What's happening to the older cows? Understanding the geriatric cow



Ian J Lean BVSc, DVSc, PhD, MANZCVS Scibus & University of Sydney
Helen M Golder PhD Scibus & University of Sydney
Jose EP Santos PhD University of Florida, USA
Stephen E LeBlanc PhD University of Guelph, Canada
Todd Duffield PhD University of Guelph, Canada
David Sheedy MVPM University of Sydney

Delivery Organisations



Partner Organisations





Why Bother?



- By changing the age structure we can produce > 16% more milk
- We have 8% more x-bred calves or pure-bred heifers to sell
- Can apply more selection pressure
- Decrease GHG intensity and total
- WHAT IS STOPPING US &
- WHAT ARE THE DOWNSIDES??







- Something may be a good opportunity **but....** is it worth the effort?
- Why is there a bother with getting that extra milk?





- We got together with friends & colleagues to gather more than 36,000 cows of data from OZ, USA and Canada collected in carefully conducted studies
- We wanted to look at the health, reproduction, body condition and metabolism of these cows to help direct our future studies in DairyUP
- Our goal was to look at why we are losing cows!!
- Key issues include profit, cow care, social license our goal is to De-risk the dairy business and have 'happy cows'
- H_A: We hypothesized that parity, production system (categorized as pasture-based or intensively fed with a mixed or component-fed ration), milk, milk-fat or -protein percentage, and milk solids production would influence survival, reproductive, health and metabolism.



- 13 studies 32,783
- We excluded non-Holstein
- TMR fed 28,675; Pasture 4,108
- Key outcomes
- Hazard of not-being bred
- Time to pregnancy
- Pregnancy to first mating
- Odds of pregnancy in a lactation
- Influence of milk, milk fat, protein
- Production and percentage of solids





Statistical analysis



- Survival analysis models were also used to evaluate time not bred over the first 120 DIM (HNBRED), and HPREG. Cox's proportional Hazards conditions were met.
- For pregnant in the lactation (OPAL) and Preg to 1^{st} service LR used.
- Similar models for disease and linear mixed models for metabolites
- All models evaluated the fixed effects of parity (1 to \geq 5),
- production 'system' (pasture or intensively fed),
- and centered study year and the random effect was cow nested within Group.
- The linear and quadratic effect of centered production variables (milk yield or fat% or protein%, fat yield, protein yield, or milk solids yield) were also evaluated and the random or frailty effect was Group.
- Interactions of parity with production variables were tested and included when these improved the model fit as assessed by AIC and BIC.
- A backward stepwise approach was used to remove non-significant terms (P > 0.05) from all survival and logistic regression models.



Summary of 9 prospective studies used in the survival database



Unlocking potential

Reference	Study year	Country	Production system	N cows	Intervention	Observation period (d)
Duffield et al. (1999a)	1994	СА	TMR	996	Monensin	95
Duffield et al. (2002)	1998	СА	TMR	152	Monensin	120
LeBlanc et al. (2002)	1998	СА	TMR	975	Vitamin	120
Golder et al. (2019)	2016	USA	TMR	6,395	Enzyme	210
Lean et al. (unpublished)	2003	AU	Other	330	Micronutrient	329
Vieira-Neto et al. (2021a)	2012	USA	TMR	9,076	Observational	300
Pinedo et al. (2020)	2013	USA	TMR	11,489	Observational	305
Golder et al. (2021) Exp. 1	2017	AU	Other	764	Calcidiol	305
Golder et al. (unpublished)	2020	AU	TMR	603	Amino acid	305
Total				30,780		



What did our survival data look like?



- Survival 30,780
- We excluded non-Holstein
- The mean for all parities was 2.28 SD 1.46
- Pasture 1,697
- Key outcomes
- All removals
- Deaths
- Sales





Parity, study year, and feeding system and interactions on time to death or being sold, time to sale only, or time to death only.

Hazard ratio \pm SE and P-values from models including parity, study year, and production system, and interaction between parity and production system.

