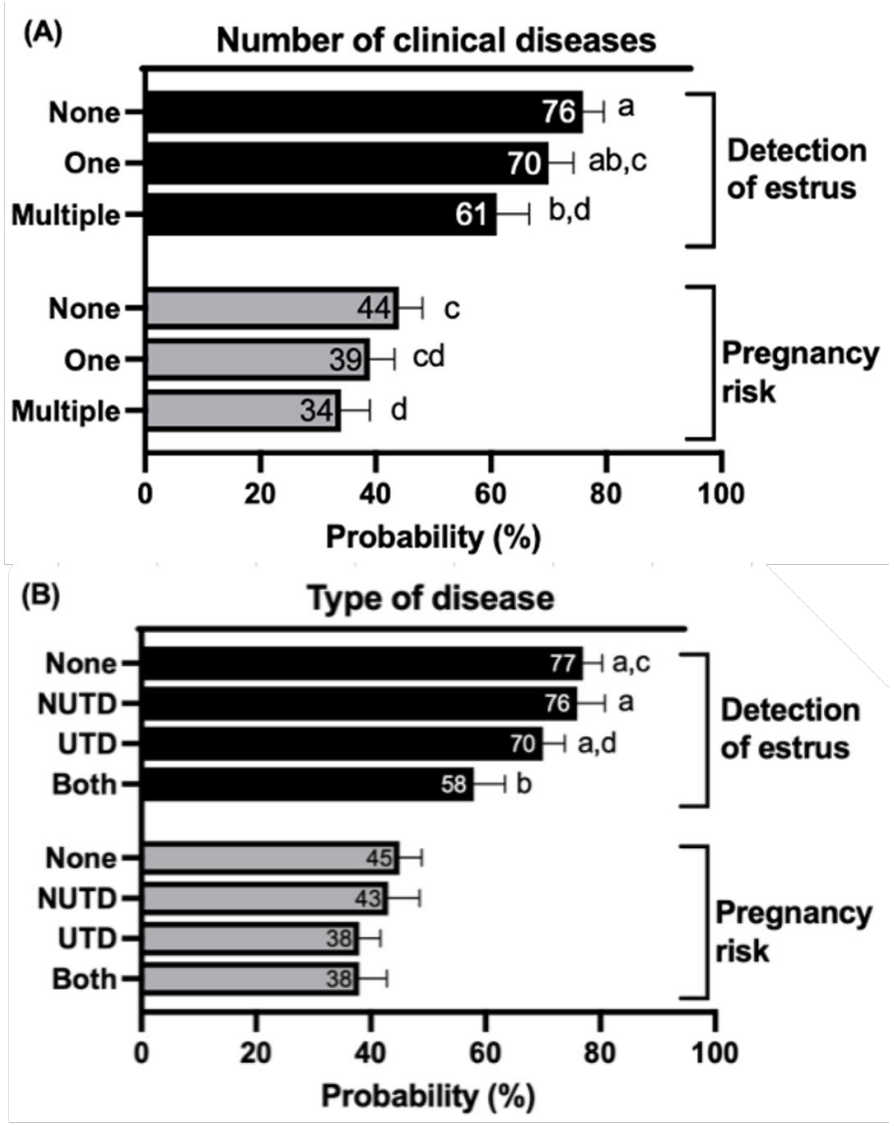
***RP, PVD, lameness***
***BCS loss (≥ 0.50-point)***




- *Elevated haptoglobin (HP): ≥ 0.5 g/L at 6 (± 2) DIM*
- *Hyperketonemia: ≥2 samples of BHB ≥0.9mM (4 DIM) or ≥0.7mM (8, 11, or 15 DIM)*
- *Endometritis: ≥ 2.4% PMN at 35 (± 3) DIM*
- *Delayed cyclicity: Acyclic by 49 (± 3) DIM*
- *BCS loss: ≥ 0.50-point loss from 3 wk prepartum to 9 wk postpartum vs. no loss*

