
Survival analysis:

An introduction

Mark Stevenson

Faculty of Veterinary and Agricultural Sciences

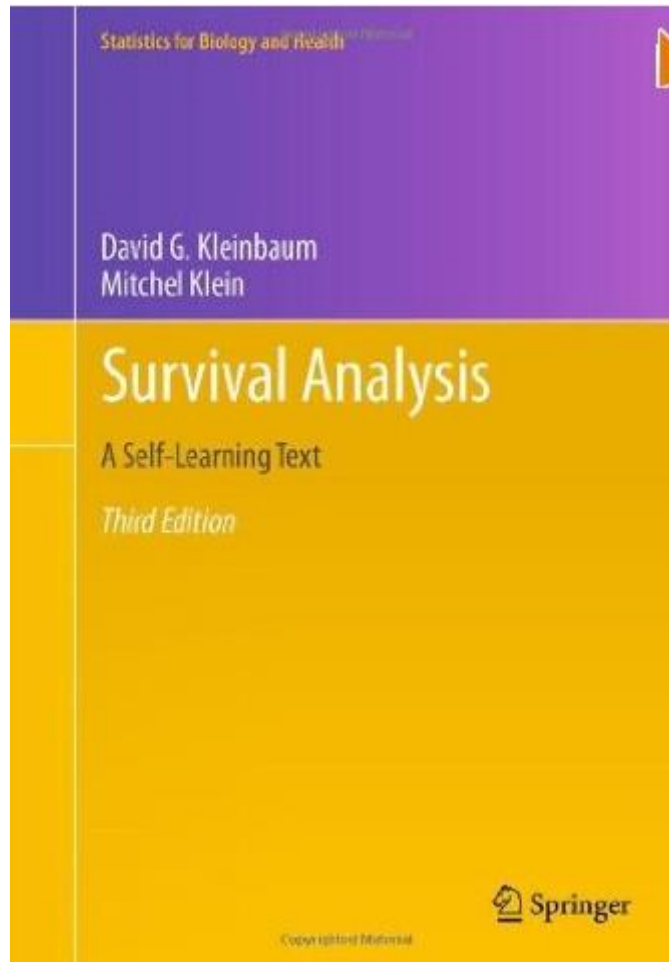
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Roadmap

- Text books
- Background
- Survival and hazard
- Examples
- Censoring
- Ties
- Data structure

Text books

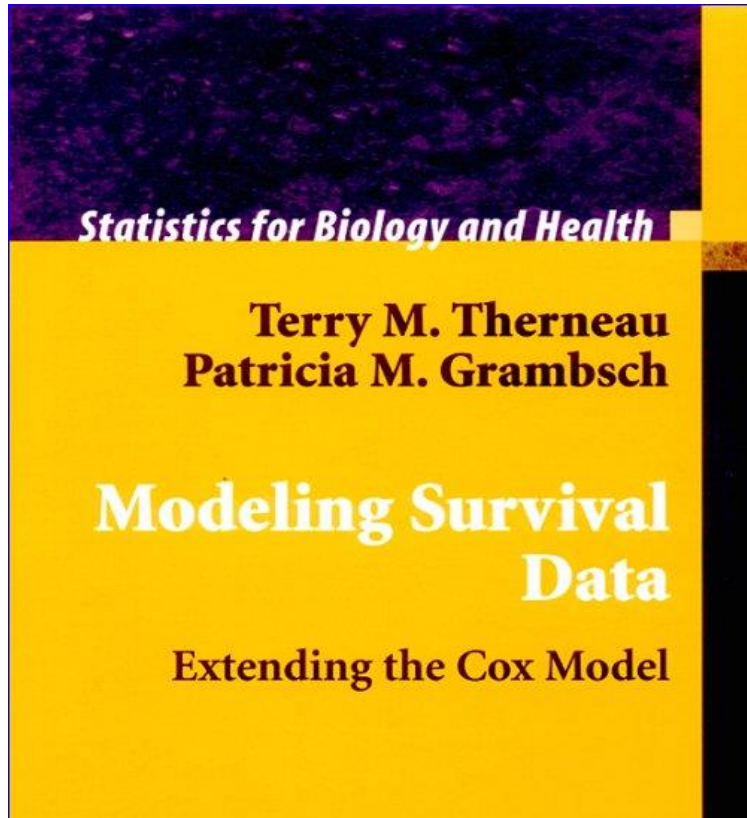


Kleinbaum D, Klein M. Survival Analysis: A Self-Learning Text. New York; Springer-Verlag; 2011.

Thorough coverage of subject. Includes software examples (SAS, SPSS, R).

Rating: +++

Text books



Therneau T, Grambsch P. Modeling Survival Data: Extending the Cox Model. New York; Springer-Verlag; 2001.

Comprehensive coverage of advanced topics.
Therneau is an excellent writer. Gives S-PLUS (\equiv R) and SAS code.

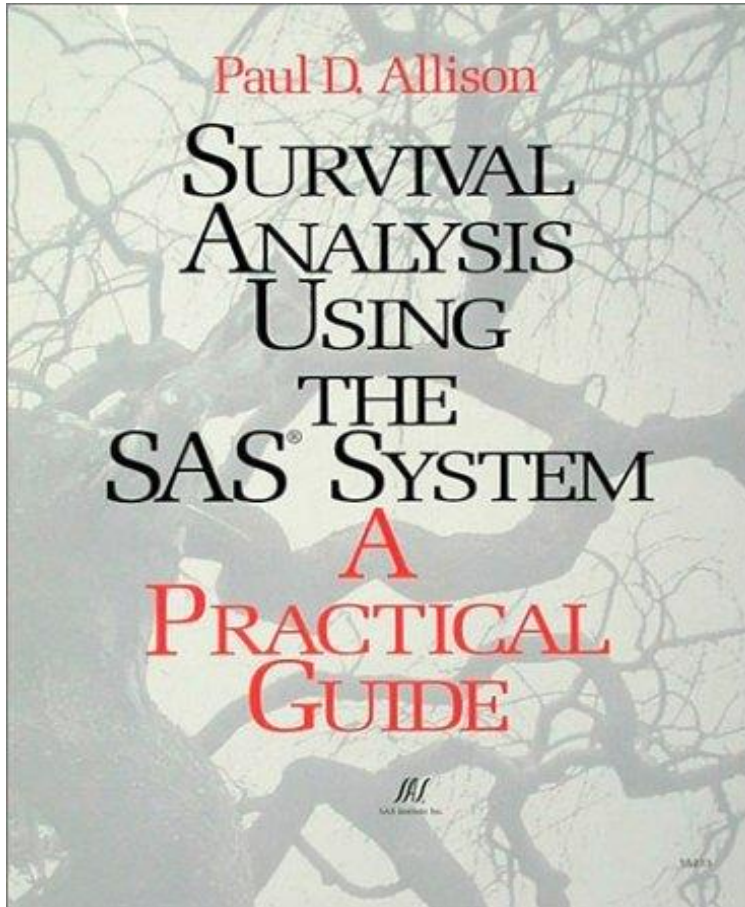
Rating: +++

Text books

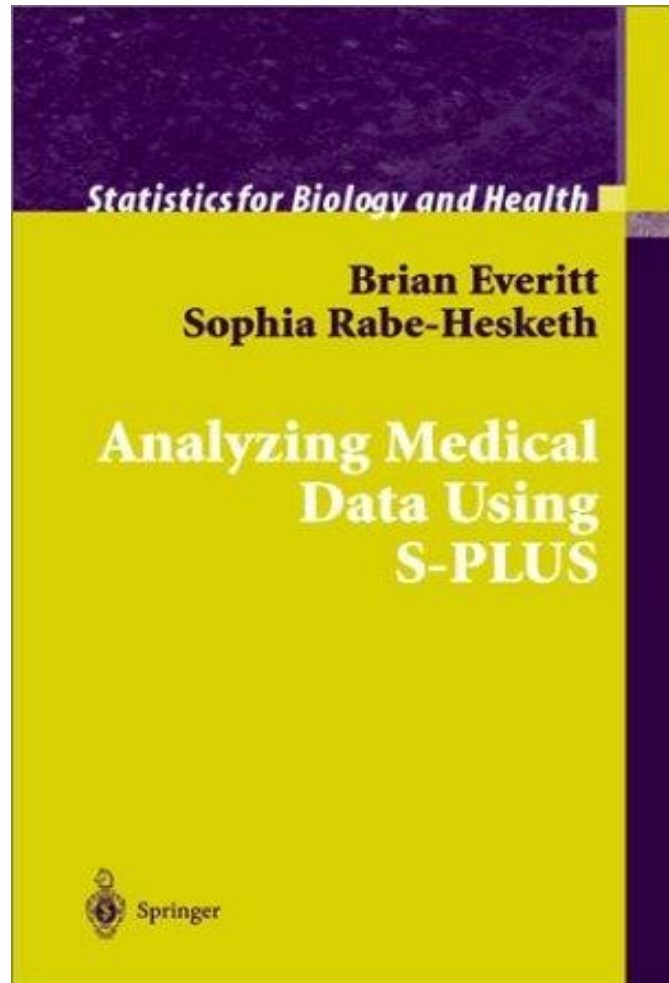
Allison P. Survival Analysis Using the SAS System A Practical Guide. New York: SAS Publishing; 1995.

A little dated now. SAS only.

Rating: ++



Text books



Everitt B, Rabe-Hesketh S. Analyzing Medical Data Using S-PLUS. New York; Springer Verlag; 2001.

Practical coverage of a wide range of analytical techniques used in epidemiology. Covers the basics of survival analysis – not advanced topics.

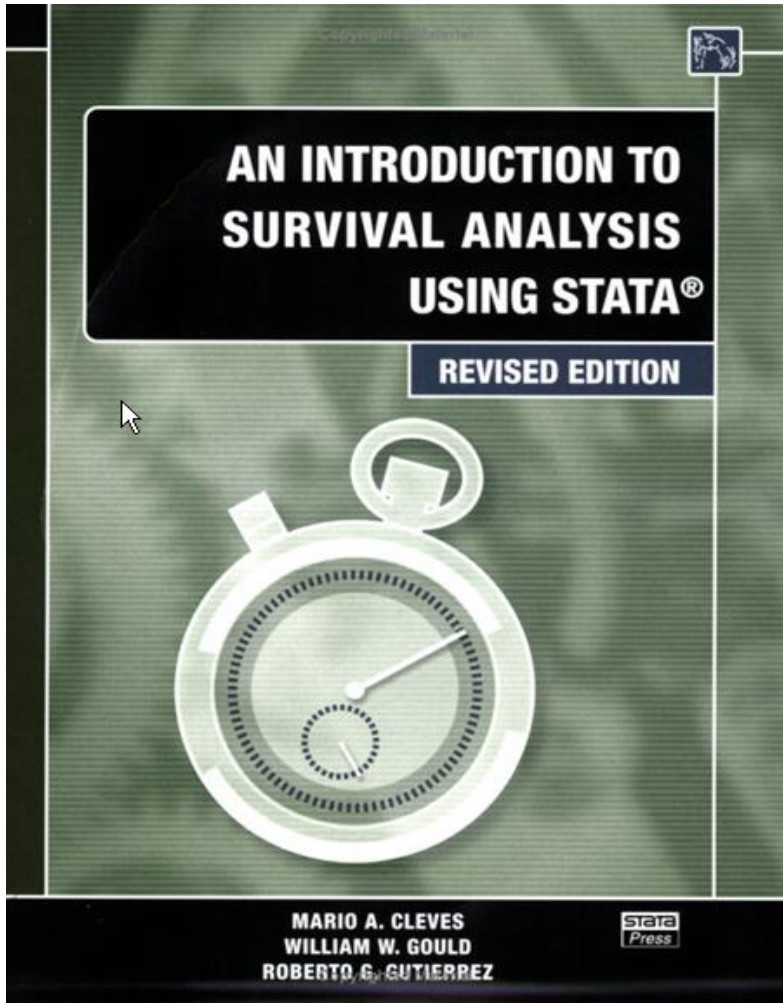
Rating: ++

Text books

Cleves MA, Gould WW, Gutierrez RG. An Introduction to Survival Analysis Using STATA. New York; STATA Press; 2003.

Practical coverage of a wide range of analytical techniques used in epidemiology. Good coverage of advanced topics.

Rating: +++



Text books

- Others
 - Collett D. Modelling Survival Data in Medical Research. London; Chapman and Hall; 1994.
 - Hosmer D, Lemeshow S. Applied Survival Analysis Regression Modeling of Time to Event Data. London; John Wiley and Sons; 1999.