Measure	Ν	2	3	4	≥ 5	Main effect	Study year	Production system	Parity × system
Died or sold	30,780	0.86 ± 0.17 ^{de} (0.387)	0.71 ± 0.16 ^{ae} (0.459)	0.91 ± 0.24 ^{abe} (0.718)	1.83 ± 0.28 ^{abcd} (<0.001)	<0.001	NS	NS	<0.001
Sold	30,780	0.66 ± 0.16 ^e (0.082)	0.58 ± 0.15 ^e (0.031)	0.68 ± 0.21° (0.217)	1.54 ± 0.26 ^{abcd} (0.012)	<0.001	NS	NS	<0.001
Died	30,780	1.57 ± 0.14 ^{abde} (<0.001)	2.77 ± 0.25 ^{abde} (<0.001)	3.95 ± 0.38 ^{abc} (<0.001)	4.27 ± 0.43 ^{abc} (<0.001)	<0.001	0.001	NS	NS

TMR (intensively fed) vs pasture fed, the referent is pasture fed: NS non-significant and excluded from the model



Summary of the 13 studies used in the reproductive database

Study year	Country	Production system	N cows	Milk compo- nent data	Intervention	Period of observation for pregnancy (d)	Reference
1992	Australia	Pasture	237	N	observational	368	Curtis (1997) Curtis and Lean (1998)
1994	Australia	TMR	81	Y	protein & genetic merit	150	Westwood et al. (2000) Westwood et al. (2002)
1995	Canada	TMR	796	N	Monensin	490	Duffield et al. (1999a) Duffield et al. (1999b)
1999	Australia	Pasture	765	Y	observational	302	Moss et al. (2002)
2002	Australia	Pasture	283	Y	protected fat	131	Lean et al. (unpublished)
2003	Australia	Pasture	336	Ν	micronutrient	198	Lean et al. (unpublished)
2005	Australia	Pasture	610	Ν	observational	235	DeGaris et al. (2010)
2012	USA	TMR	9,075	Ν	observational	300	Vieira-Neto et al. (2021b)
2013	USA	TMR	11,728	Ν	observational	305	Pinedo et al. (2020)
2016	USA	TMR	6392	Y	enzyme	350	Golder et al. (2019)
2017	Australia	Pasture	764	Y	calcidiol	300	Exp. 1 Golder et al. (2021)
2017	Australia	Pasture	1,113	Y	calcidiol	300	Exp. 2 Golder et al. (2021)
2020	Australia	TMR	603	Y	amino acid	487	Golder et al. (unpublished)



Hazard of not being bred



- Kaplan-Meier survival curves for the days to removal before first insemination [i.e., the hazard of not being bred (HNBRED) or censoring for the hazard of being inseminated at least once] by parity.
- The data are from 32,356 cows.
- Parity ≥5 cows had 2.45 times greater HNBRED than parity 1 cows.
- Parity 2 cows had reduced hazard of HNBRED than parity 1
- Parities 3 and 4 had greater hazard of not being inseminated than parity 1 and lesser hazard than parity ≥5.





Time to pregnant



- Survival curves for days to pregnancy by parity
- The data are from 32,969 cows in 13 studies
- All parity groups differed in the daily probability of pregnancy which declined with parity
- Parity 5+ v 1 HR 0.73



How is milk production involved?

- Association of milk yield (kg/d) at approximately 70 DIM centred on Group with relative predicted hazard of pregnancy
- The data are from 20,071 cows
- All parity groups differed in probability or hazard of pregnancy
- Parity 1 cows had the greatest daily probability of pregnancy and parity ≥5, the least probability of pregnancy
- Low producers and high producers within a Group were less likely to go in calf each day





Milk protein% and relative predicted hazard of pregnancy



 Association of milk protein percent centered on Group within herd at approximately 70 DIM with the relative predicted hazard of being pregnant.

The data are from 8,761 cows in 7 studies.

- Parity ≥5 cows had lesser daily probability of pregnancy than other parities.
- Parity 1 did not differ from parity 2;
- however, parity 3 and 4 cows had a lesser hazard of pregnancy than parity 1 and 2 cows which did not differ from each other.



Associations of odds of pregnancy to first breeding (PREG1) with parity, and milk production variables (approx. 70 DIM) controlling for parity, study year, and production system.