# Transition health associations with estrus and pregnancy

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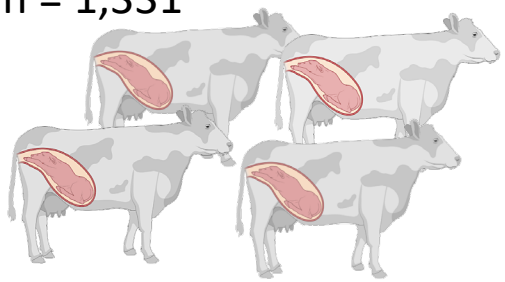
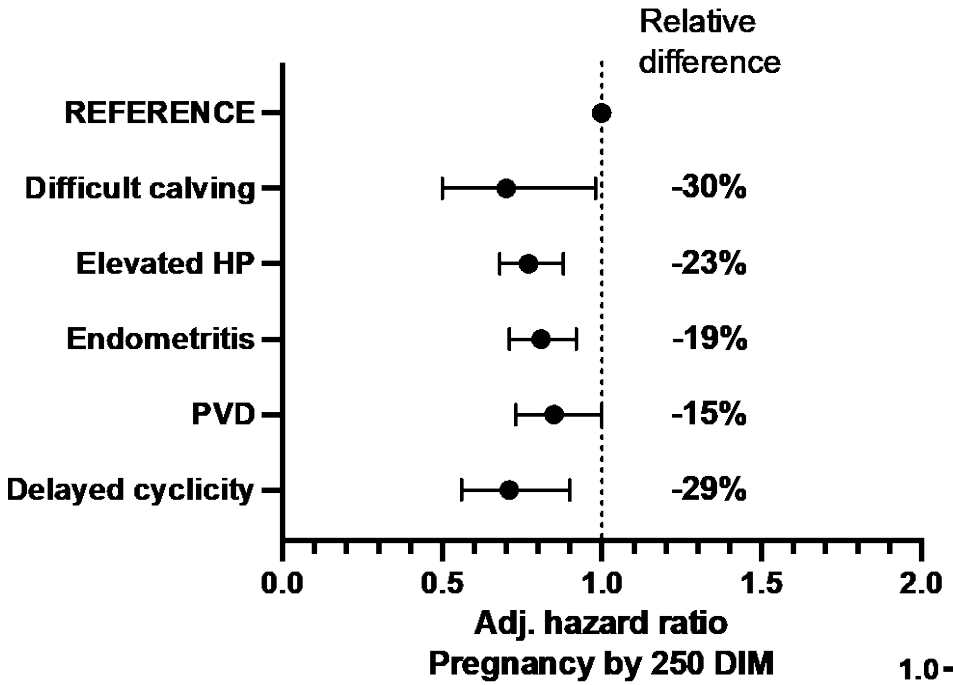
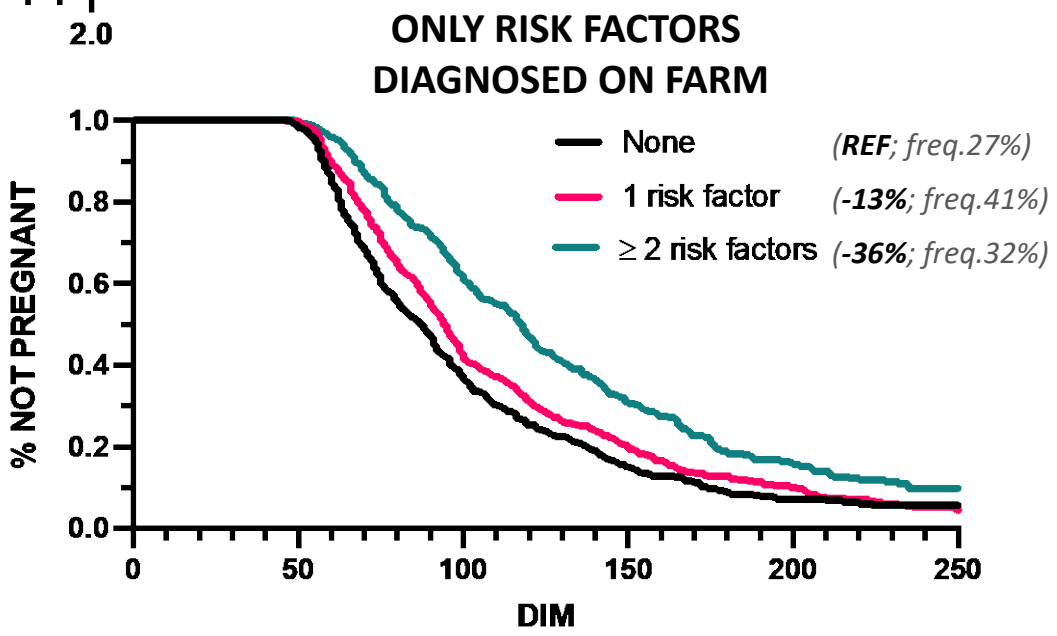
# Time to pregnancy