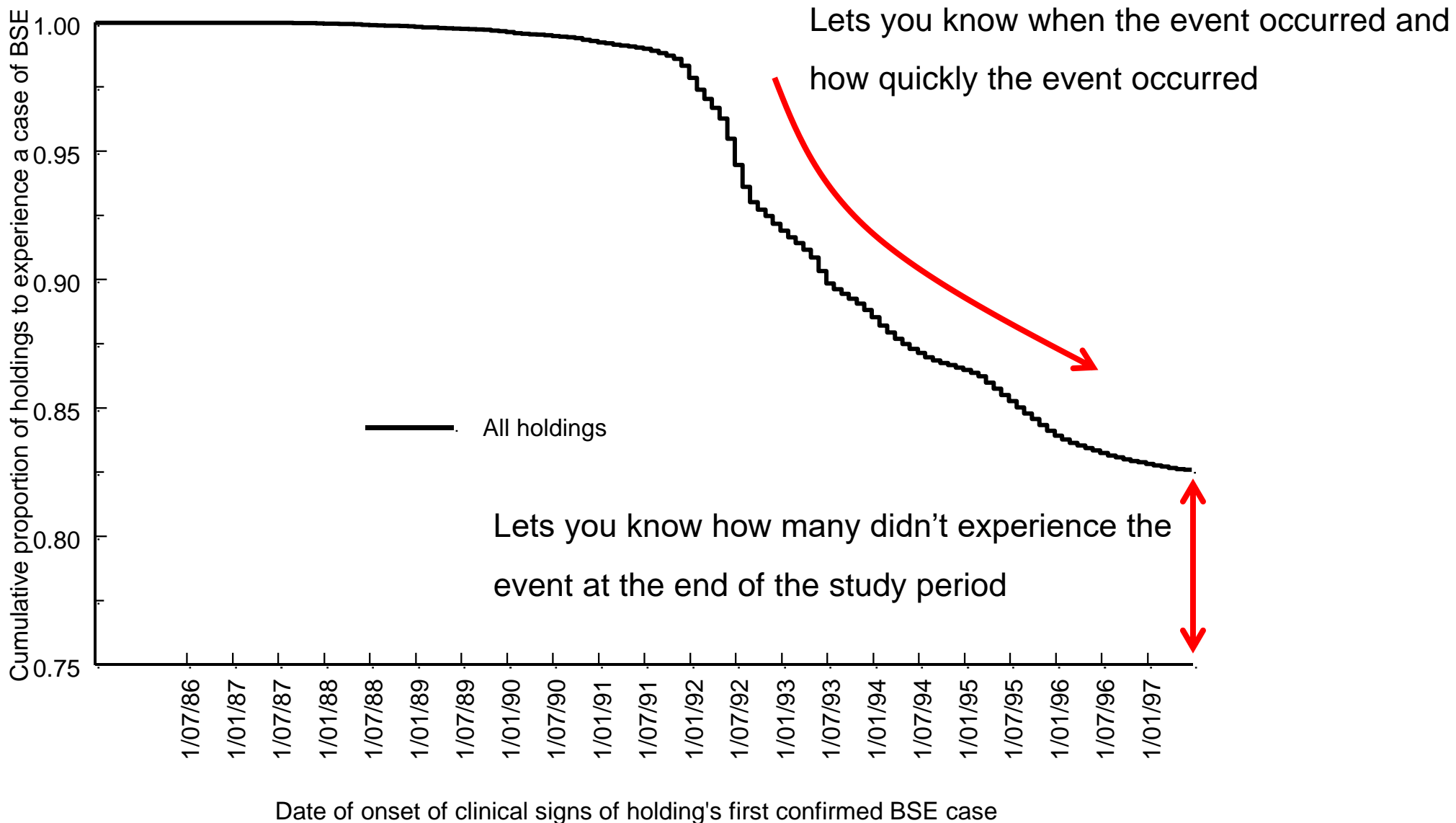
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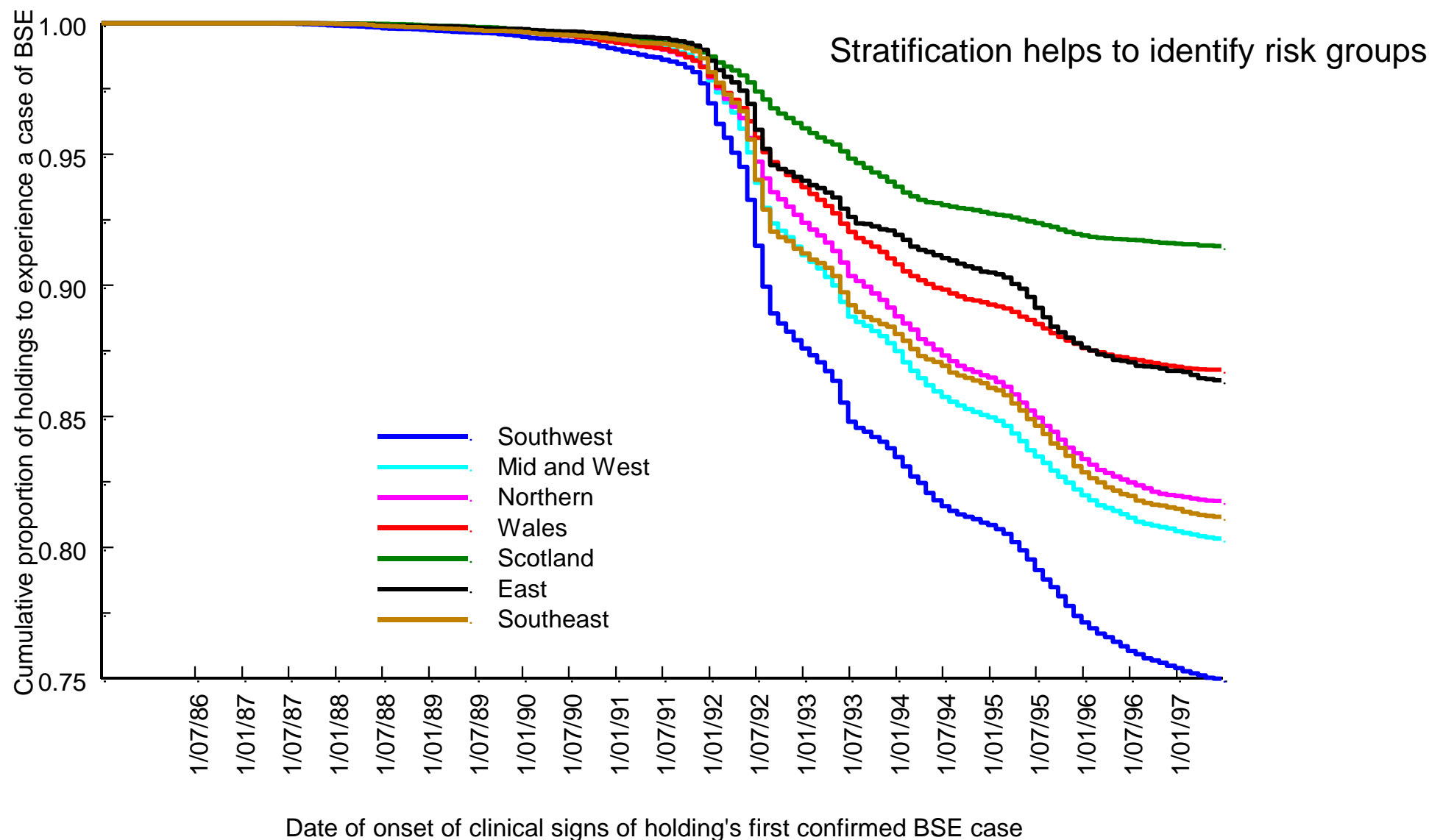
Background

- Survival analysis \equiv analysis of time to event data
- Many applications in vet epidemiology:
 - length of productive life
 - date of first disease case on property
 - age at seroconversion
- Terms you may have heard:
 - survival function (Kaplan-Meier survival curves)
 - Cox proportional hazards regression

Days to index BSE case - British cattle holdings.



Days to index BSE case - British cattle holdings.



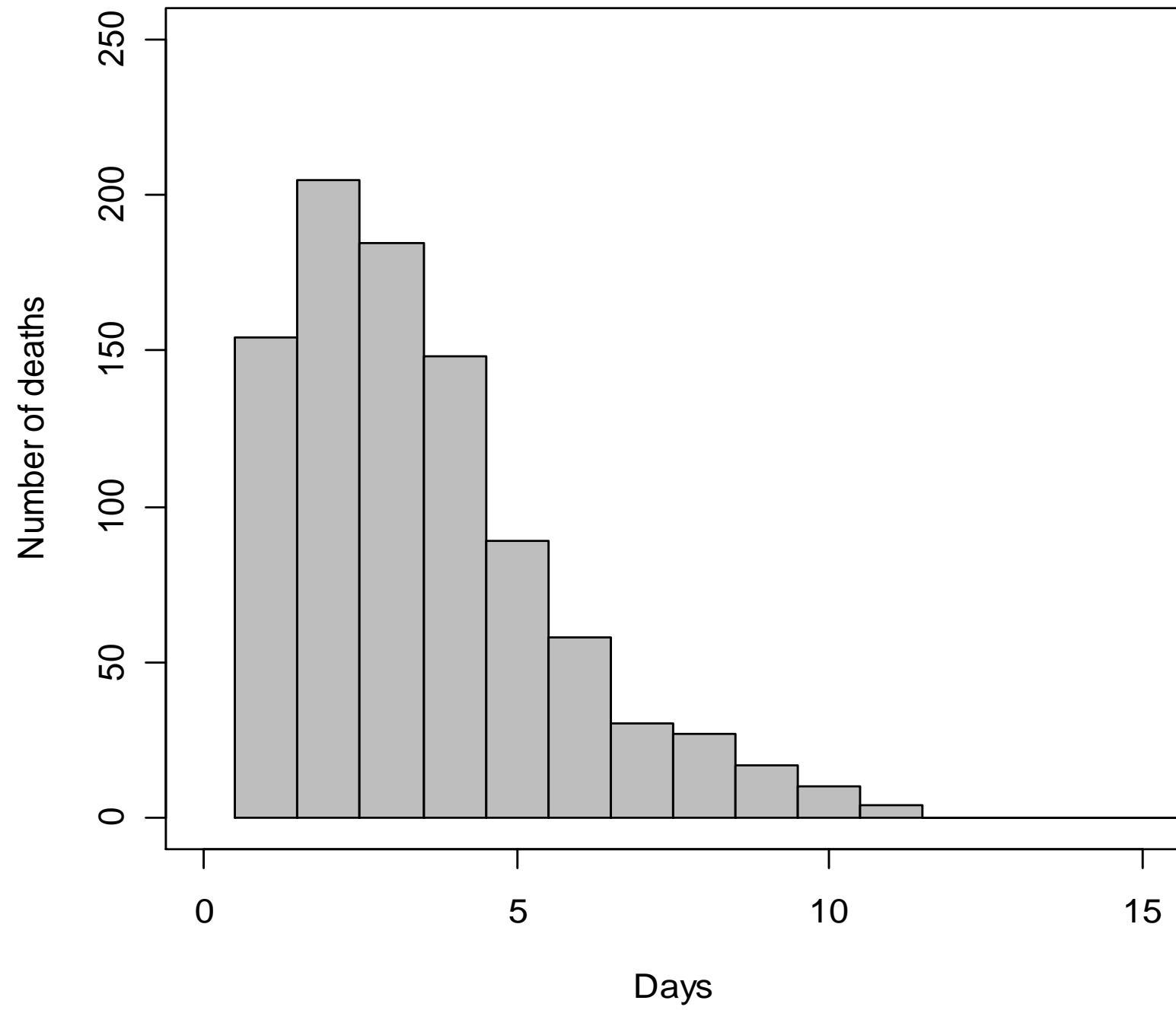
Background

- Survival \equiv time taken for event to occur
- Failure \equiv occurrence of event of interest
- Censoring \equiv subjects that don't show the event of interest during observation period
 - event didn't happen during the period of observation
 - the subject was withdrawn from study for a reason not related to event of interest

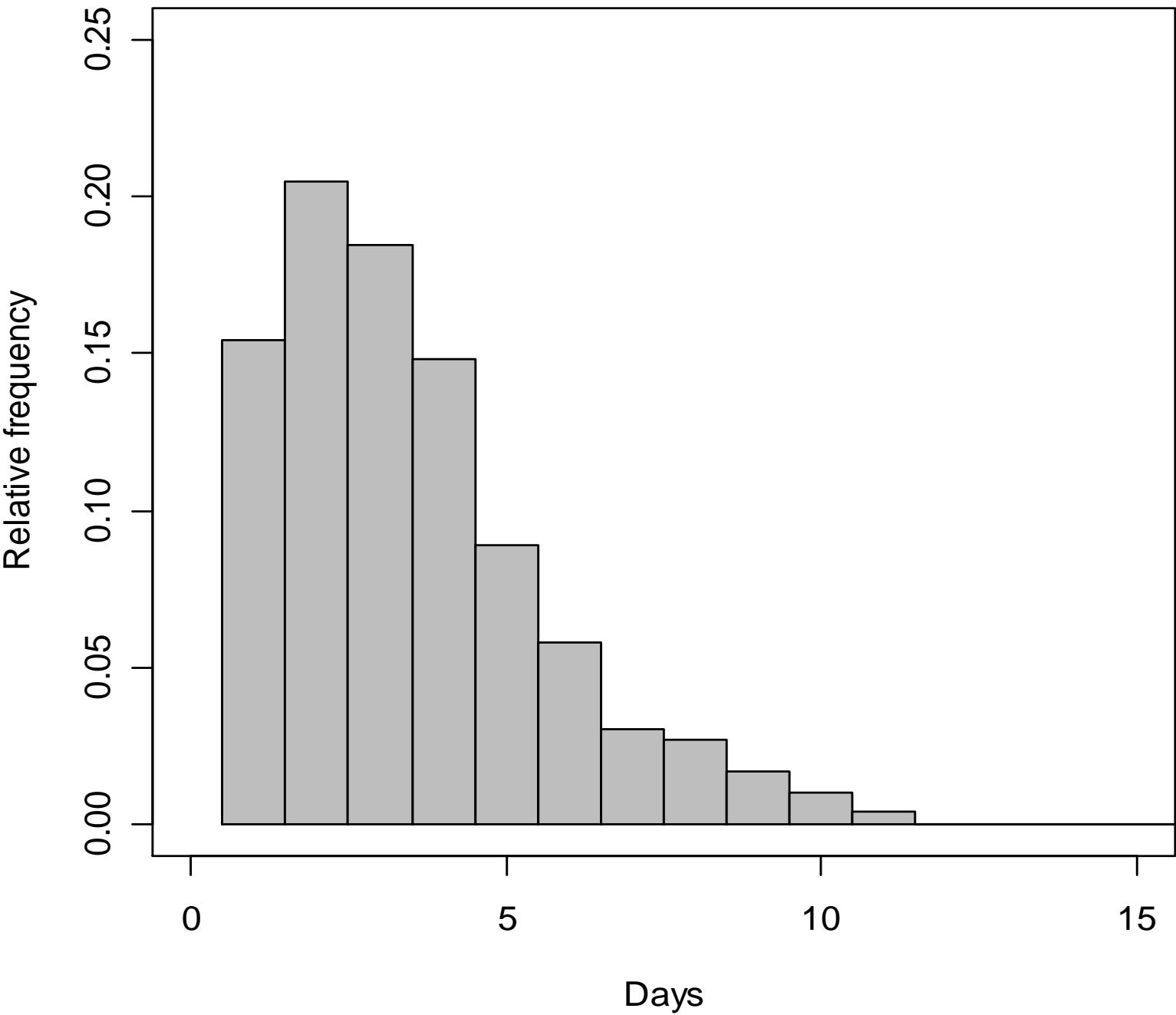
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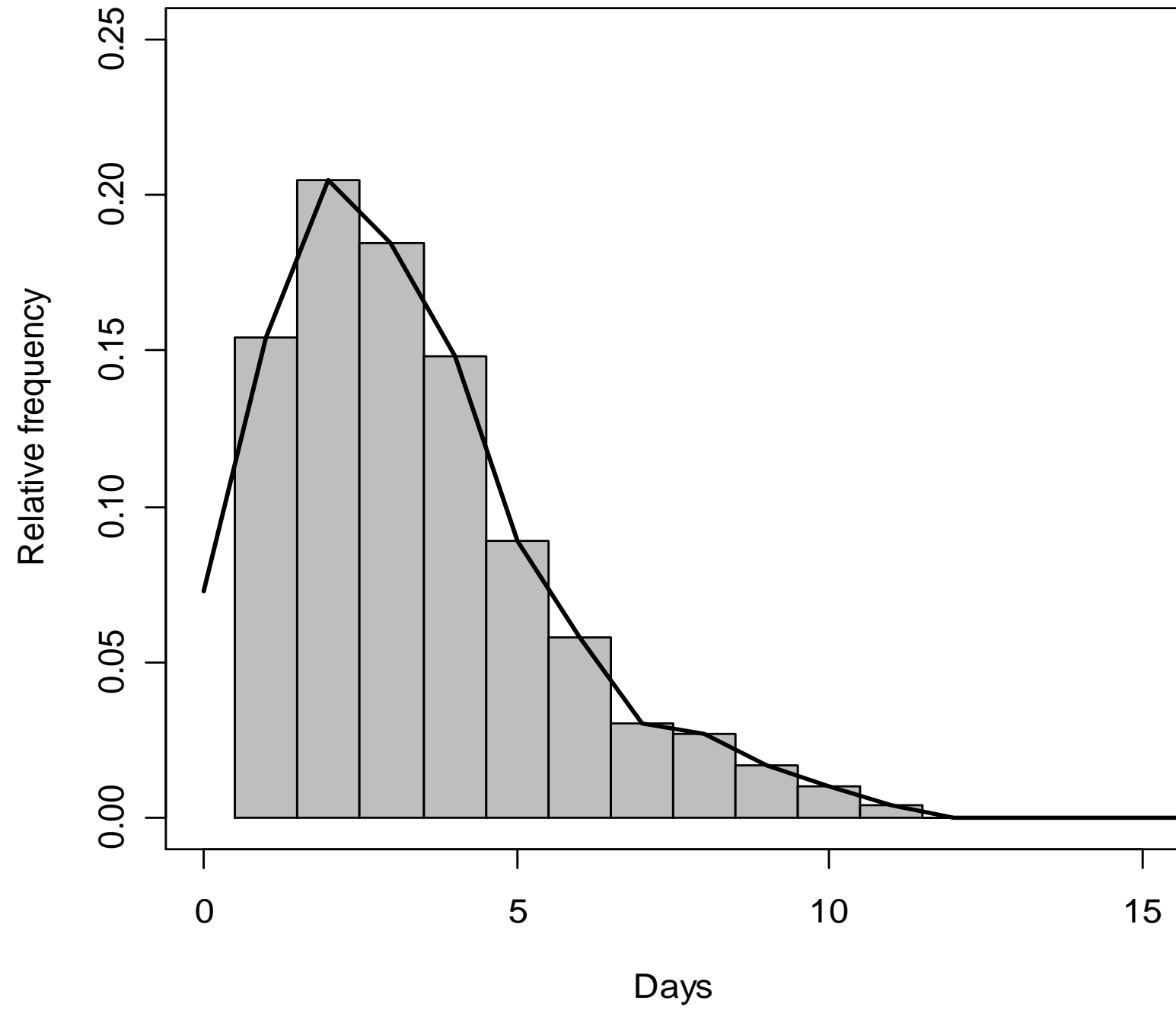
Frequency histogram showing the number of deaths as a function of time.