Measure	n		Parity (Parity 1 i	Production	Effect of milk production variable			
		2	3	4	≥ 5	system	Linear	Quadratic
Whole population	23,637							
Univariable parity	23,637	0.87 ± 0.03a (<0.001)	0.81 ± 0.03ad (<0.001)	0.92 ± 0.05c (0.115)	0.86 ± 0.05a (0.009)			
Milk yield sub- population								
Univariable parity	21,964	0.87 ± 0.03ac (<0.001)	0.79 ± 0.03abd (<0.001)	0.94 ± 0.05c (0.227)	0.86 ± 0.05a (0.014)			
Milk yield (kg/d)	21,964	0.96 ± 0.04c (0.260)	0.84 ± 0.04ab (0.001)	1.00 ± 0.06 (0.988)	0.92 ± 0.06 (0.195)	NS	1.00 ± 0.00 (0.048)	NS

^aDiffers from parity 1; ^bDiffers from parity 2; ^cDiffers from parity 3; ^dDiffers from parity 4; eDiffers from parity 5

The problem is overall pregnancy Scibus (OPAL) Not so much at first service DairyUP

- Milk yield (kg/d) at approximately 70 DIM centred on Group and relative predicted coefficient for odds of pregnancy in a lactation
- All parities differed, with parity 1 cows having the greatest odds and parity \geq 5, the least odds of pregnancy in the lactation OR parity 5+ v 1 = 0.36
- Being near average production or even well above (up to 20L per day above) improved the probability of getting pregnant in a lactation.
- Despite similar pregnancy at 1st service, increased parity resulted in increased failure!



Summary of responses for milk production, milk fat percentage and yield, milk protein percentage and yield, and yield of milk solids with reproductive outcomes.



– L indicates a negative linear association and Q a quadratic association.

Milk measures	Hazard of not being bred (HNBRED) ¹	Time to pregnancy (HPREG) ²	Pregnancy to first breeding (PREG1)	Pregnancy in a lactation (OPAL)
Production (kg/d)	Q	Q	– L	Q
Fat (%)	– L	– L	– L	Q
Fat yield (kg/d)	– L	– L	NS	– L
Protein (%)	Q	Q	Q	Q
Protein yield (kg/d)	Q	– L	– L	Q
Total solids yield (kg/d)	Q	– L	– L	Q

¹Probability or hazard of not being bred over time ²Probability or hazard of being pregnant over time

Summary of reproduction?



- Reproductive failure was the major source of removal in this study
- In general, increased parity reduces reproductive performance
- However, very similar performance at *first insemination*
- It is a failure to be mated and ultimately not going in calf
- BOTH low production and very high production are risk factors for time to pregnancy and OPAL
- Production only has a small effect on pregnancy at first insemination
- We do have nutritional and hormonal methods to improve reproduction



Are there any problems with increasing longevity?

Dicordor		Parity1 (P-value)							
Disorder		2	3	4	≥5				
Clinical hypocalcemia3	15,793	-	3.52 ± 0.74bde (<0.001)	8.61 ± 1.78bc (<0.001)	20.02 ± 3.94bcd (<0.001)				
Mastitis	27,857	1.16 ± 0.05acde (0.001)	1.69 ± 0.08abde (<0.001)	1.91 ± 0.11abce (<0.001)	2.46 ± 0.15 abcd (<0.001)				
Lameness	26,464	1.55 ± 0.10acde (<0.001)	3.09 ± 0.21abde (<0.001)	4.32 ± 0.34abce (<0.001)	5.63 ± 0.48abcd (<0.001)				
Dystocia	26,653	0.55 ± 0.03ae (<0.001)	0.49 ± 0.04ae (<0.001)	0.50 ± 0.05ae (<0.001)	0.70 ± 0.07abcd (<0.001)				
Retained placenta	27,607	1.49 ± 0.10acde (<0.001)	1.85 ± 0.13abe (<0.001)	2.01 ± 0.17ab (<0.001)	2.34 ± 0.20abc (<0.001)				
Metritis	27,571	0.57 ± 0.02a (<0.001)	0.55 ± 0.03a (<0.001)	0.52 ± 0.03a (<0.001)	0.59 ± 0.04a (<0.001)				
Endometritis	22,412	0.85 ± 0.04a (0.001)	0.91 ± 0.06 (0.109)	0.81 ± 0.06a (0.007)	0.97 ± 0.08 (0.738)				
Displaced abomasum	25,721	1.50 ± 0.19acde (0.002)	3.97 ± 0.46abe (<0.001)	3.66 ± 0.51ab (<0.001)	2.92 ± 0.45abc (<0.001)				
Clinical ketosis	12,593	1.47 ± 0.26acde (0.029)	3.90 ± 0.65ab (<0,001)	3.728 ± 0.73ab (<0.001)	4.89 ± 0.96ab (<0.001)				
Subclinical ketosis	11,964	1.06 ± 0.06cde (0.343)	2.05 ± 0.13ab (<0.001)	1.83 ± 0.15ab (<0.001)	1.50 ± 0.14ab (<0.001)				
Pneumonia/ respiratory	20,758	1.49 ± 0.18a (0.001)	1.53 ± 0.21a (0.002)	1.54 ± 0.26a (0.009)	1.72 ± 0.32a (0.004)				

