Case study

Presenting complaint

- I have too many cases of metritis. This problem has gotten worse in the last few months.

Initial inspection

- WHAT is the problem?
  - Define
  - Quantify

CHAIN	FDAT	LACT	EASE	Twins	RP	DDRY	METR	Days METR	FSTPJ
1575	01-Jul-05	1	2			0	1	4	9160
1554	02-Jul-05	1	1			0			10290
1560	02-Jul-05	1	0		1	0	1	4	10600
1577	02-Jul-05	1	2		1	0			12130
1566	03-Jul-05	1	2			0			8740
1227	04-Jul-05	3	0			24			11190
1214	06-Jul-05	3	0			36	1	3	7940
1034	08-Jul-05	4	1	1	1	68			8800
1346	09-Jul-05	2	0			29			10440
1562	11-Jul-05	1	2			0	1	5	11310
1233	14-Jul-05	3	0			34			8960
1412	14-Jul-05	2	0	1		34			8420
1457	15-Jul-05	2	0			35			9870
1268	16-Jul-05	3	0			36			8240
1570	18-Jul-05	1	0		1	0	1	4	10390
1427	19-Jul-05	2	1			39			8370
1571	22-Jul-05	1	1			0			10190
1084	23-Jul-05	3	0			37			7280
1274	23-Jul-05	3	0			83			7520
1456	24-Jul-05	2	0			44			9270
1619	26-Jul-05	1	1			0			14480
662	30-Jul-05	5	1		1	50	1	4	0

Question 1

After considering the data presented on the metritis incidence in this herd, the **Presenting Complaint** is:

1. not really a problem
2. a small problem
3. a significant problem

Question 2

After considering the data presented on the metritis incidence in this herd, **WHAT** is the primary problem in this herd:

1. over diagnosis of metritis
2. dystocia in heifers
3. a seasonal pattern of metritis
4. dry period length
5. incidence of retained placenta

Questions 3-6

Question 3

After considering the data, **WHO** is primarily affected with metritis in this herd:

1. first-calf heifers
2. second lactation cows
3. third + lactation cows
4. no pattern

Question 4

After considering the data, has the incidence of metritis in this herd changed over time:

1. No pattern
2. Increased in July-September
3. Increased in October-December

Question 5

After considering the metritis data in this herd, a metritis case should be defined as:

1. Any occurrence recorded
2. When associated with another problem
3. A case of specified duration of antibiotic treatment
4. A case that is treated and has production loss

Question 6

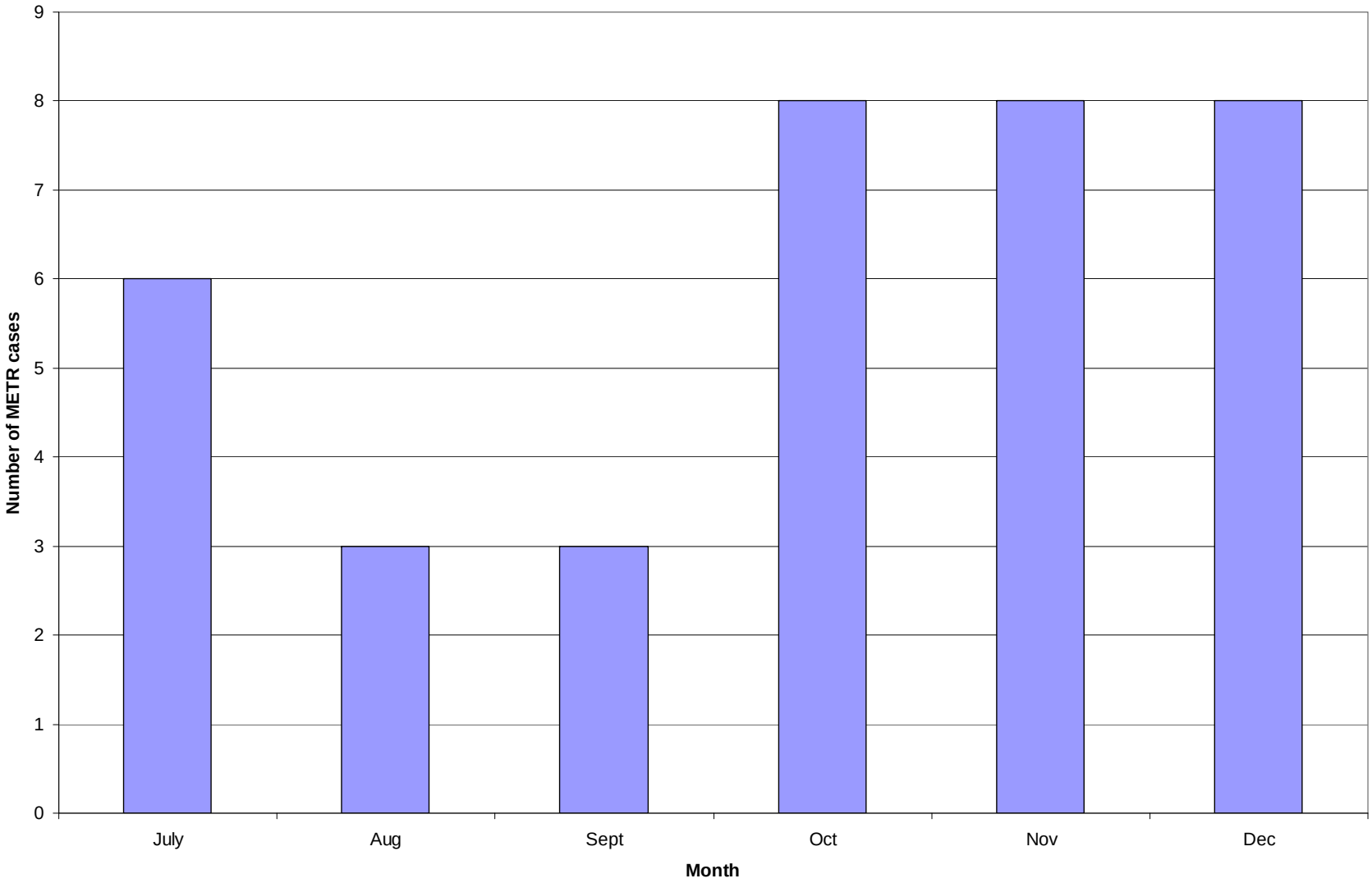
After considering the data presented from this herd, the impact of a case of metritis on an individual cow is:

1. Increased production
2. No effect on production
3. Decreased production

- How many cases have you had?