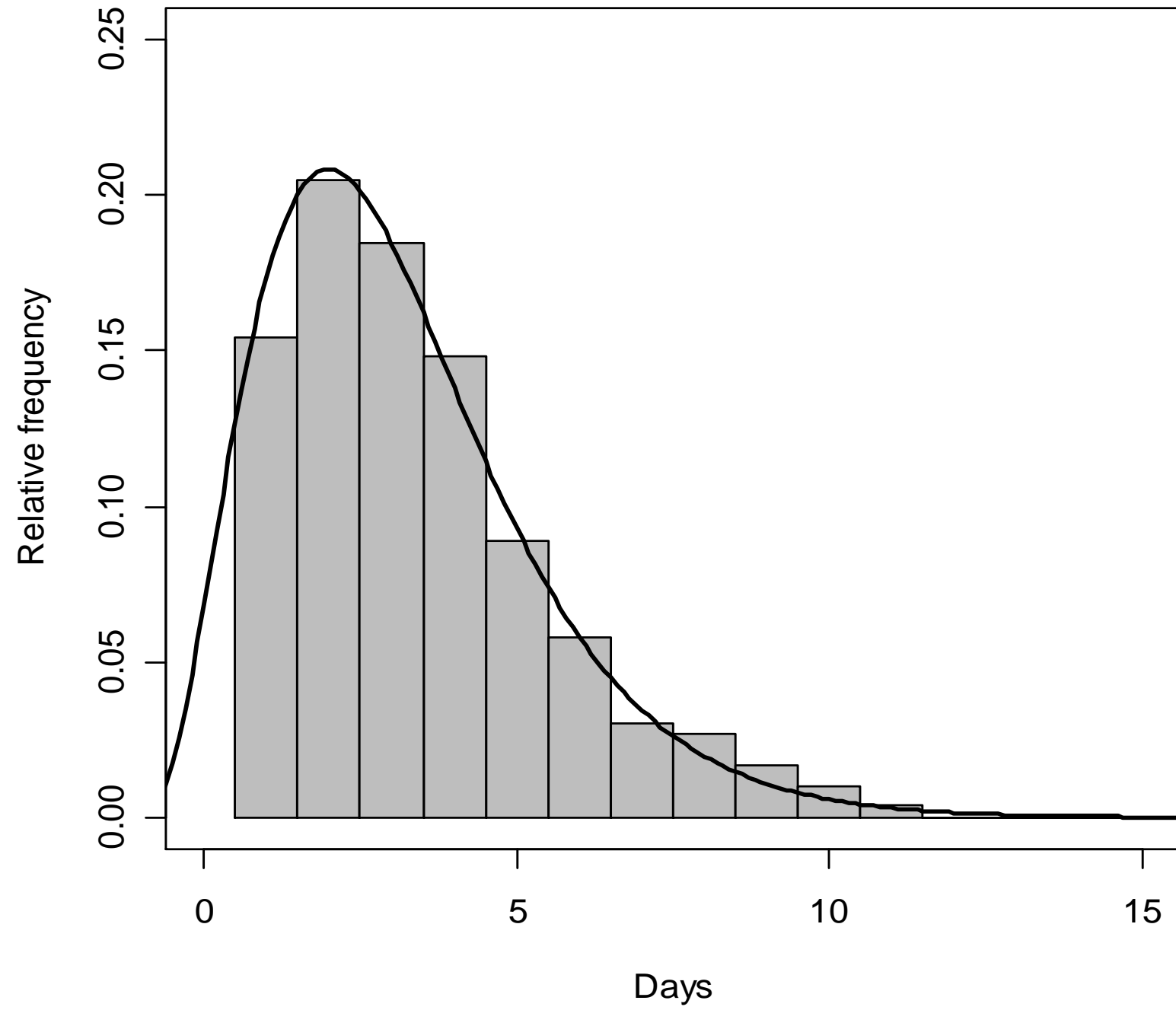
Frequency histogram showing the relative frequency of deaths as a function of time.



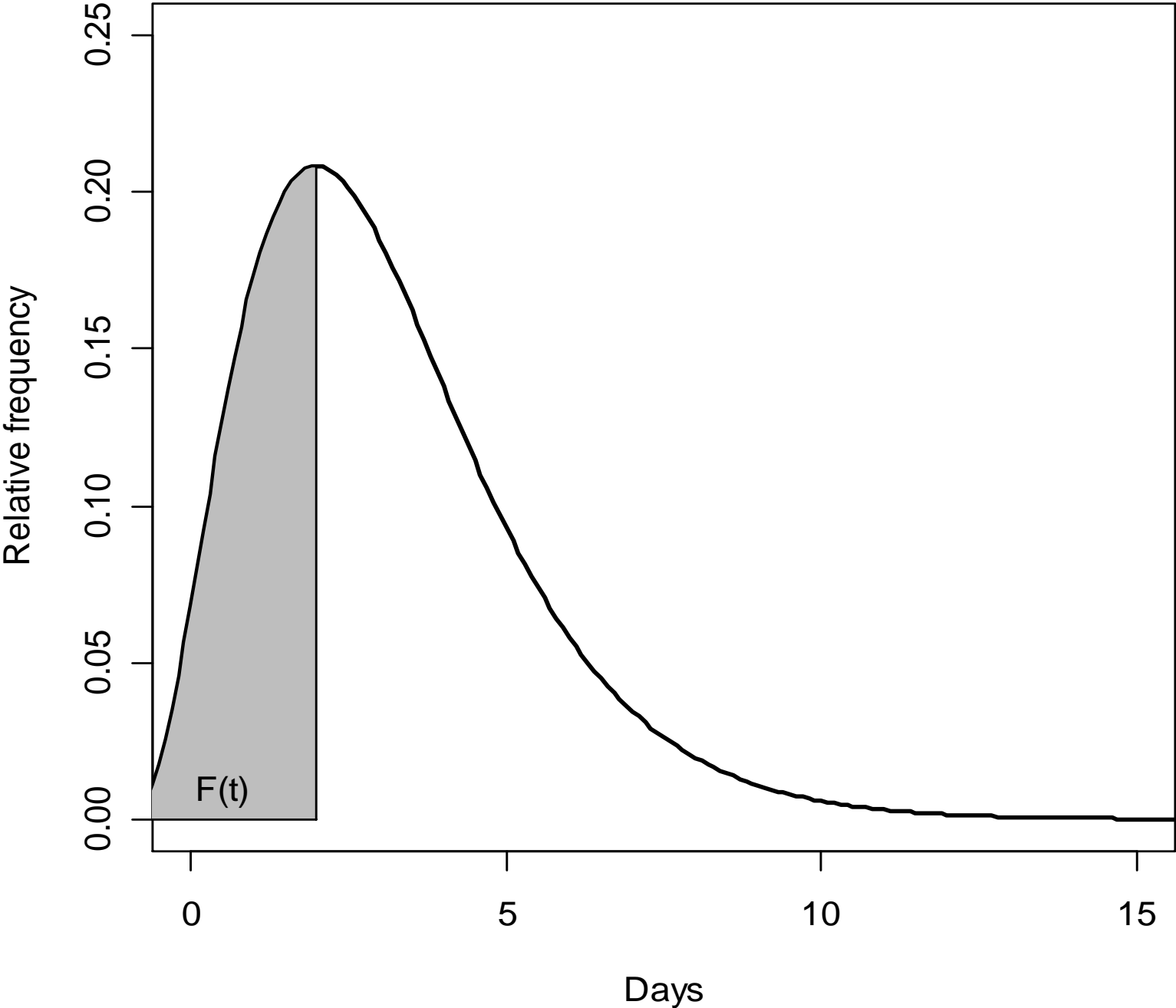
$f(t)$ = death density function.



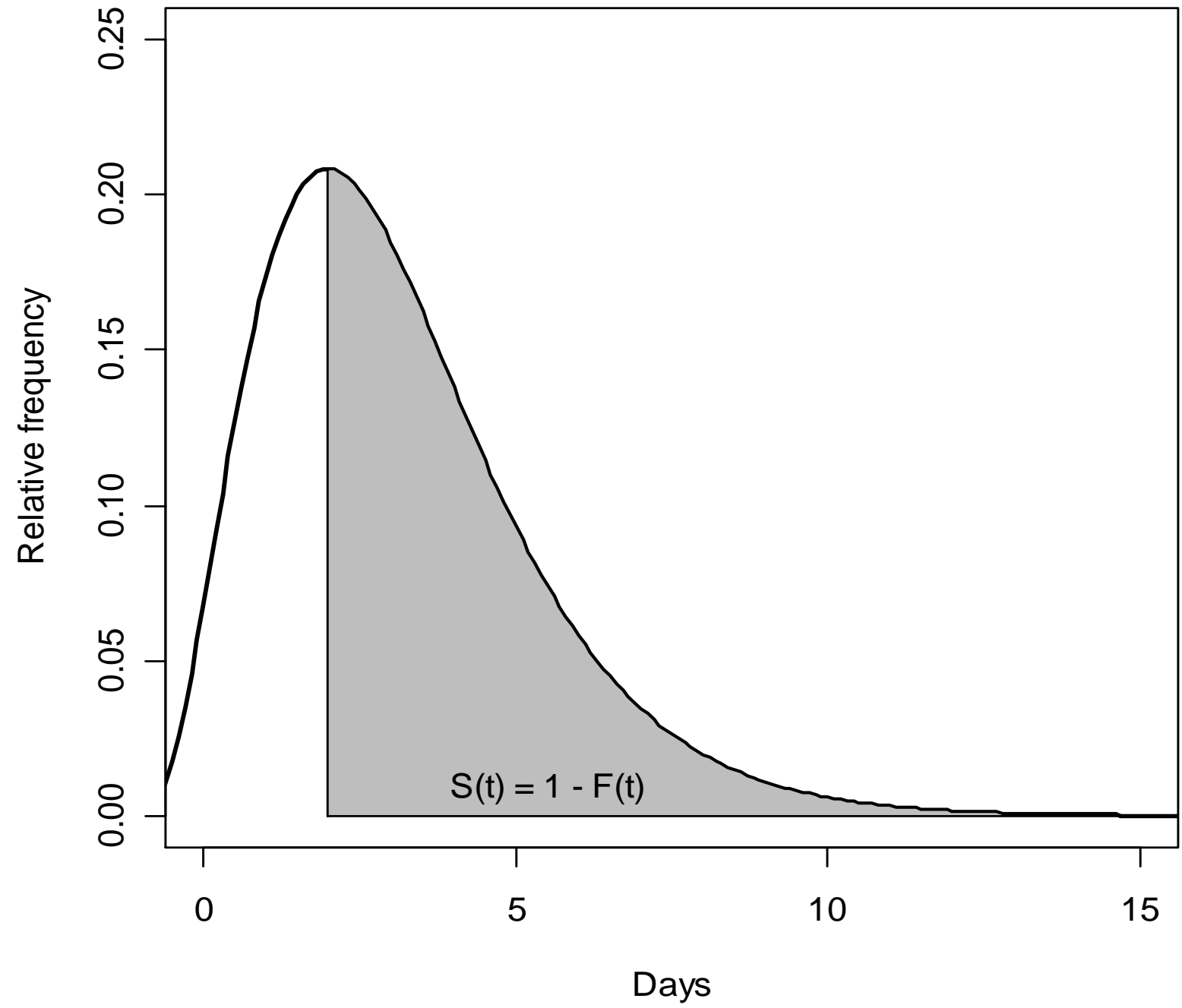
$f(t)$ = death density function.