n = 1,331

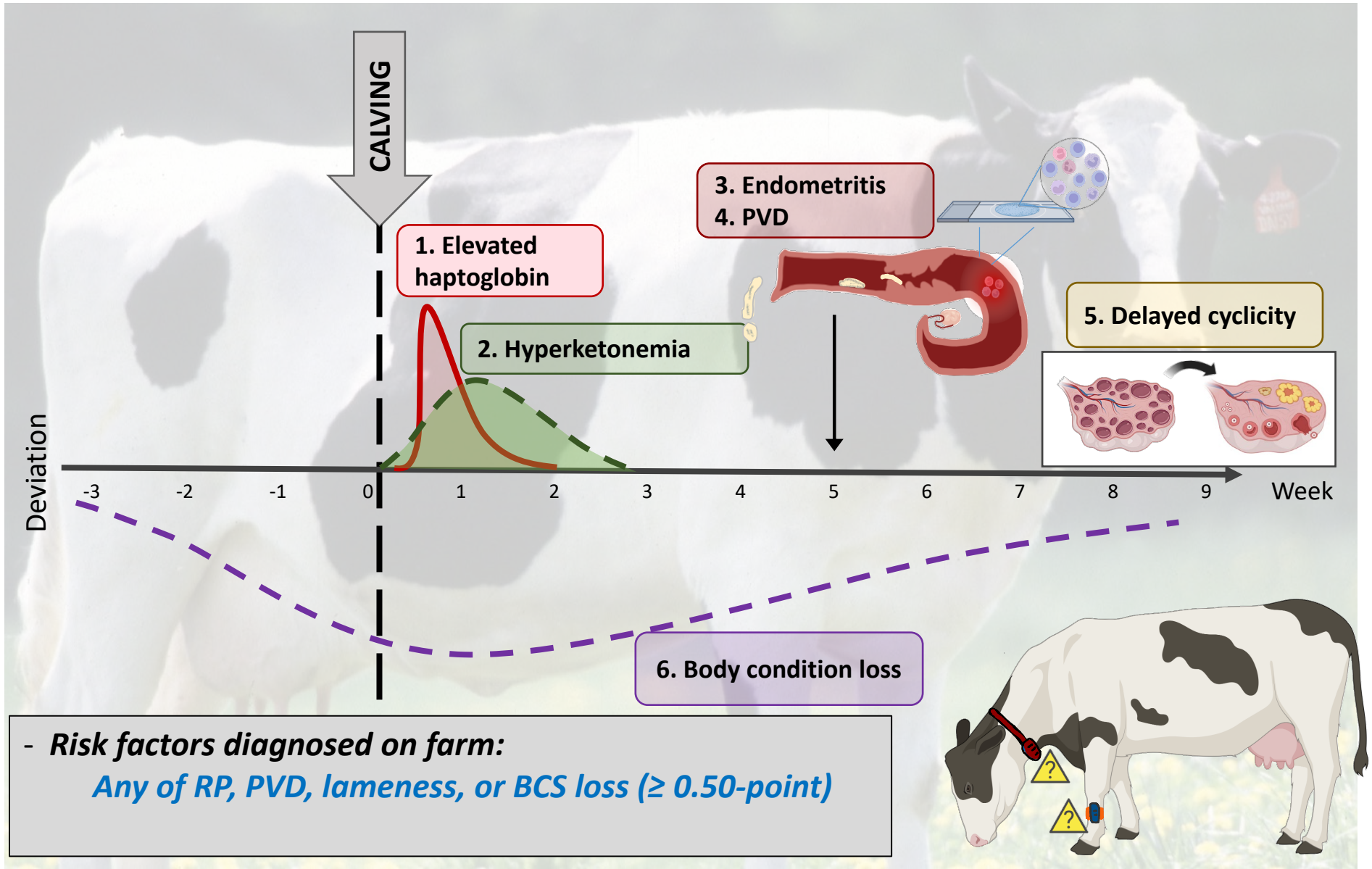





- *Elevated Hp: ≥ 0.5 g/L at 6 (± 2) DIM*
- *Endometritis: ≥ 2.4% PMN at 35 (± 3) DIM*
- *Delayed cyclicity: Acyclic by 63 (± 3) DIM*
- *Risk factors diagnosed on pregnancy: Difficult calving, metritis, PVD, lameness, or BCS loss (≥ 0.50-point)*

# Risk factors for reduced probability of estrus detection




- ***Risk factors diagnosed on farm:***
  ***Any of RP, PVD, lameness, or BCS loss (≥ 0.50-point)***

# Transition checklist

## Goal: Optimize metabolic health & immune function

## Means: Manage cows to maintain feed intake

**Management**

- Feed daily for 3-5% left over; ideally ≥ 2X/d
- ≥ 75 cm (30") feed bunk space per cow
- ≤ 85% cows: freestalls
- > 14 $m^2$ (130 $ft^2$) of bedded pack/cow
- Build for 130-140% of average monthly calvings
- Large enough stalls; adaptation to stalls
- < 24 h in calving pen
- Minimize group changes
- Separate heifers if it does not violate the above
- Heat abatement (fans, soakers) when THI > 68
- BCS = 3.0 - 3.25 at calving
- Diagnose & treat PVD at 4-6 weeks

**Transition diet**

- 2-stage dry period; 3-4 weeks on close-up diet
- Meet but do not exceed E requirement 8 to 3 weeks prepartum; 1100 g MP per day
- Water ad lib; 10 cm linear per cow; 2 sources per pen
- Vitamin E: far-off: 1000 IU /d; close-up: 2000 IU/d; 0.3 ppm selenium (Ideally ~ 6 mg/d)
- DCAD < -100 mEq/kg; urine pH 6.0 – 6.5

**Monitoring**

- NEFA <0.3-0.4 in last week prepartum; <0.7-1.0 in week 1
- BHB < 0.8 mM in week -1
- BHB < 1.1 mM in week 1
- BHB < 1.2 mM weeks 2 – 3
- Ca > 2.15 mmol/l at 4 DIM

Stephen LeBlanc November 2022

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