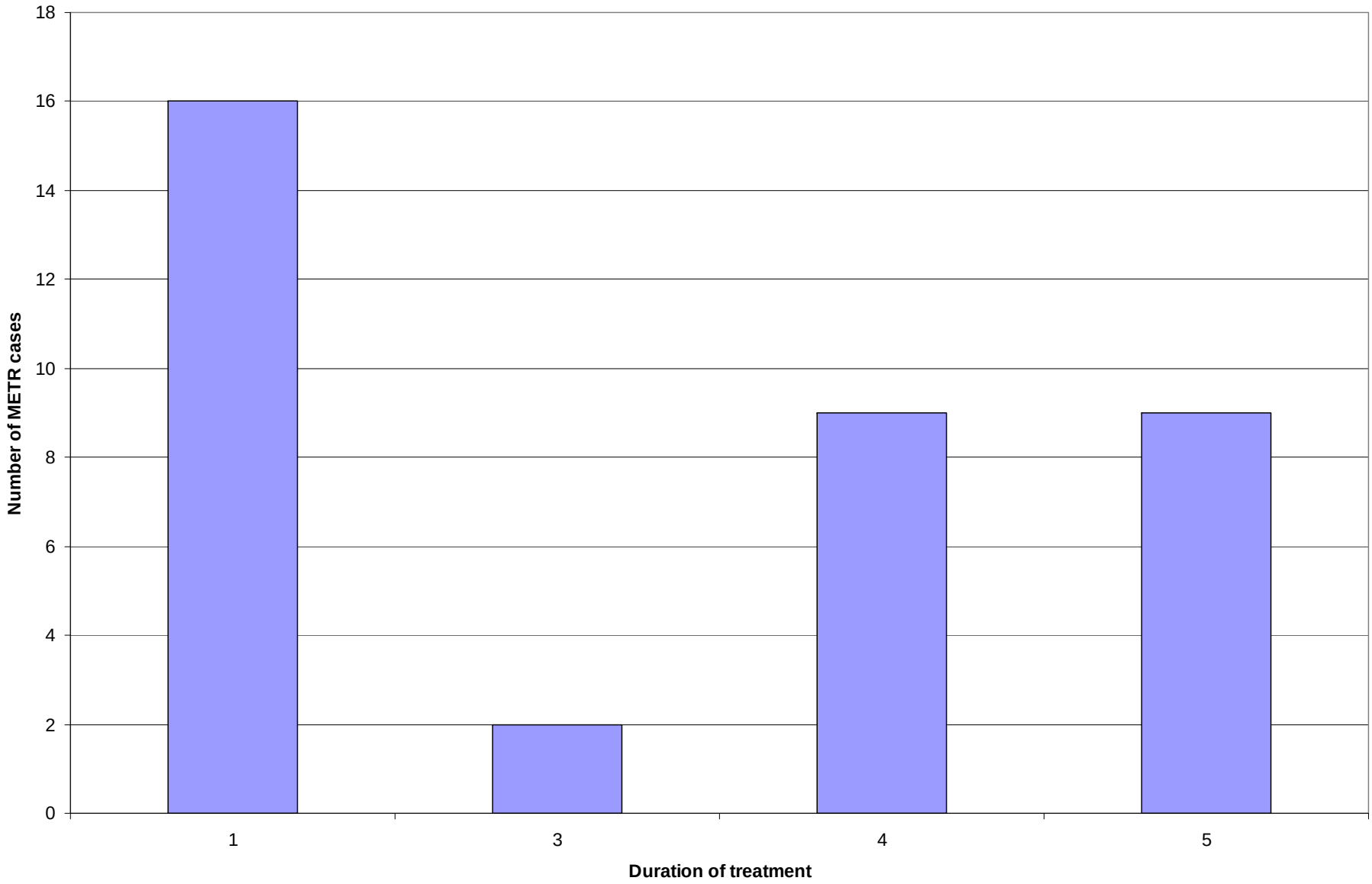
- EVENTS\5
- EGRAPH

When


9
8
7
6
5
4
3
2
1
0
Number of METR cases
July
Aug
Sept
Oct
Nov
Dec
Month

- What is a case of metritis?
- How do you record them in Dairy Comp?

What?


18
16
14
12
10
8
6
4
2
0
Number of METR cases
1
3
4
5
Duration of treatment

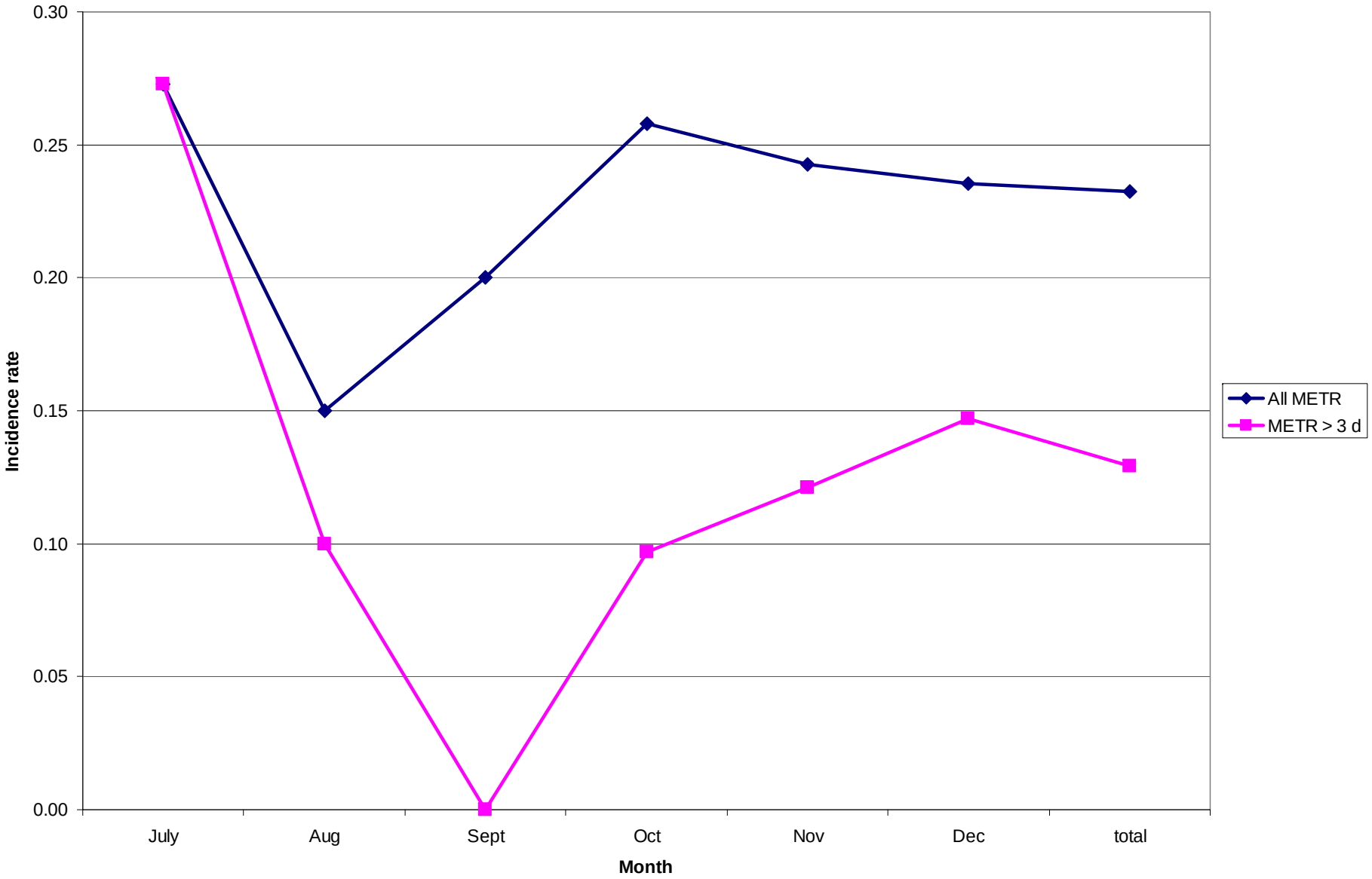
Descriptive stats

- Metritis
  - All: 36/155 = 23%
  - METR > 3 d: 20/155 = 13%
- Twins: 11/155 = 7%
- RP: 19/155 = 12%
- Calving
  - Unassisted: 89/155 = 57%
  - Easy: 46/155 = 30%
  - Hard: 20/155 = 13%

- How many cows calved – what's the denominator?

- EVENTS\5

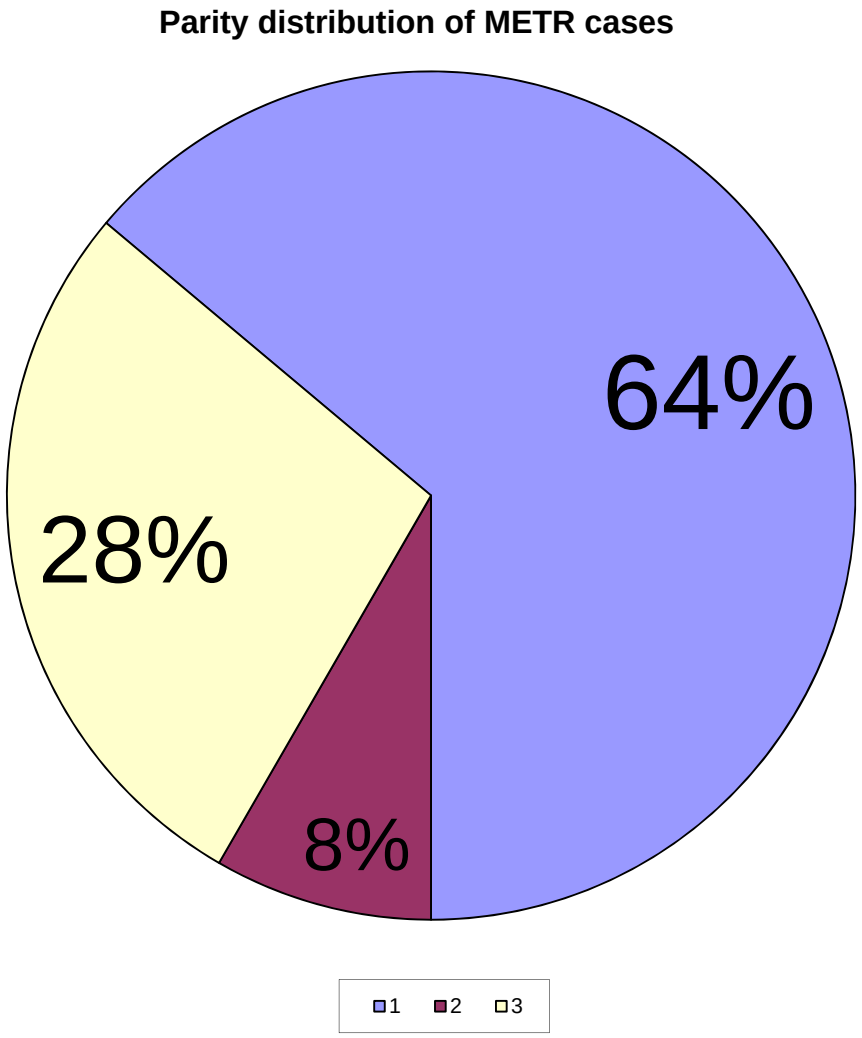
Rates


0.30
0.25
0.20
0.15
0.10
0.05
0.00
Incidence rate
July
Aug
Sept
Oct
Nov
Dec
total
Month
All METR
METR > 3 d

Who is affected?