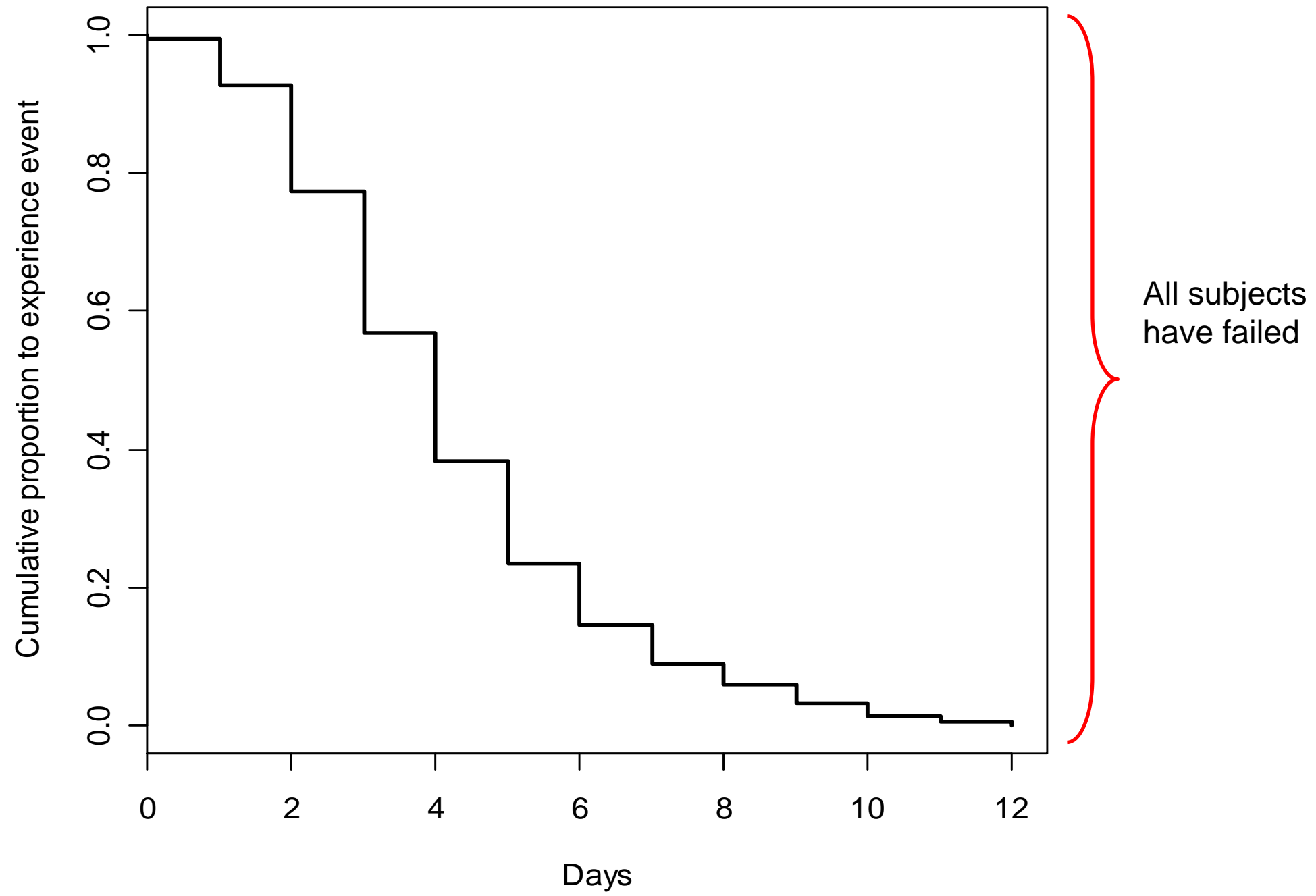
$F(t)$ = the failure function = the proportion not surviving past time t .



$S(t)$ = survival function = the proportion of the group that survive up to time $t = 1 - F(t)$.



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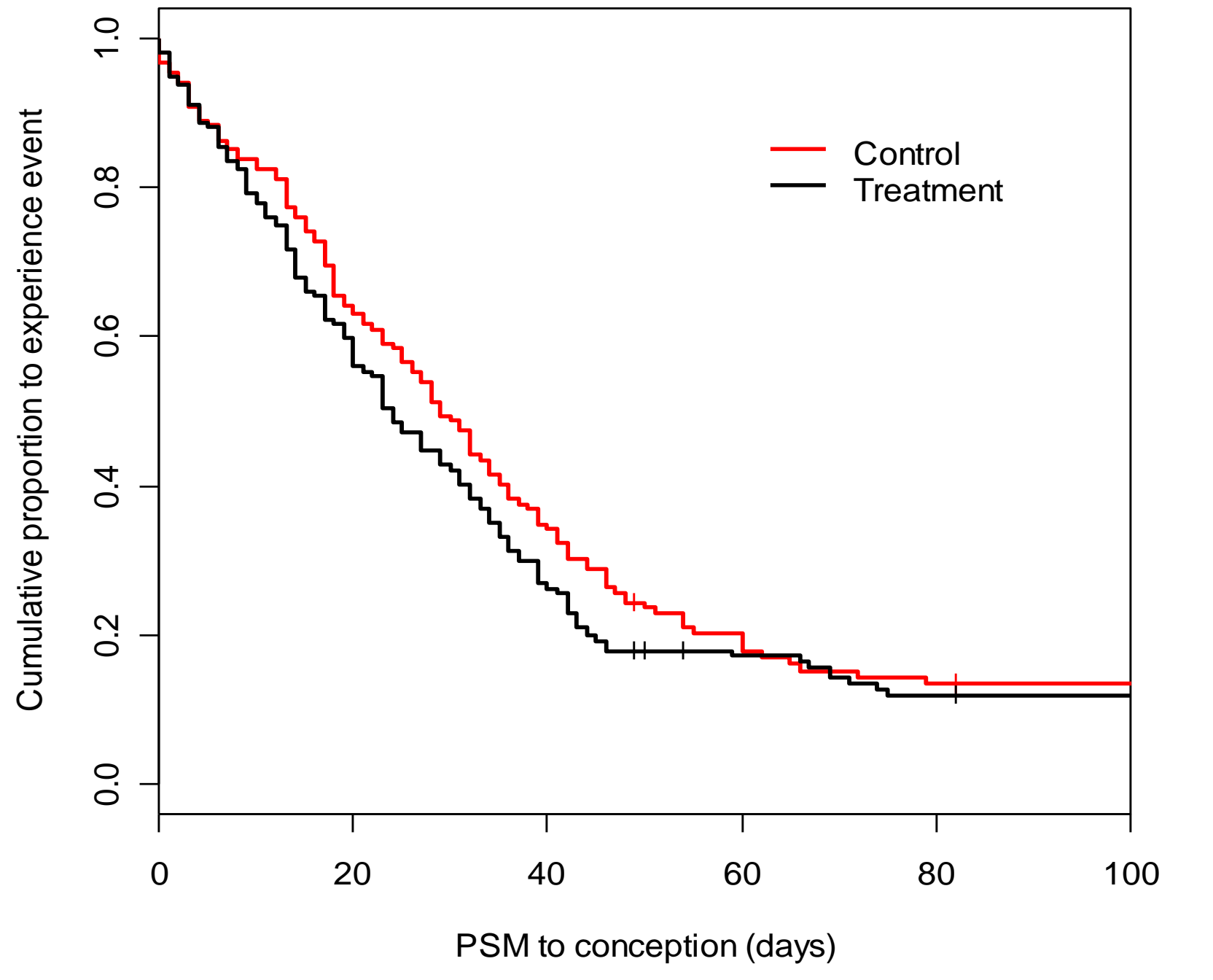


Survival and hazard

- Effect of post-calving oral calcium chloride treatment on fertility in dairy cattle ...



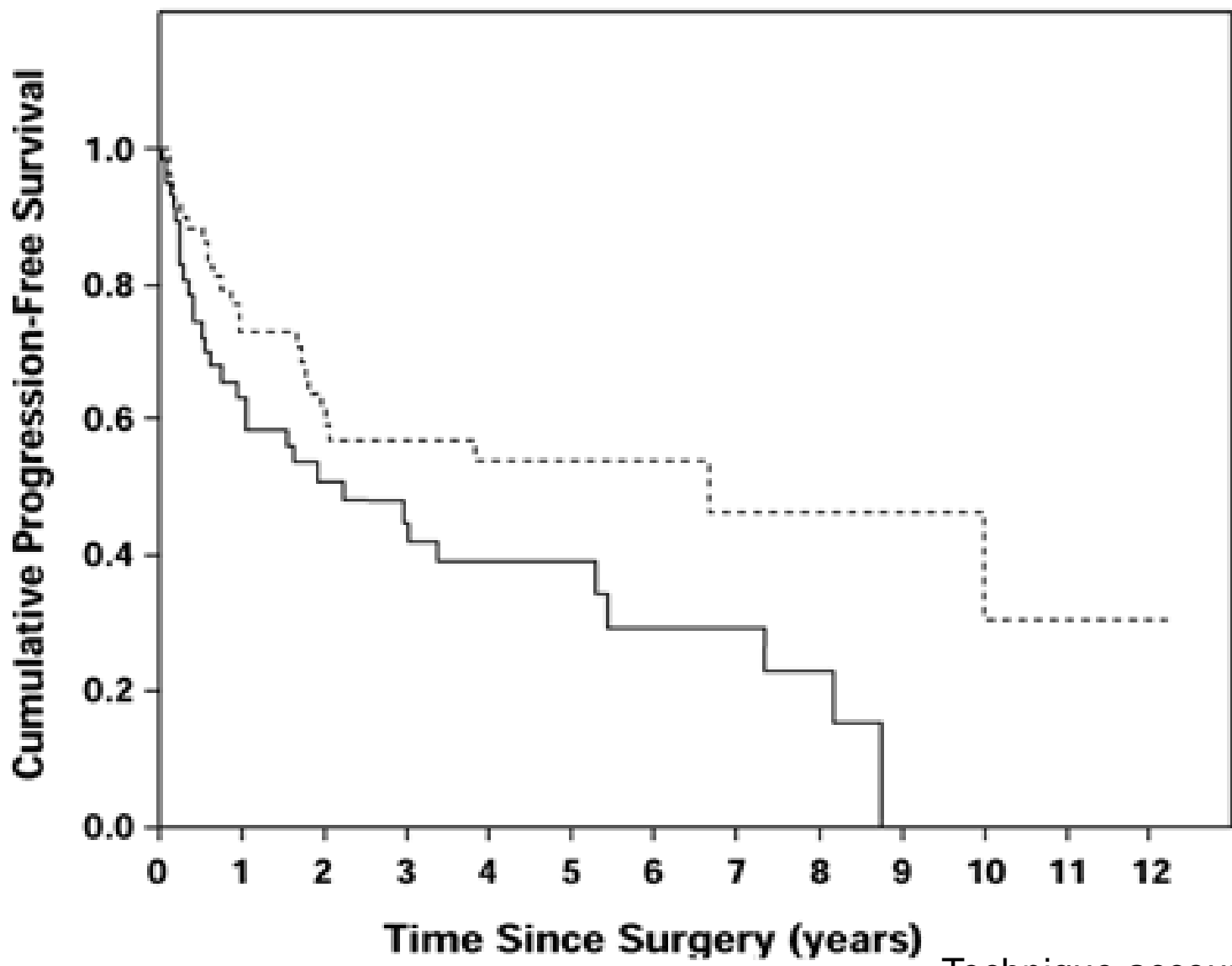
Effect of post-calving oral calcium chloride treatment on fertility in dairy cattle.



Survival and hazard

- Treatment of neoplasia in humans ...

Progression-free survival time post surgery.



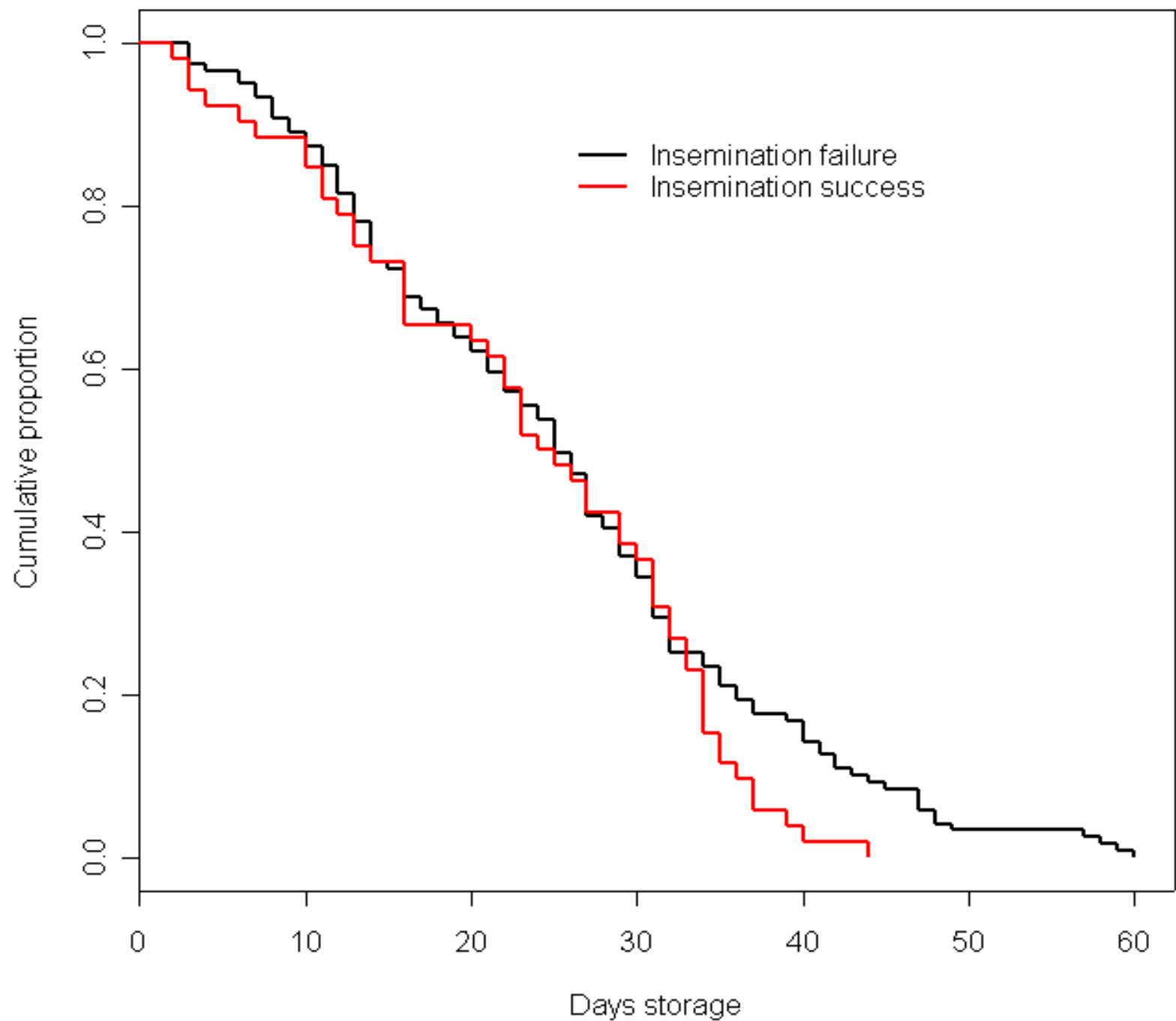
Technique accounts for changing population structure: often instability in the 'tail' of computed survival functions (small numbers of subjects left to experience event of interest).

Survival and hazard

- Insemination outcome (success or failure) as a function of semen storage time ...



Effect of semen storage time on insemination outcome.



Survival and hazard

- The problem of the disappearing teaspoons ...