Glucose and parity: Difference from group centered mean pre-calving, at calving, immediately after calving and at peak



DairyUP

NEFA and parity: Difference from group centered mean precalving, at calving, immediately after calving and at peak



BHB and parity: Difference from group centered mean precalving, at calving, immediately after calving and at peak

Dair



Cholesterol and parity: Difference from group centered mean precalving, immediately after calving and at peak



DairyUP

Unlocking potential

Pre-calving (-3 to -1 DIM)
Post-Calving (1-3 DIM)
Peak Milk

BHB and parity: Difference from group centered mean precalving, at calving, immediately after calving and at peak

UP

Dair



Summary of longevity & Metabolism?



- There are differences in survival with older cows ie 5+ parity markedly more likely to die. They are at greater risk for removal overall.
- There are marked differences in concentrations of metabolites for cows of 5+ parity that are reflected in differences in disease.
- These marked differences in risk of death and concentrations of metabolites with parity at all times evaluated are consistent with reduced reproduction, health, and body condition for higher parity cows
- The findings demonstrate the considerable risk of confounding in evaluation if simple cut-points for parity are used to diagnose subclinical disorders.
- There is a need to use parity-controlled models with greater complexity (ie not simply nulli and pluriparous) to better understand older dairy cows and the changes in metabolism associated with age that underpin the increases in health risks with increased parity.
- Critically, what do we need to do to modify the risks



Cow Parity

Cow Parity

Cow Parity

5+



What might be causing this? Cows gain weight but lose BCS







Parity 3								
_								
		┢╌┟╴	++					
	==	┢╋	┢╋					
ōō	ōō		Ħ					

- Within parity, expect 25% for each BCS/BW category
- Parity 1: 61% High BCS/Low BW
- Parity ≥5: 56% Low BCS/High BW



Low BCS & Low BW
 Low BCS & High BW
 High BCS & Low BW
 High BCS & High BW



What might be causing this? Cows gain weight but lose BCS



Proportion of cows in each category of BCS and BW Holstein

Proportion of cows in each category of BCS and BW Other Breeds





Where to now? Define and improve



- We have strong evidence of impaired metabolism with increased parity (another presentation).
- In order to fix it, we need to better define the causes BUT we have many solutions available – ration balancing, better protein nutrition, fat nutrition, some reproductive treatments etc.
- Where will we look protein nutrition, rumen function, calcium and bone, cholesterol and fats.
- Why do older cows lose BCS? What does this mean in terms of reproduction and health?
- Will facility design or management help?



DairyUP Unlocking potential

Thanks

- Collaborators
- Past students who contributed data sets
- Colleagues in Dairy UP
- Corporate and public good supporters of the research included in the original studies



Statistical analysis - BCS



- All outcomes (pre-calving BCS, peak-milk BCS, BCS change and peak-milk BW) were all centered around study Group mean to help control for study year, genetic differences and other unknown confounding variables between studies.
- Ordinary least-squares linear regressions performed using for each of the four outcomes using *regress* (STATA 16): intragroup correlation between study groups were controlled using clustered sandwich estimators, *vce(cluster Group)*.
- Main fixed effects were parity (1 to ≥ 5), production system (pasture or TMR) and day of observation.
- Interactions of parity with system were evaluated.
- A manual, forward stepwise model was used with model selection determined by minimum AIC.