- What is the parity of the affected animals?

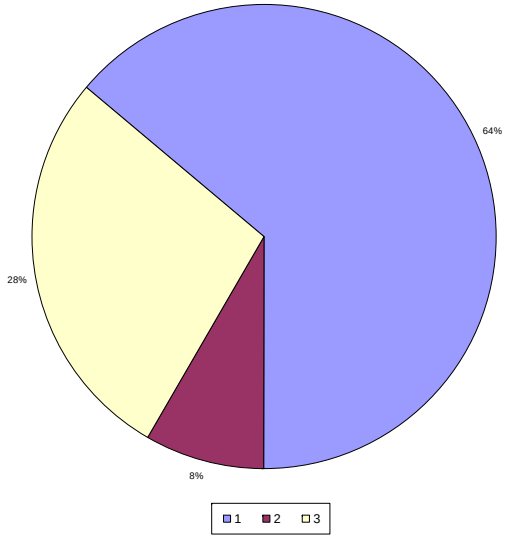
Distribution of cases



Who is affected?

- Is there a difference in metritis risk among parities?

Parity distribution of METR cases

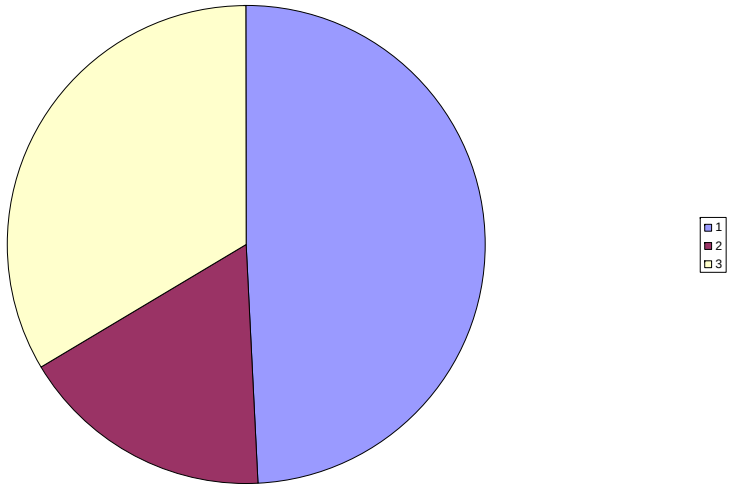


64% of cases are in heifers

This is "proportional morbidity"

= cases/cases

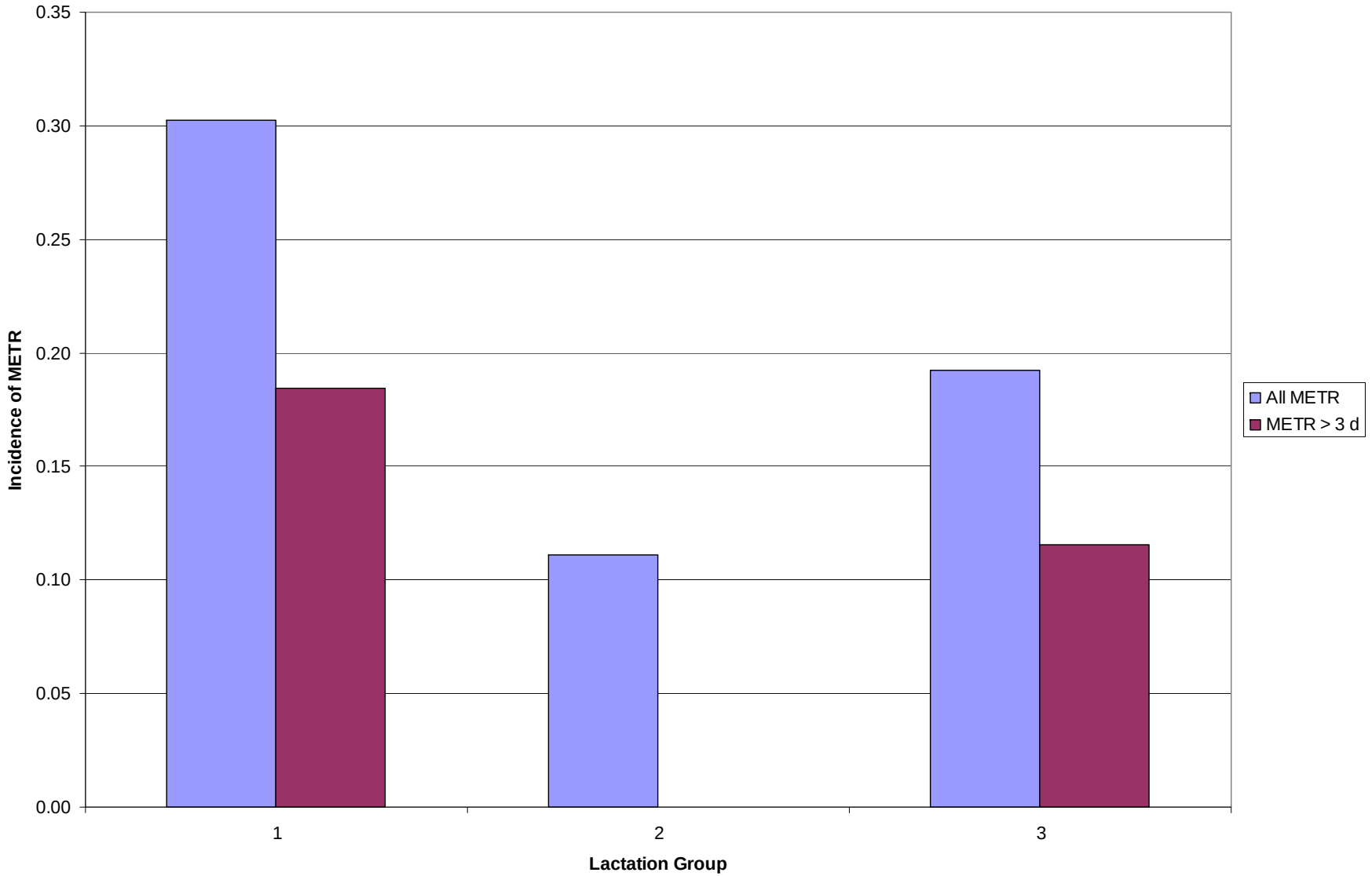
Parity distribution of the herd



But heifers make up 49% of calvings

Risk = cases/number at risk

Metritis Risks by Parity



Metritis risks by parity

	METR			
LCTGP	Yes	No	total	Risk
1	23	53	76	30%
2	3	27	27	11%
3	10	42	52	19%
	36	119	155	23%

P = .09

Metritis risks by parity

METR > 3 d

LCTGP	Yes	No	total	Risk
1	14	62	76	18%
2	0	27	27	0%
3	6	46	52	12%
	20	135	155	13%