The case of the disappearing teaspoons: longitudinal cohort study of the displacement of teaspoons in an Australian research institute

Megan S C Lim, Margaret E Hellard, Campbell K Aitken

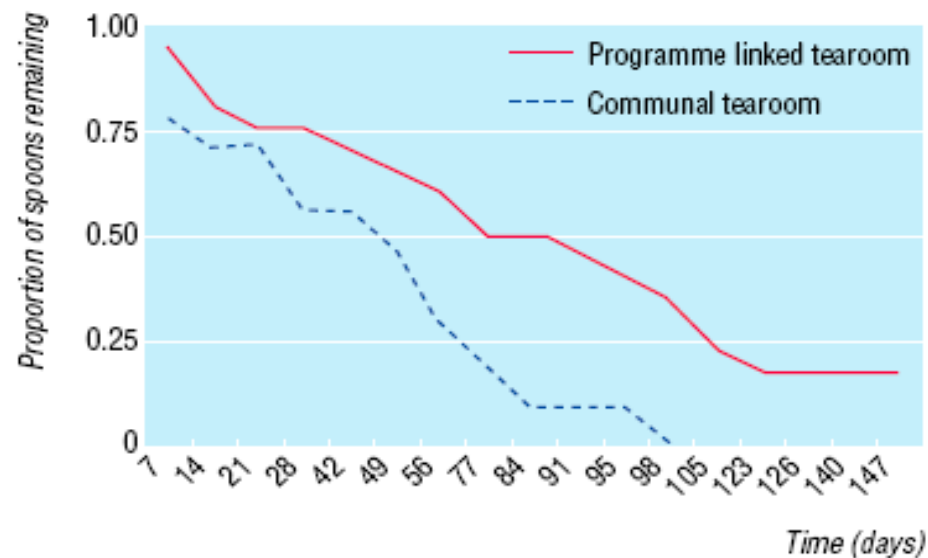


Fig 1 Proportion of teaspoons remaining by final tearoom type

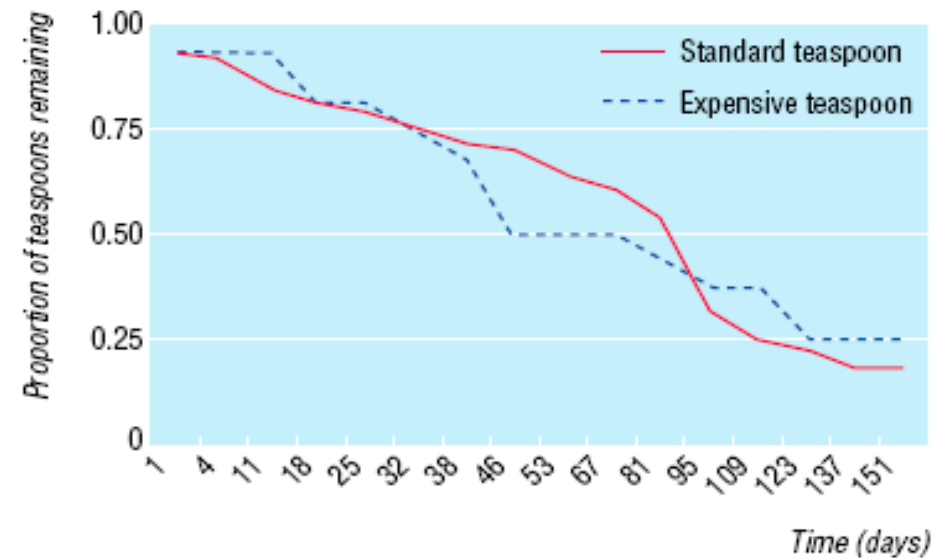


Fig 2 Proportion of teaspoons remaining by teaspoon type



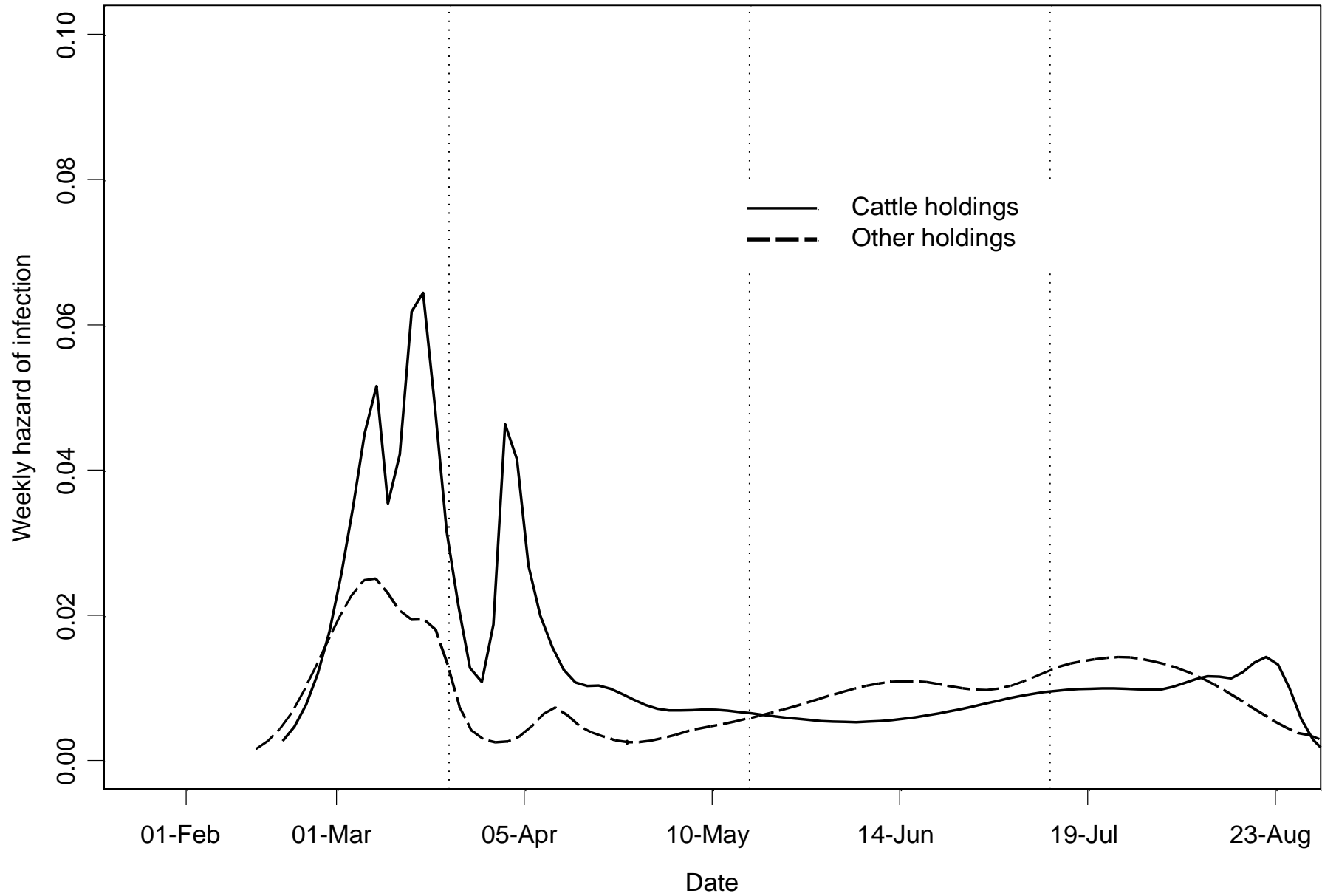
Lim, M., Hellard, M., Aitken, C., 2006. The case of the disappearing teaspoons: longitudinal cohort study of the displacement of teaspoons in an Australian research institute. *British Medical Journal* 331, 1498 - 1500.

Survival and hazard

- Instantaneous hazard
 - $h(t)$
 - \equiv 'hazard' (Dohoo, Martin and Stryhn)
 - equals the probability of an event occurring at time t , given that it has not occurred already



Weekly instantaneous hazard of FMD in Cumbria, February – September 2001.



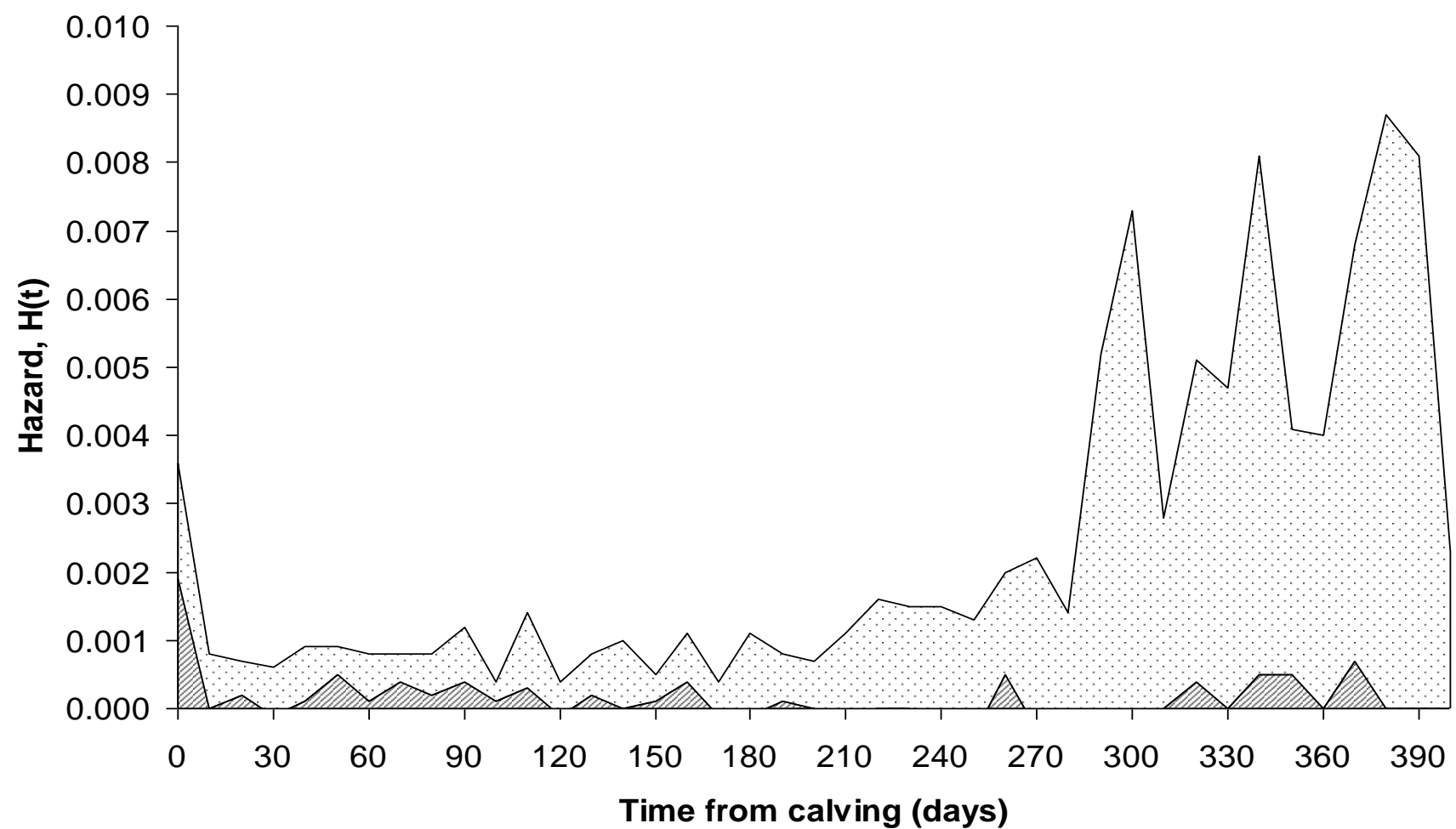
Wilesmith, J., Stevenson, M., King, C., Morris, R., 2003. Spatio-temporal epidemiology of foot-and-mouth disease in two counties of Great Britain in 2001. Preventive Veterinary Medicine 61, 157 - 170.

Survival and hazard

- Length of productive life in dairy herds ...

Hazard of sale and death in NSW dairy cattle.

Dark shading shows hazard of death, light shading hazard of sale.

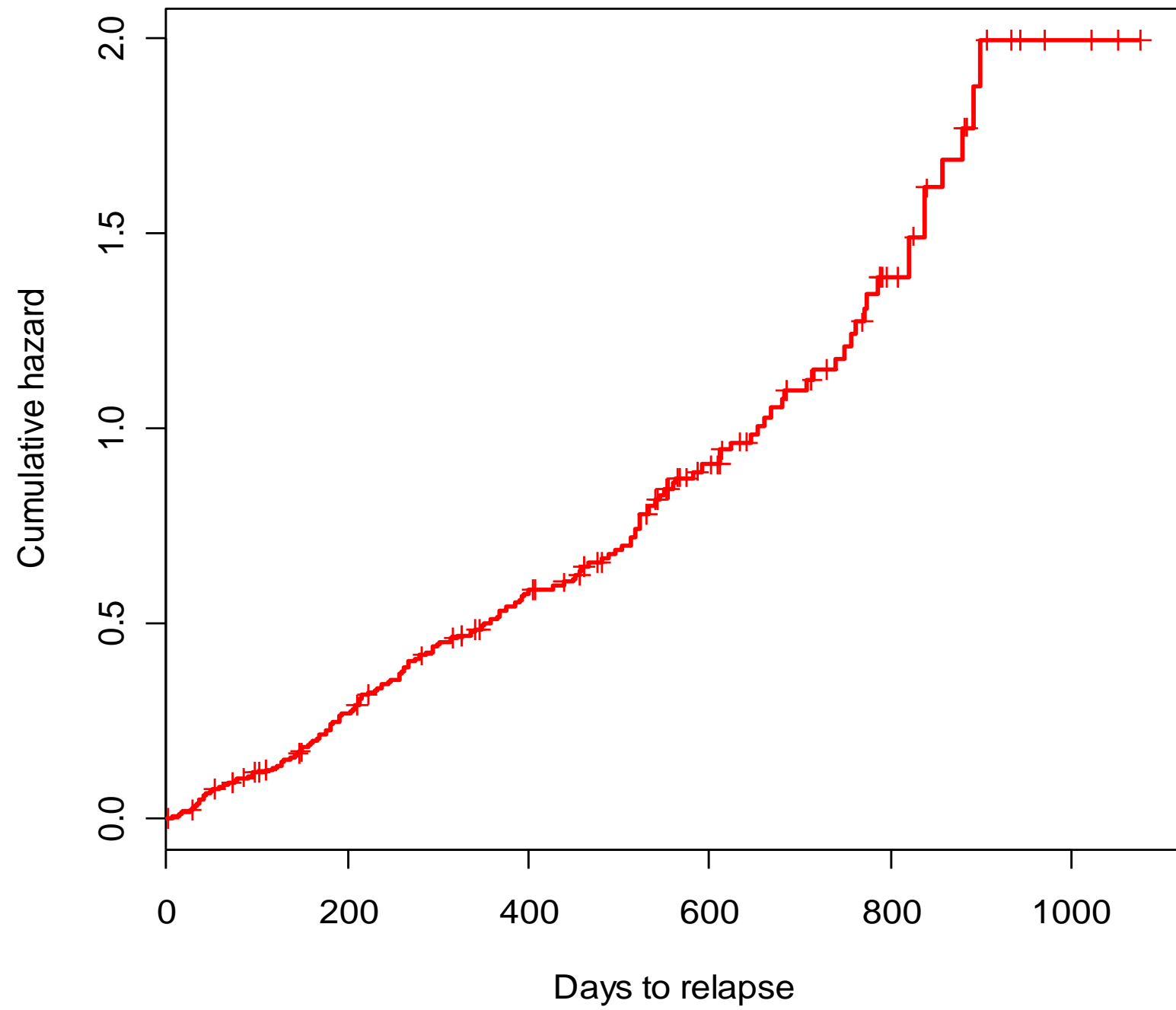


Stevenson, M., Lean, I., 1998. Descriptive epidemiological study on culling and deaths in eight dairy herds. Australian Veterinary Journal 76, 482 - 488.