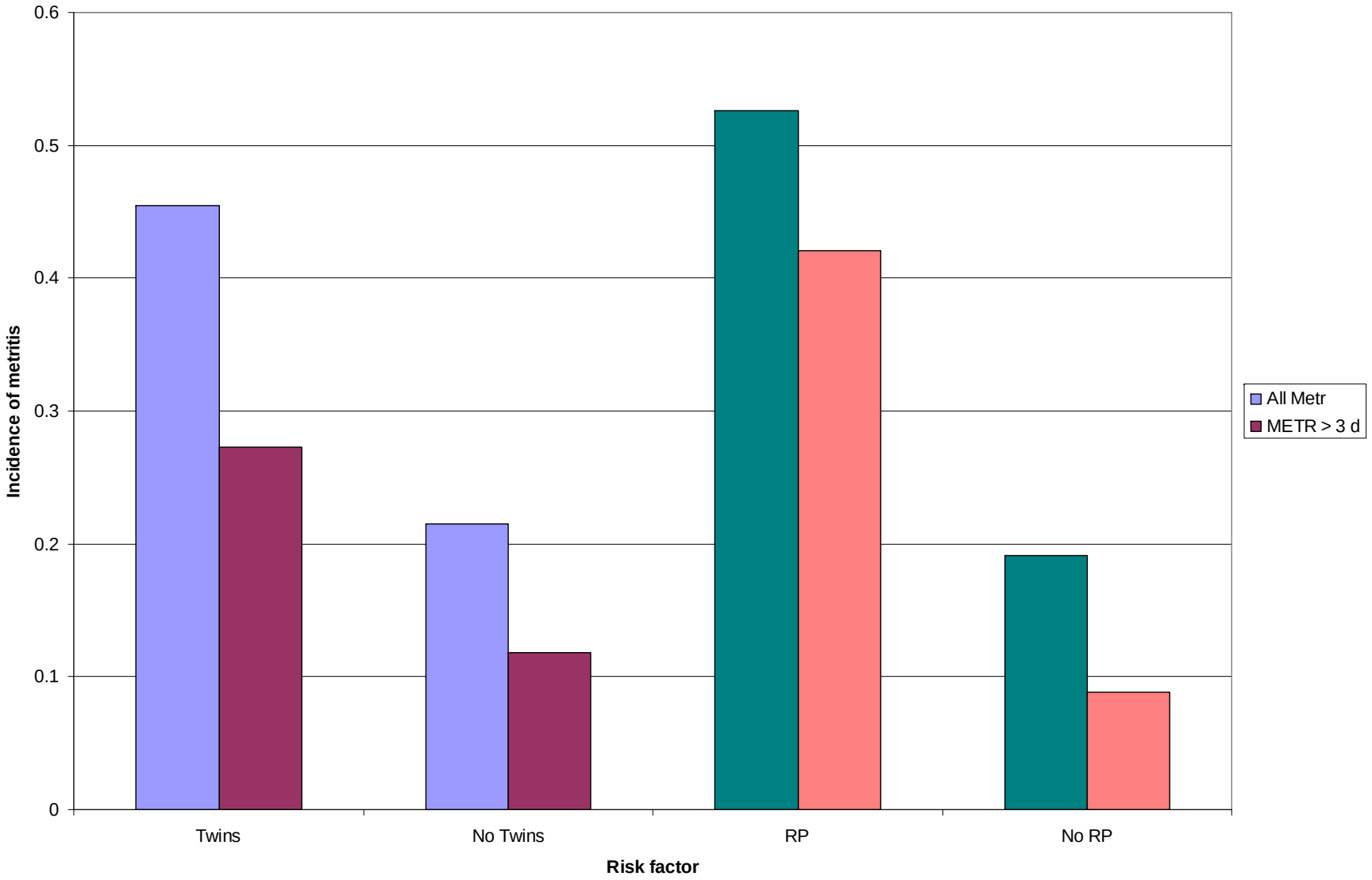
P = .05

Is

- Twins
- RP
- Calving ease

associated with metritis?

Twins and RP


0.6
0.5
0.4
0.3
0.2
0.1
0
Incidence of metritis
Twins
No Twins
RP
No RP
Risk factor
All Metr
METR > 3 d

Association of Twins with METR

	METR			
Twins	Yes	No	total	Risk
Yes	5	6	11	45%
No	31	113	144	22%
	36	119	155	

OR = 3.0 RR = 2.1 P = 0.13 (Fisher's exact)

Association of Twins with METR

	METR > 3 d			
Twins	Yes	No	total	Risk
Yes	3	8	11	27%
No	17	127	144	12%
	20	135	155	

OR = 2.8 RR = 2.3 P = 0.15 (Fisher's exact)

Association of RP with METR

	METR			
RP	Yes	No	total	Risk
Yes	10	9	19	53%
No	26	110	136	19%
	36	119	155	

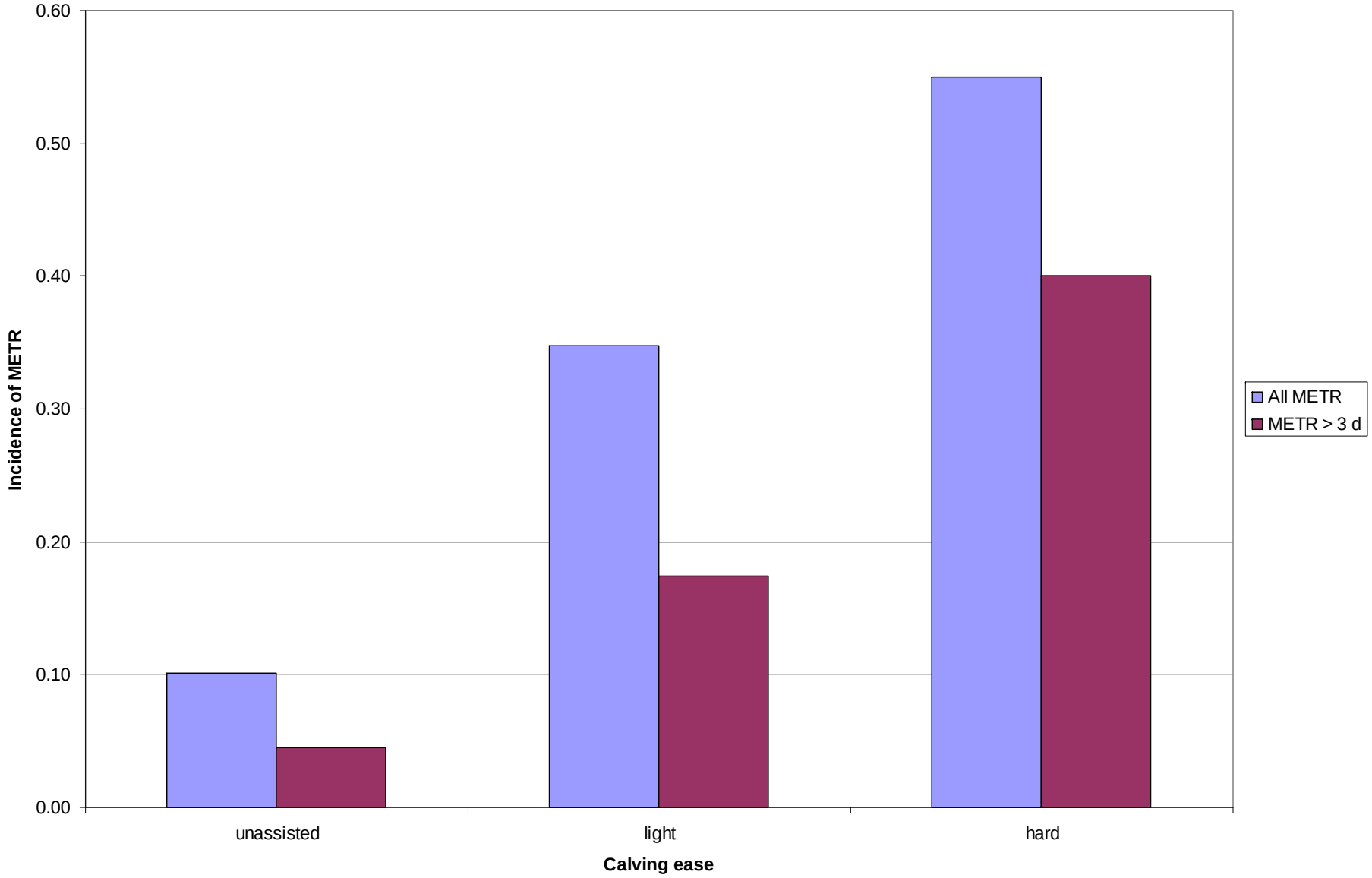
OR = 4.7 RR = 2.8 P = 0.001

Association of RP with METR

	METR > 3 d			
RP	Yes	No	total	Risk
Yes	8	11	19	42%
No	12	124	136	9%
	20	135	155	

OR = 7.5 RR = 4.7 P = 0.0001

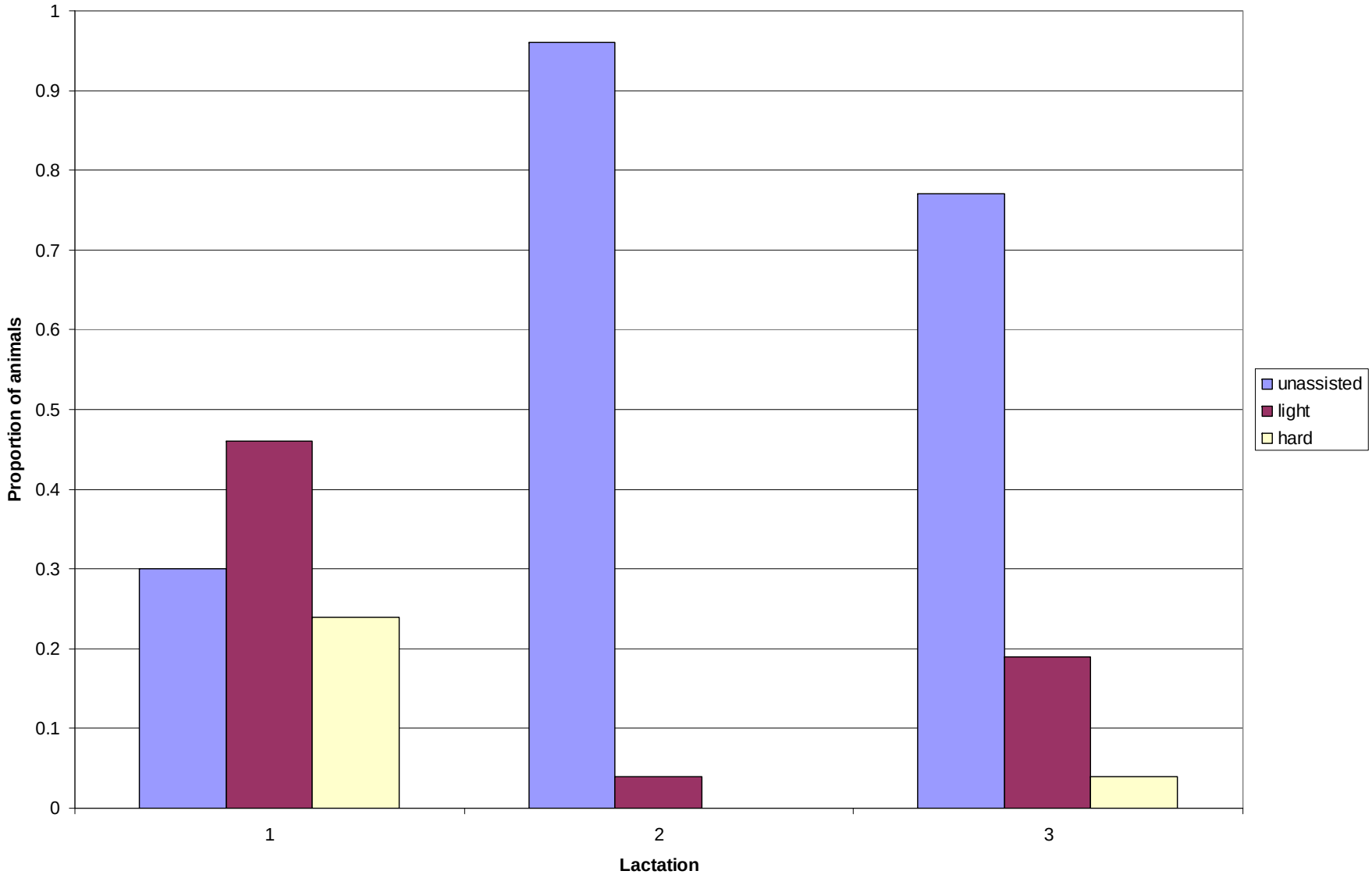
Calving ease

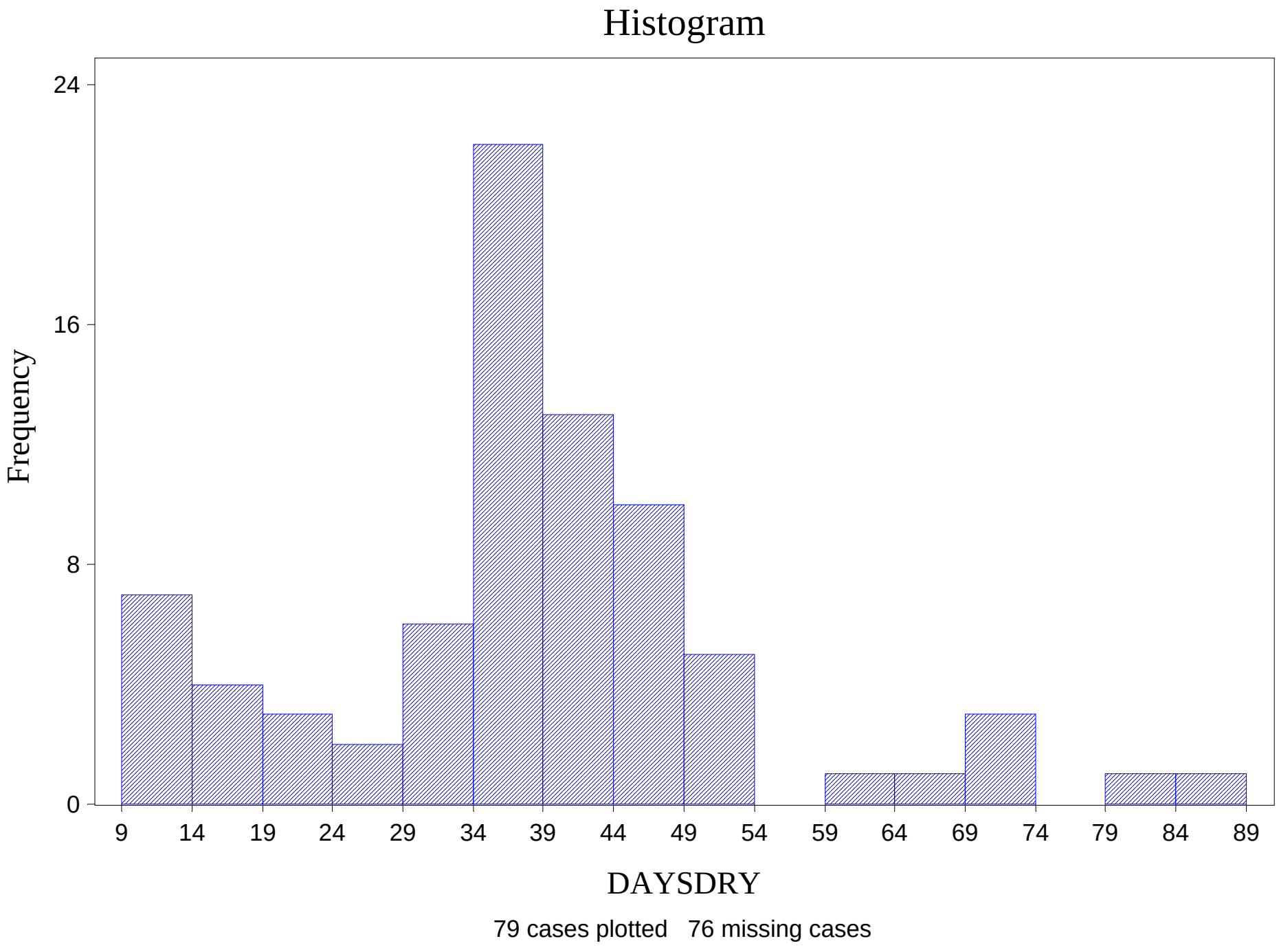


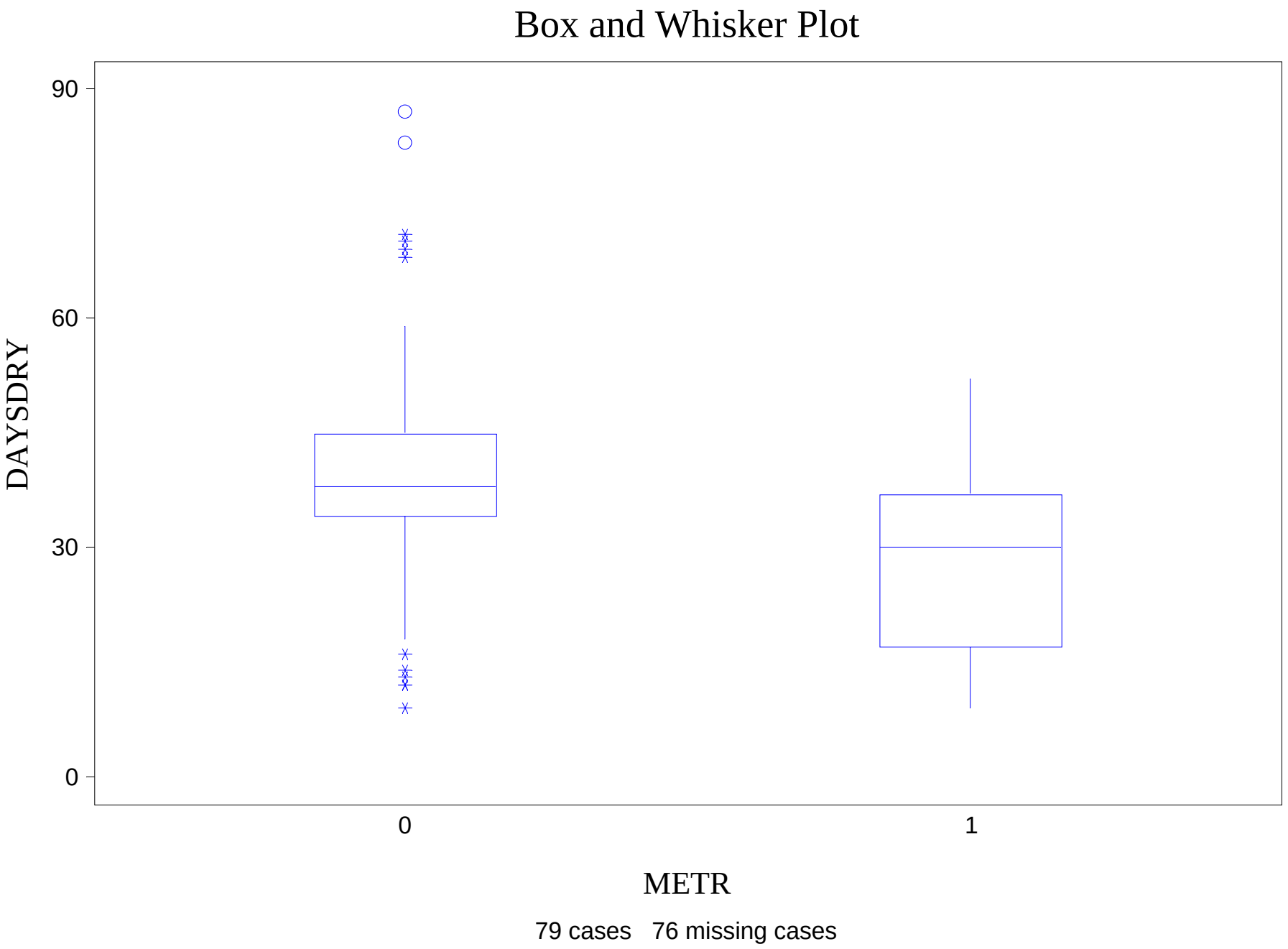
Attack rate table

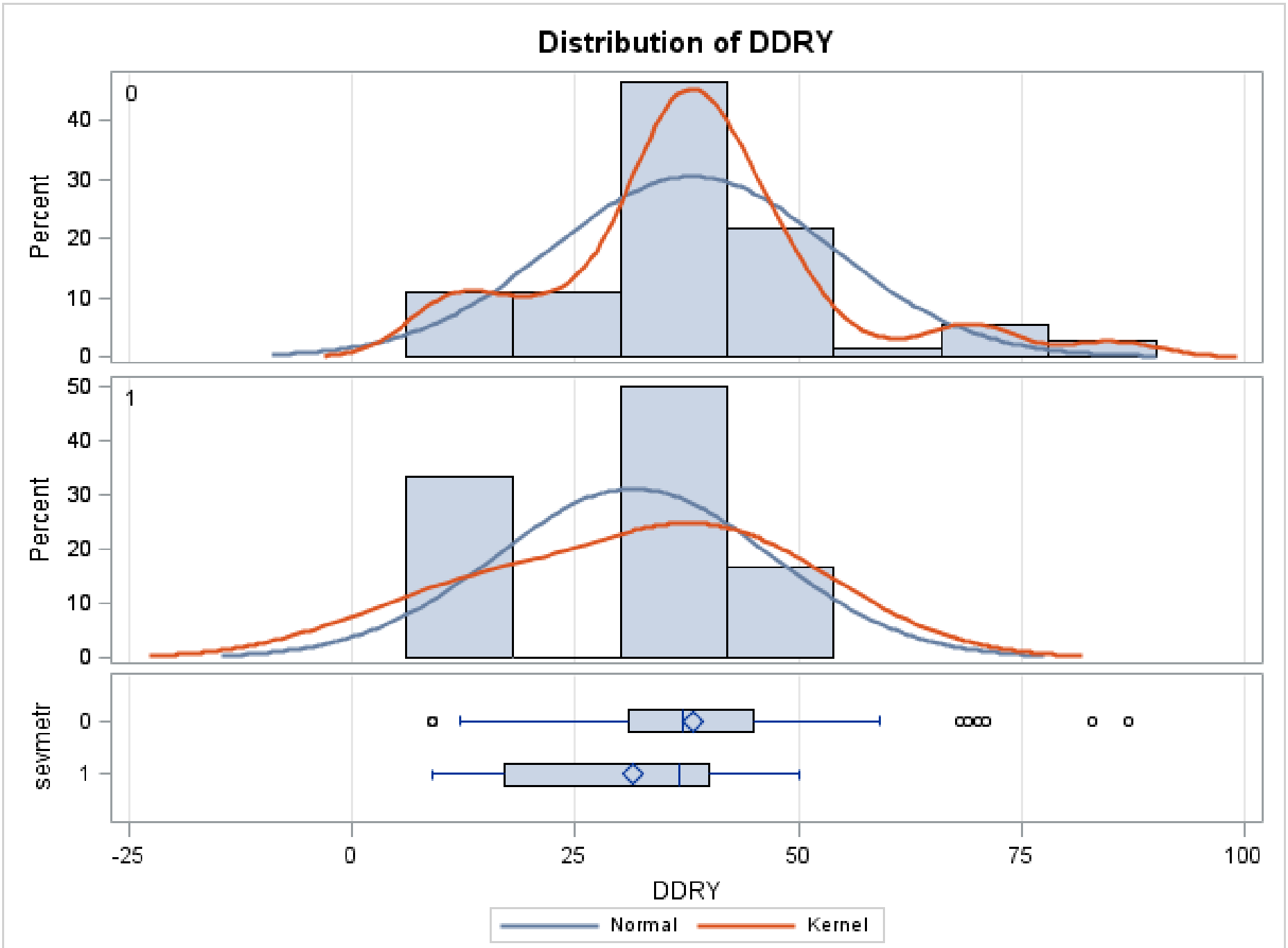
Risk factor	Exposed to the factor				Not exposed to the factor				AR Diff	OR	RR
	Number affected	Number not affected	total	Attack rate	Number affected	Number not affected	total	Attack rate			
	E1	E2	E1 + E2	E1/ (E1+E2)	U1	U2	U1+ U2	U1/ (U1+U2)			
Twins	5	6	11	45%	31	113	144	22%	+23%	3.0	2.1
RP	10	9	19	53%	26	110	136	19%	+34%	4.7	2.8
Heifer	23	53	76	30%	13	66	79	16%	+14%	2.2	2.1
Assisted calving	27	39	66	41%	9	80	89	10%	+31%	6.2	4.1
Hard calving	11	9	20	55%	13	66	79	16%	+39%	6.2	3.4