Survival and hazard

- Cumulative hazard
 - $H(t)$
 - also referred to as ‘integrated hazard’
 - equals the total amount of accumulated risk that an individual has encountered from the beginning of the observation period
 - neither a probability or rate
 - $H(t) = -\log S(t)$

Cumulative hazard of relapse in heroin addicts following discharge from rehabilitation.



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Examples

- Applications of survival analysis in veterinary epidemiology
 - describe survival (or hazard) functions
 - compare survival (or hazard) functions between groups
 - quantify factors that influence survival



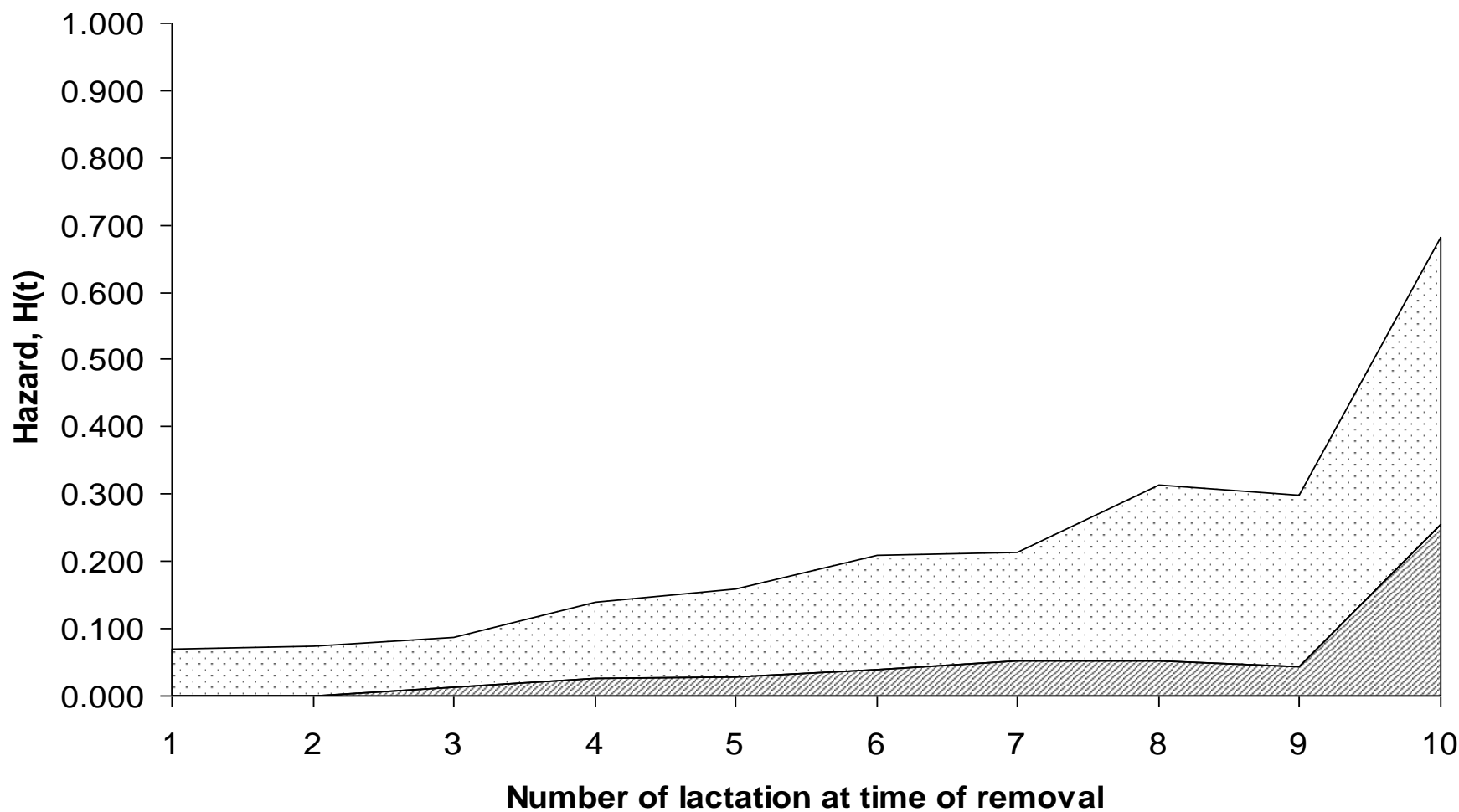








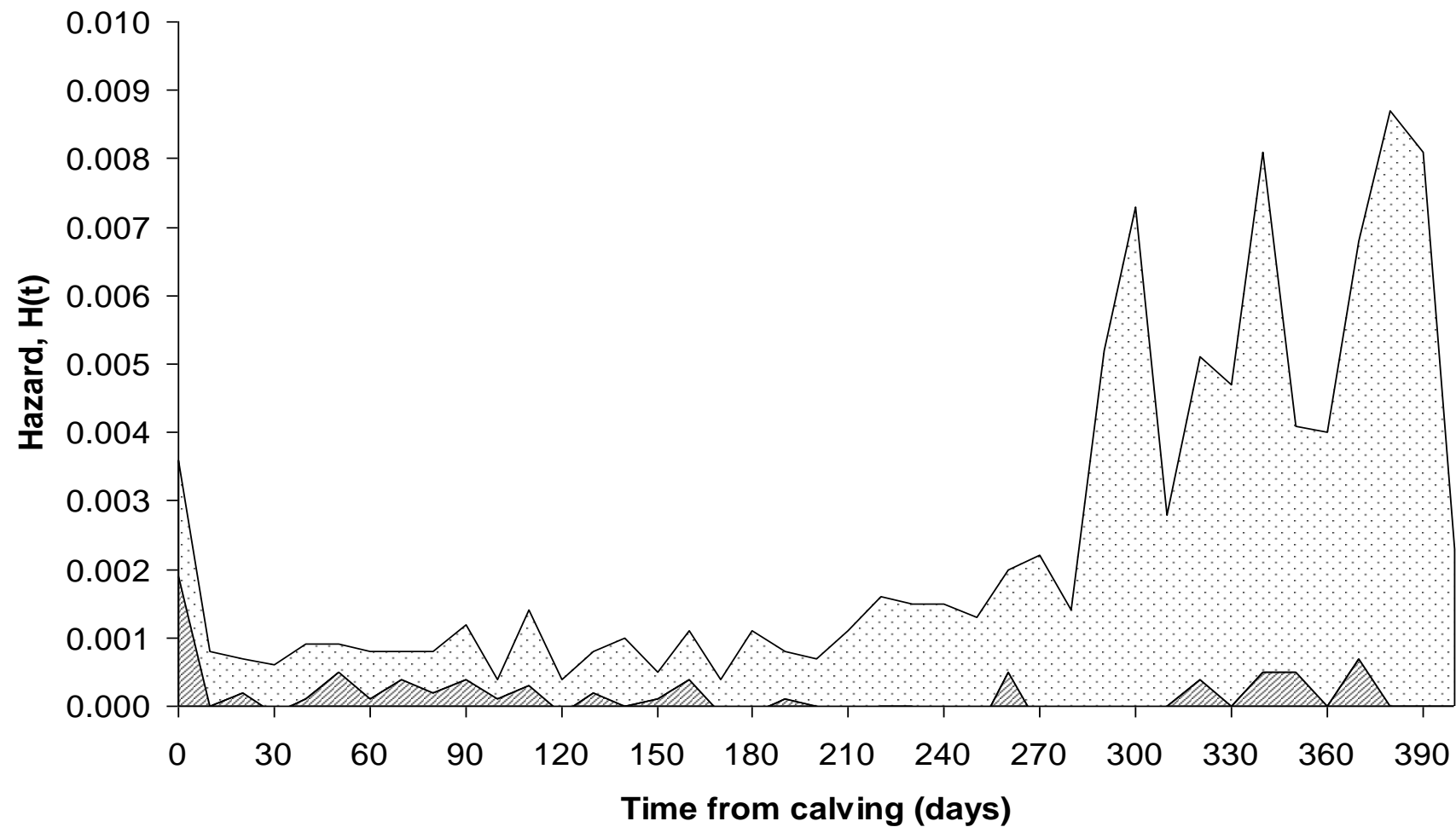
Hazard of sale and death in NSW dairy cattle as a function of lactation number.
Dark shading shows hazard of death, light shading hazard of sale.



Stevenson, M., Lean, I., 1998. Descriptive epidemiological study on culling and deaths in eight dairy herds. Australian Veterinary Journal 76, 482 - 488.

Hazard of sale and death in NSW dairy cattle as a function of days in milk.

Dark shading shows hazard of death, light shading hazard of sale.



Stevenson, M., Lean, I., 1998. Descriptive epidemiological study on culling and deaths in eight dairy herds. Australian Veterinary Journal 76, 482 - 488.

Hazard of removal for udder health disorders in NSW dairy cattle.

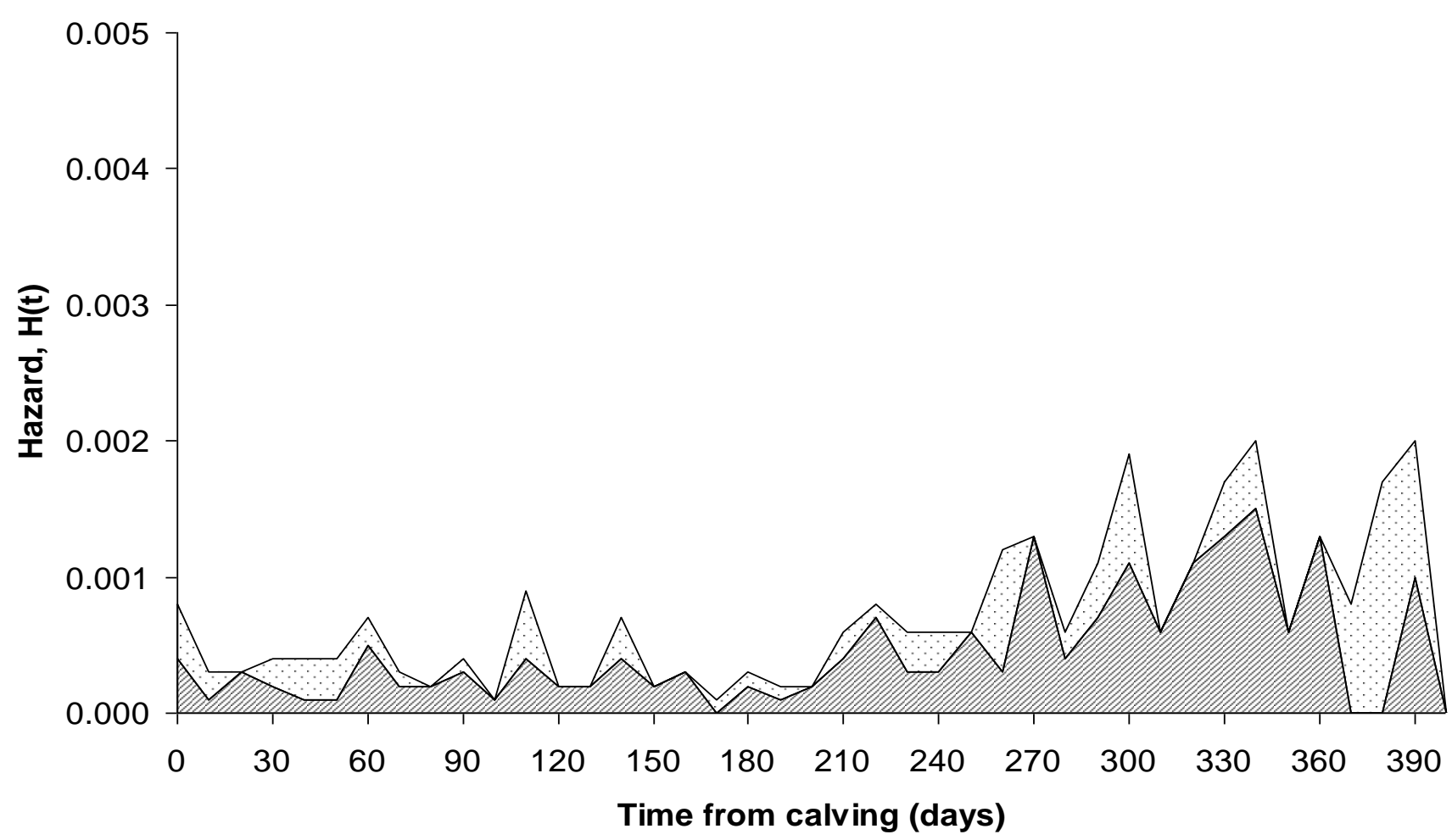
Dark shading shows hazard of removal for mastitis, light shading hazard of removal for other disorders.



Stevenson, M., Lean, I., 1998. Descriptive epidemiological study on culling and deaths in eight dairy herds. Australian Veterinary Journal 76, 482 - 488.

Hazard of removal for udder health disorders in NSW dairy cattle.

Dark shading shows hazard of removal for mastitis, light shading hazard of removal for other disorders.