Calving ease by LCTGP

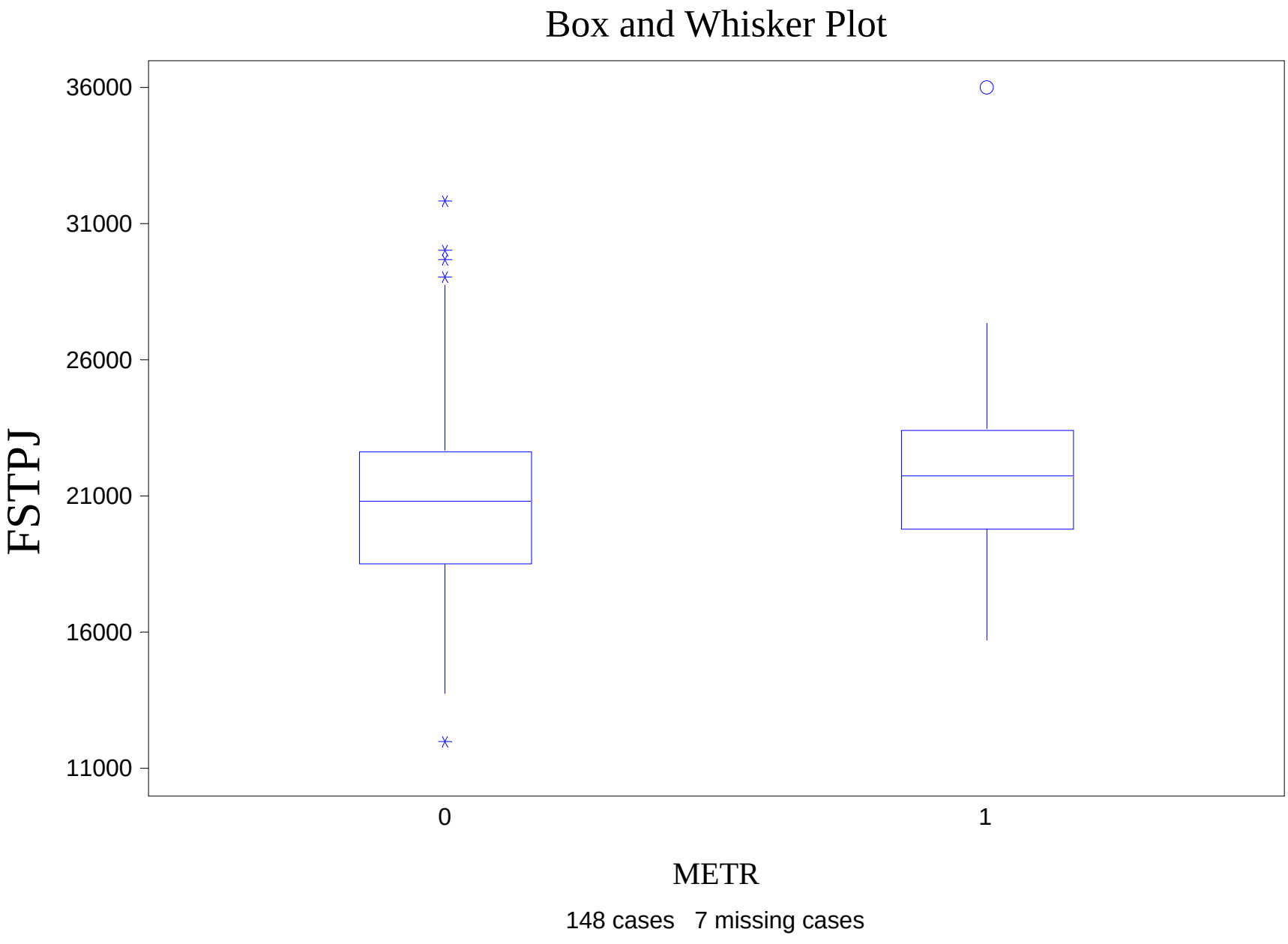


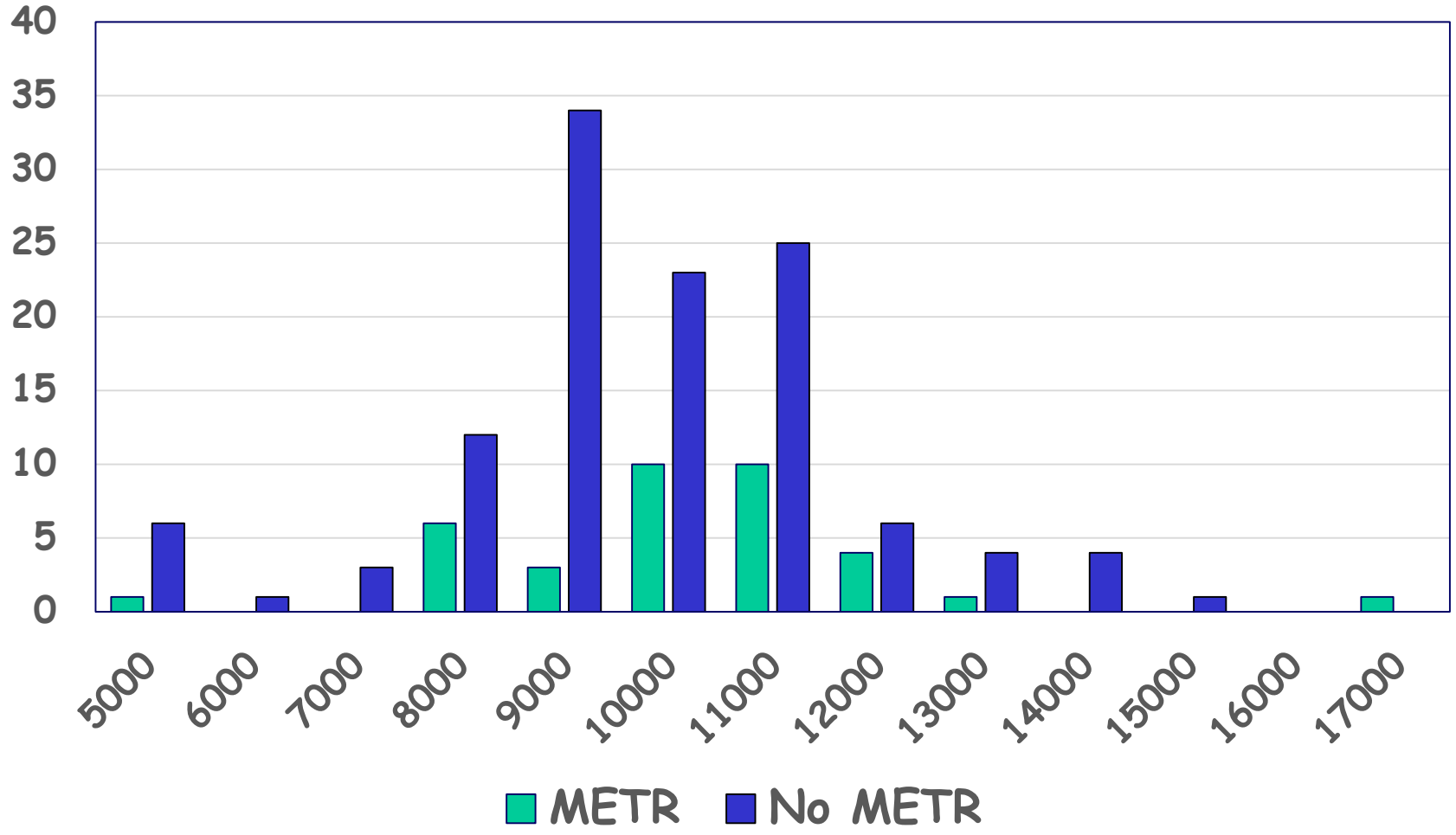

Histogram
Frequency
24
16
8
0
9
14
19
24
29
34
39
44
49
54
59
64
69
74
79
84
89
DAYSDRY
79 cases plotted 76 missing cases


Box and Whisker Plot
90
60
30
0
DAYSDRY
0
1
METR
79 cases 76 missing cases


Distribution of DDRY
0
1
Percent
sexmetr
DDRY
-25
0
25
50
75
100
Normal
Kernel

- Now, being a good production medicine vet, you will quantify the losses due to metritis in this herd.
- You compare 1st test 305ME projection (FSTPJ) for affected and unaffected cows


Box and Whisker Plot
36000
31000
26000
21000
16000
11000
FSTPJ
0
1
METR
148 cases 7 missing cases


40
35
30
25
20
15
10
5
0
5000
6000
7000
8000
9000
10000
11000
12000
13000
14000
15000
16000
17000
METR
No METR

	No METR	METR
Average FSTPJ	9486 kg	9863 kg

Awkward silence followed by…
"Is that my phone – gotta go!"

Are these numbers different?