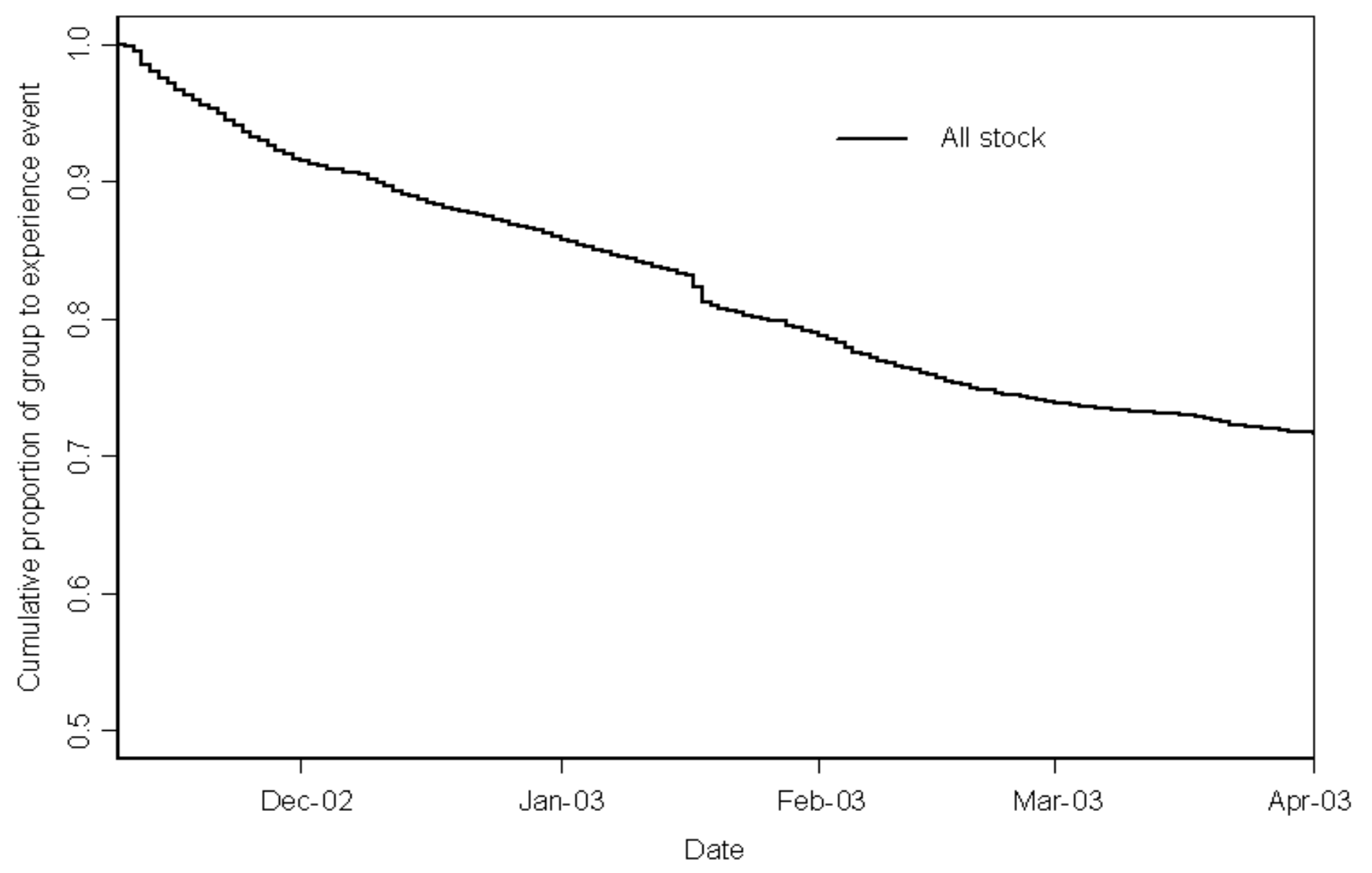


Stevenson, M., Lean, I., 1998. Descriptive epidemiological study on culling and deaths in eight dairy herds. Australian Veterinary Journal 76, 482 - 488.

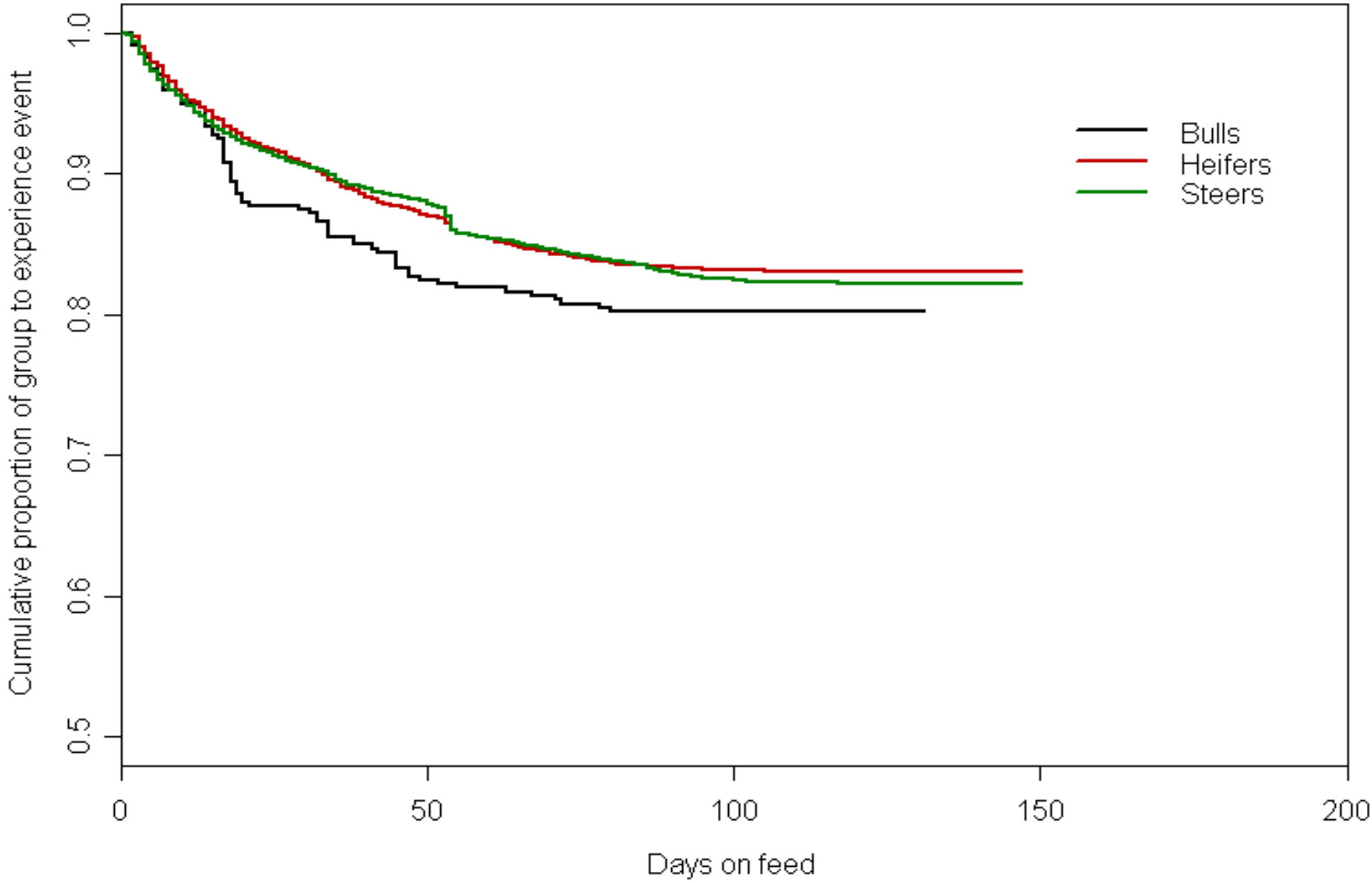
An Indonesian feedlot.



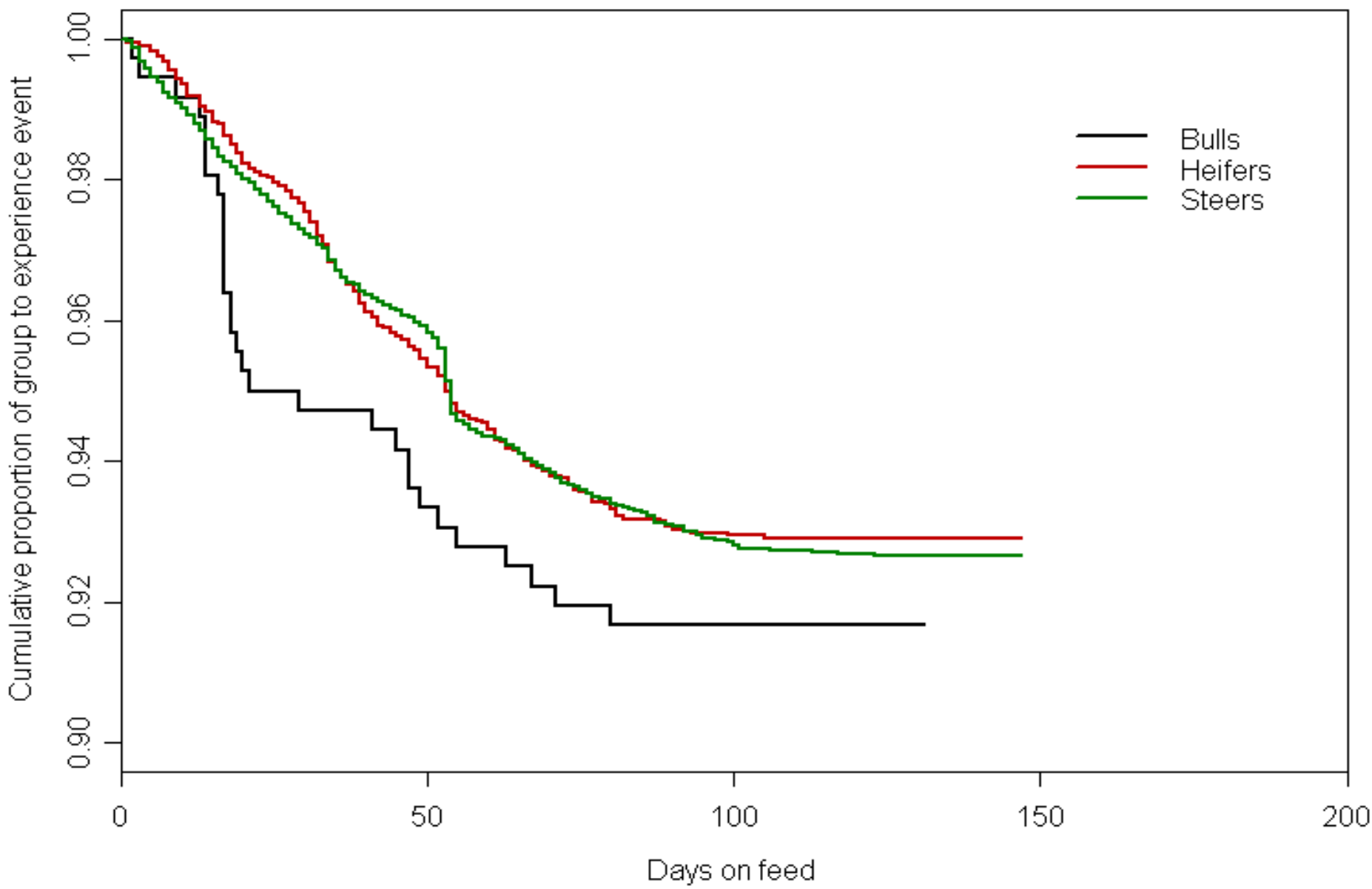
Kaplan-Meier survival curve showing cumulative proportion of animals pulled for all reasons as a function of calendar date, all stock.



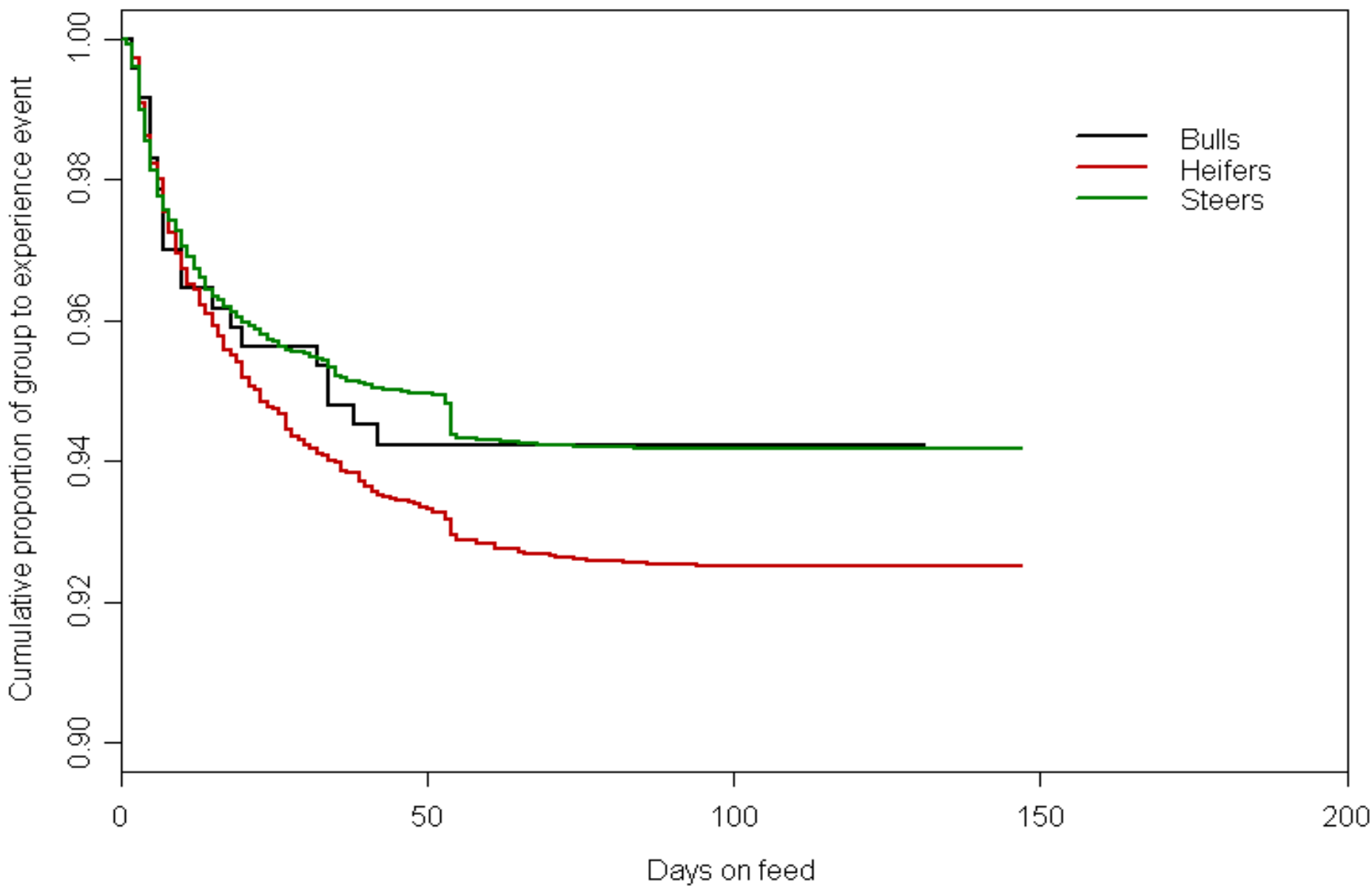
Kaplan-Meier survival curve showing cumulative proportion of animals pulled for all reasons as a function of calendar date, by stock class.