- Statistical test depends on the nature of the data
- Continuous
  - Normally distributed – compare means
    - E.g. T-test
  - Skewed – compare medians or ranks
- Categorical

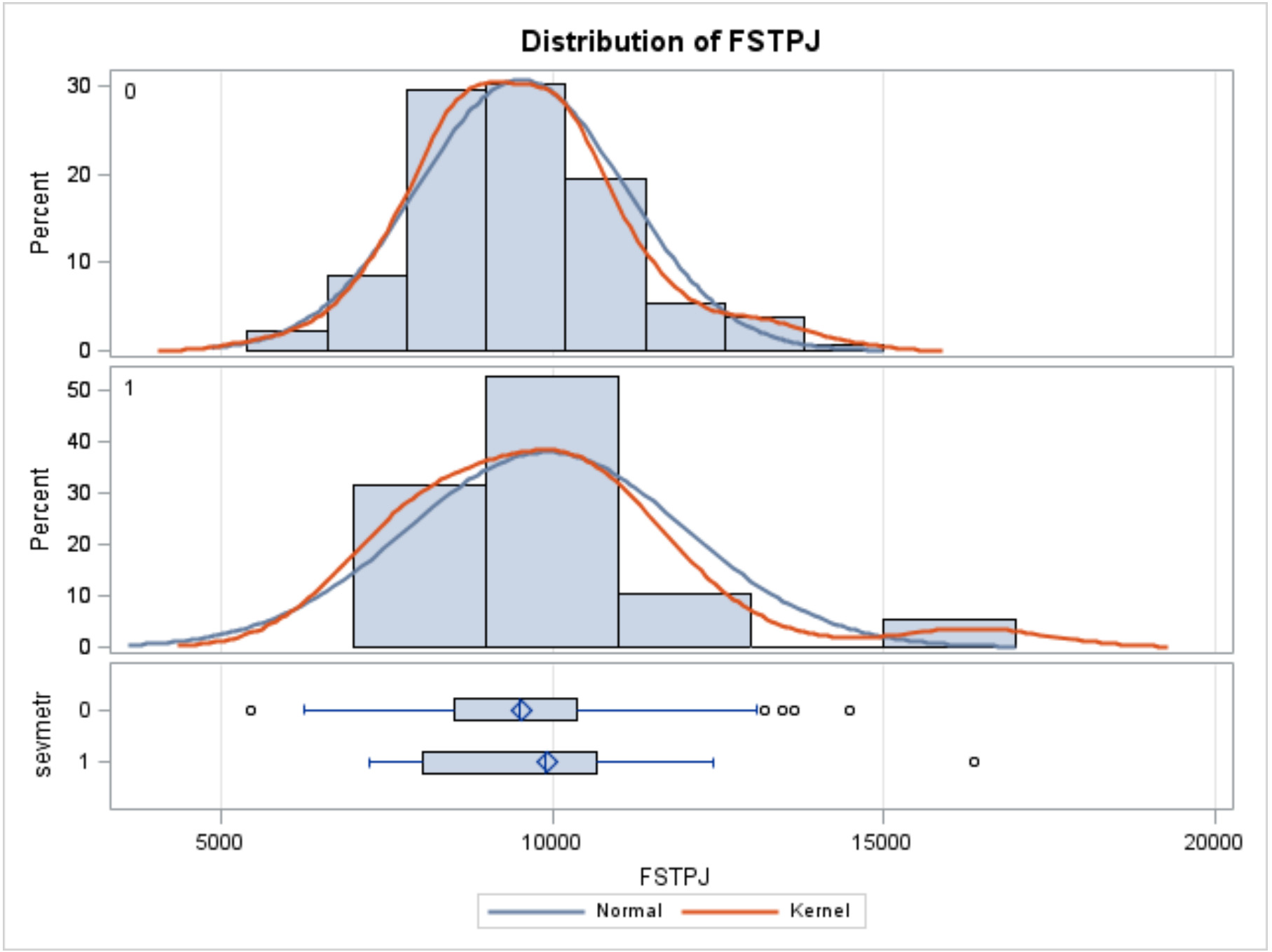
Are these numbers different?

- Depends on:
  - the magnitude of the difference
  - BUT ALSO:
  - The variance
  - The number of observations

} Standard error

Impact of METR > 3 d

	No METR > 3 d	METR > 3 d
Average	9526	9909
SD	1563	2105
n	129	19
SE	138	483
95% CI	9254 - 9798	8894 - 10924
T-test	P = 0.45	


Distribution of FSTPJ
0
1
Percent
sevmetr
FSTPJ
5000
10000
15000
20000
Normal
Kernel

Conclusions

- The rate of metritis is stable in the last 3 months
- There may a problem of over-diagnosis or inconsistent diagnosis

How much can I get for this?
Sample size calculations

Sample size calculation Estimation of prevalence

How many animals would you need to sample or test to estimate the prevalence of infection or disease in a group?

$$n = \frac{1.96^2 \mathrm{P}(1-\mathrm{P})}{\mathrm{d}^2}$$

$$n_{adj} = \frac{(N \times n)}{(N + n)}$$

n = required sample size for an infinite population

P = expected prevalence in the population

d = largest acceptable difference from the true prevalence

N = number of animals in the group under study

Sample size calculation Estimation of prevalence

example

n = required sample size for an infinite population (=138)

P = expected prevalence in the population (10%)

d = largest acceptable difference from the true prevalence (5%)

N = number of animals in the group under study (50 cows in the group)

$$n = \frac{1.96^2 .1(1-.1)}{.05^2}$$

$$n_{adj} = \frac{(50 \times 138)}{(50 + 138)}$$

$$n_{adj} = 37$$

- So turning the question around…

Given the number of animals or tests that I have or can get, how precise is my estimate of prevalence in the group?

Confidence interval for proportions

(adjusted for finite sample)

$$95\%\,\text{CI for P} = \text{P} \pm 1.96\sqrt{\frac{\text{P}(1-\text{P})}{\text{n}}\,\frac{(\text{N}-\text{n})}{\text{N}}}$$

- P = proportion of interest (e.g. prevalence of disease or test + in a group)
- n = number of samples or individuals in the denominator of the proportion of interest (i.e. number actually tested)
- N = Number of animals in the study population (i.e. number in the whole herd)

Confidence interval for proportions

(adjusted for finite sample)

$$95\%\,\text{CI for P} = 0.3 \pm 1.96\sqrt{\frac{0.3(1-0.3)}{10}\,\frac{(50-10)}{50}}$$

example

- Group of 50 animals
- Examine 10 animals or run 10 tests and 3 are affected or positive P = 3/10 = 30% = .3
- n = 10
- Estimate = .3 but 95% CI = {.05 - .55}
- Essentially, you could be 95% confident that the proportion affected was between 5% and 55%

To compare 2 groups

- To establish a statistically significant difference depends on
  - **Magnitude of difference**
  - **Variance**
  - Confidence (avoidance of Type I error) – convention = 95%
  - Power (avoidance of Type II error) – convention = 80%

		True Difference	
		Yes	No
Result of the statistical test	Different	**Correct** Power	**Type I Error** Avoid through P-value
	Not different	**Type II error** Avoid through sample size	**Correct** Confidence

Comparing proportions

CR in 1 group	CR in other group	Total sample required
35	40	2942
30	40	712
DA rate in 1 group	DA rate in other group	
3	8	652
2	4	2282

Comparing means

Mean in 1 group	Mean in other group	SD	Sample size
70	80	10	32
70	80	15	70
77	80	10	348
90	100	10	32

Comparing means

Difference	SD	Sample size
2	2	32
2	5	198
3	5	88
1	5	786

Disease detection

- How many samples do I need, to know that **the prevalence is past a meaningful threshold** (e.g. 10% of cows with NEFA > 0.4 a week before calving)
- Depends on
  - Group/herd size
  - Estimated prevalence
  - Confidence required

How many NEFA samples?

Group size	Est. Prev.	Confidence	Sample
100	10%	75%	13
1000	10%	75%	14
50	10%	75%	12
50	20%	75%	6
50	10%	95%	22

So what's the bottom line?

- Neither groups nor budgets are infinite
- Take-home: when the number of observations is low, confidence interval will be wide (i.e. precision is low)
- **Monitoring and problem solving do not rely on finding statistically significant differences**
  - **Statistically significant association ≠ causation**
  - **<u>Important</u> differences may not be statistically significant**

Caveat

- When comparing 2 groups (especially before and after a change, as opposed to randomized treatment at the same time) in addition to sufficient statistical power and analysis, it is critical to ask, "Is the effect of interest the only thing that is different between the groups?"
- It often isn't e.g. parity distribution, seasonal effects, other changes in feed and management, etc.
- These other variables must be considered and accounted for in assessing the difference between groups

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Pamela L. Ruegg, DVM, MPVM

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Hood of the Truck Statistics for Food Animal Practitioners

Barrett D. Slenning, MS, DVM, MPVM

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Determining Cause and Effect in Herds

John M. Gay, DVM, PhD