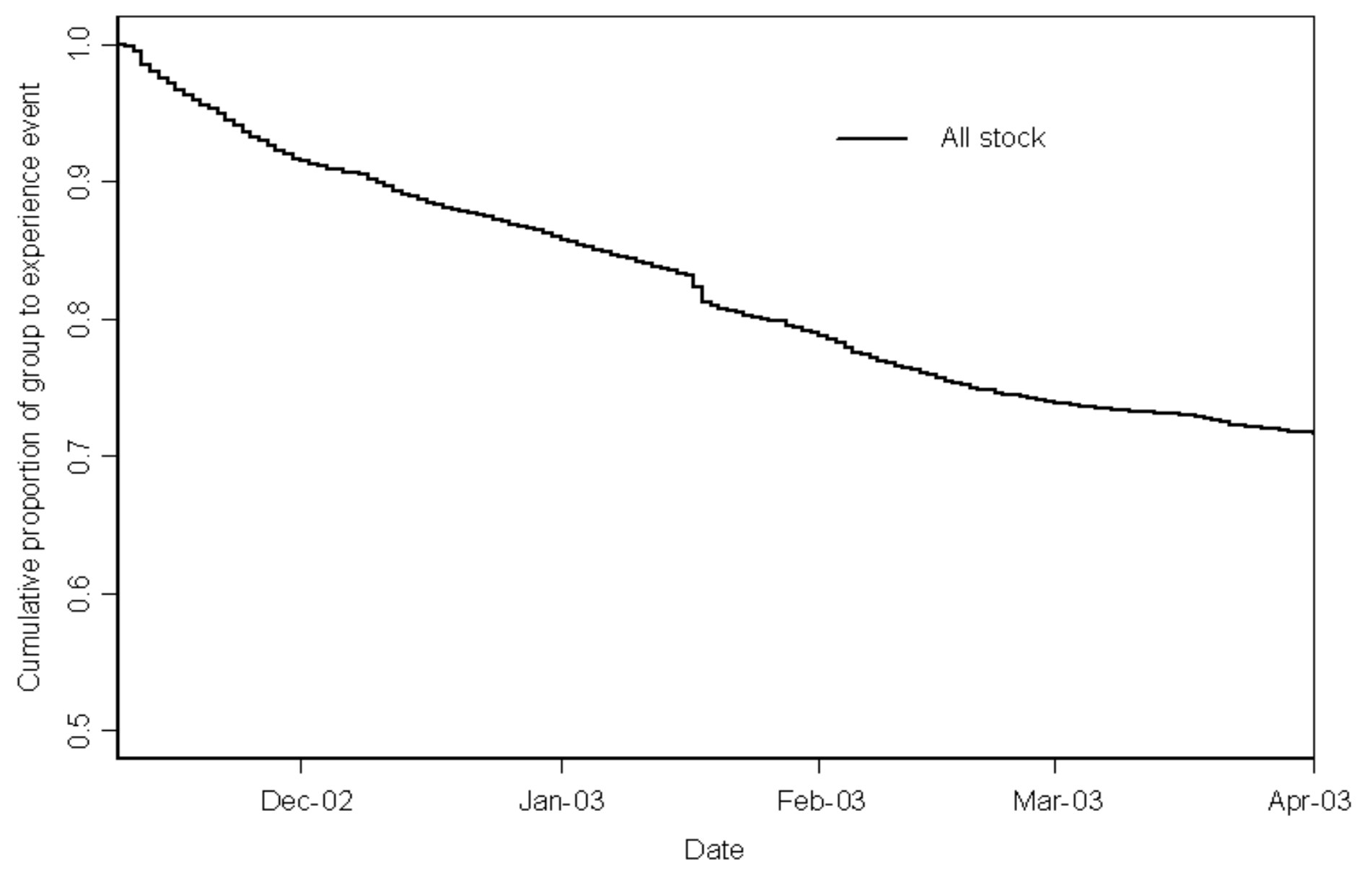
Kaplan-Meier survival curve showing cumulative proportion of animals pulled for lameness as a function of calendar date, by stock class.



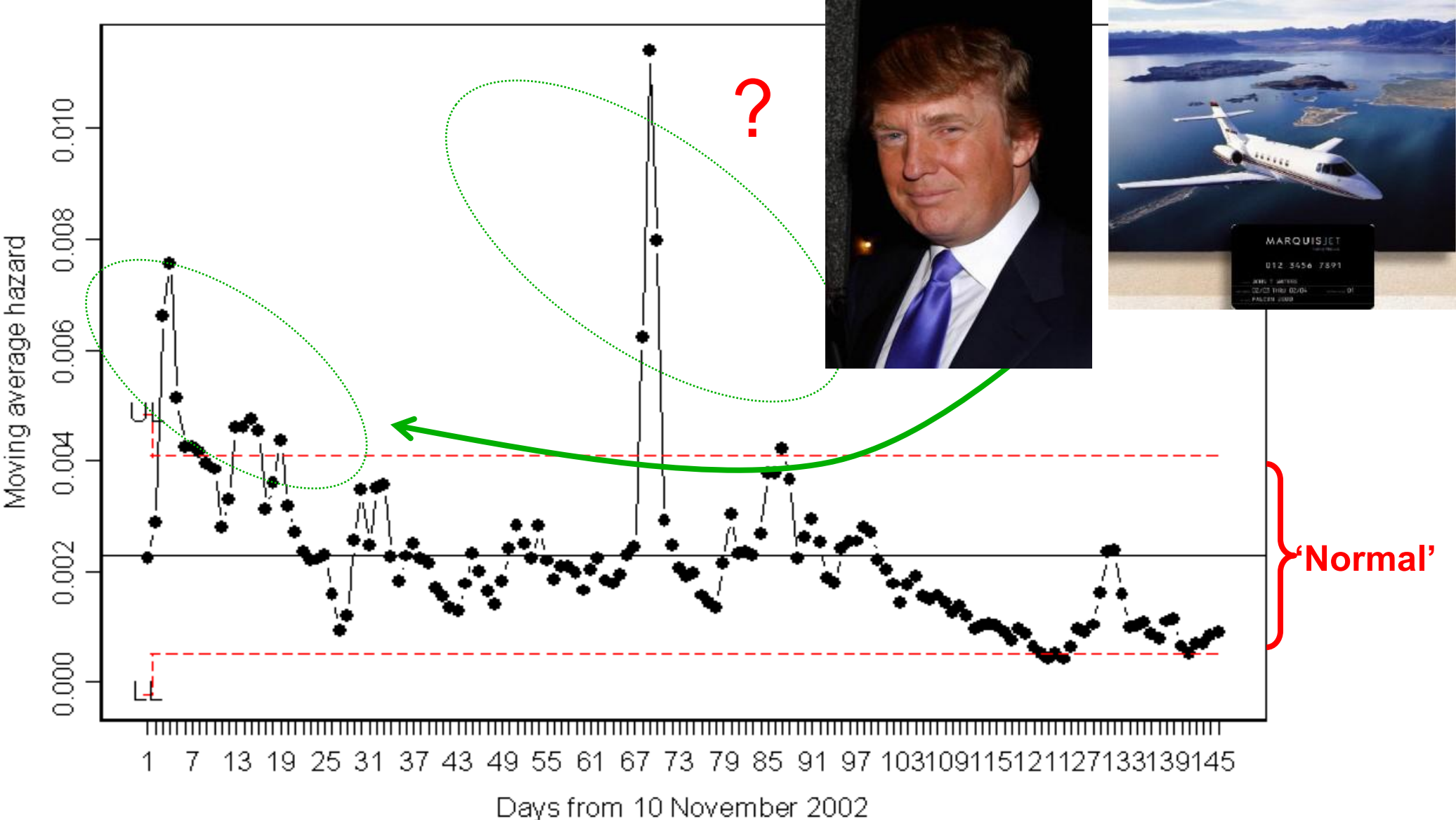
Kaplan-Meier survival curve showing cumulative proportion of animals pulled for weakness as a function of calendar date, by stock class.



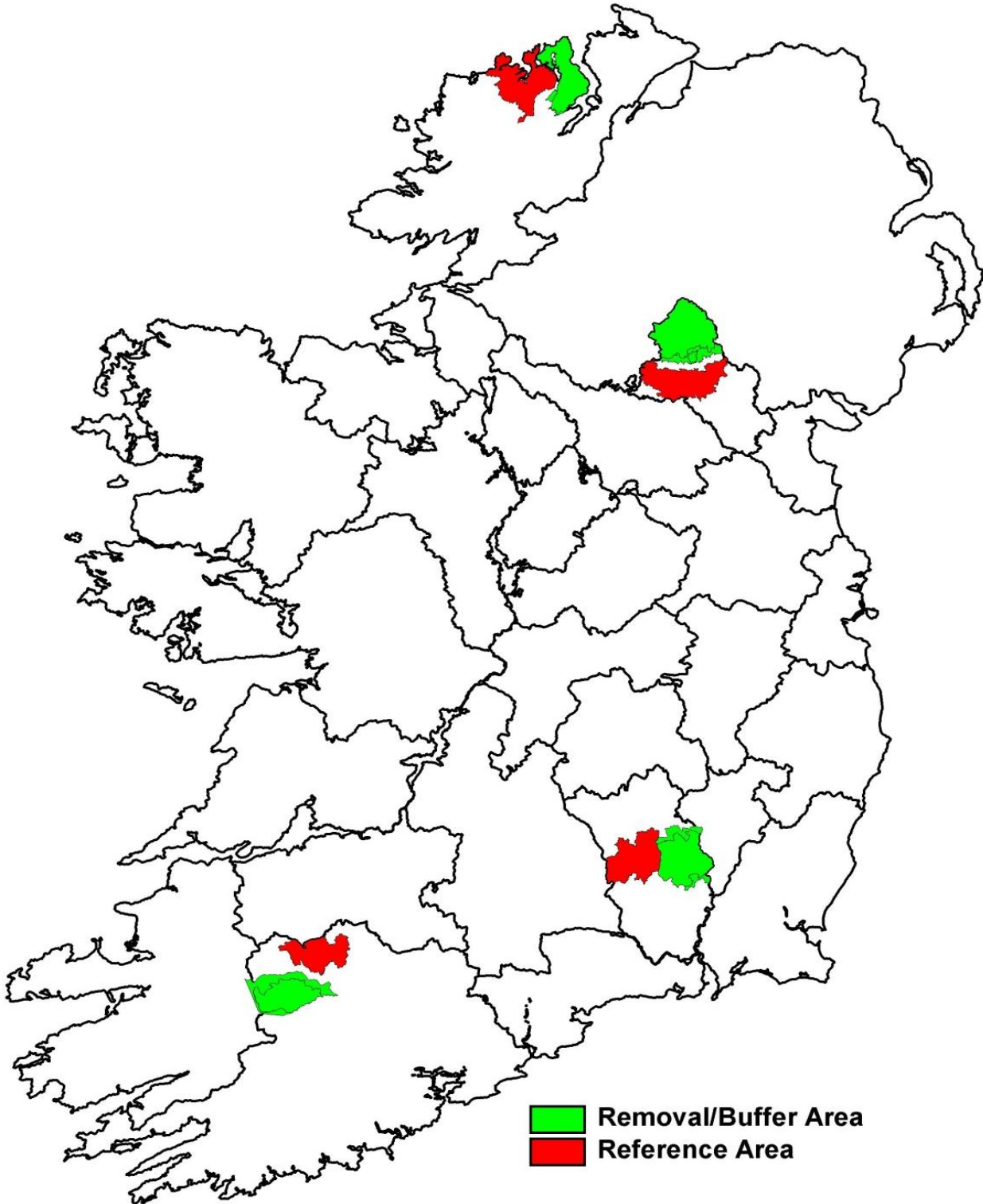
Kaplan-Meier survival curve showing cumulative proportion of animals 'pulled' as a function of calendar date, all stock.



Instantaneous hazard of being pulled for all reasons as a function of calendar date, all stock.



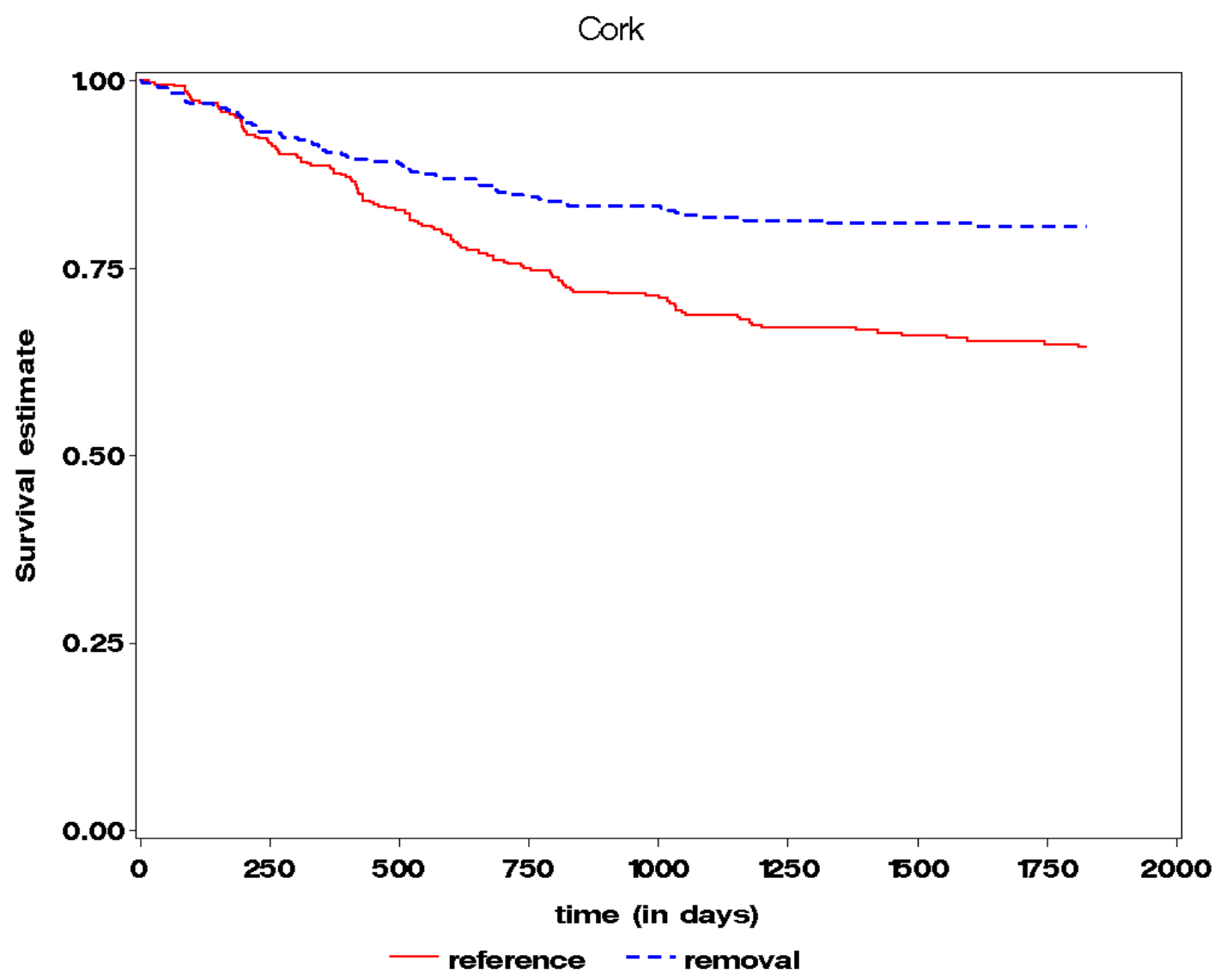
Ireland: four area badger removal project, 1997 – 2002.

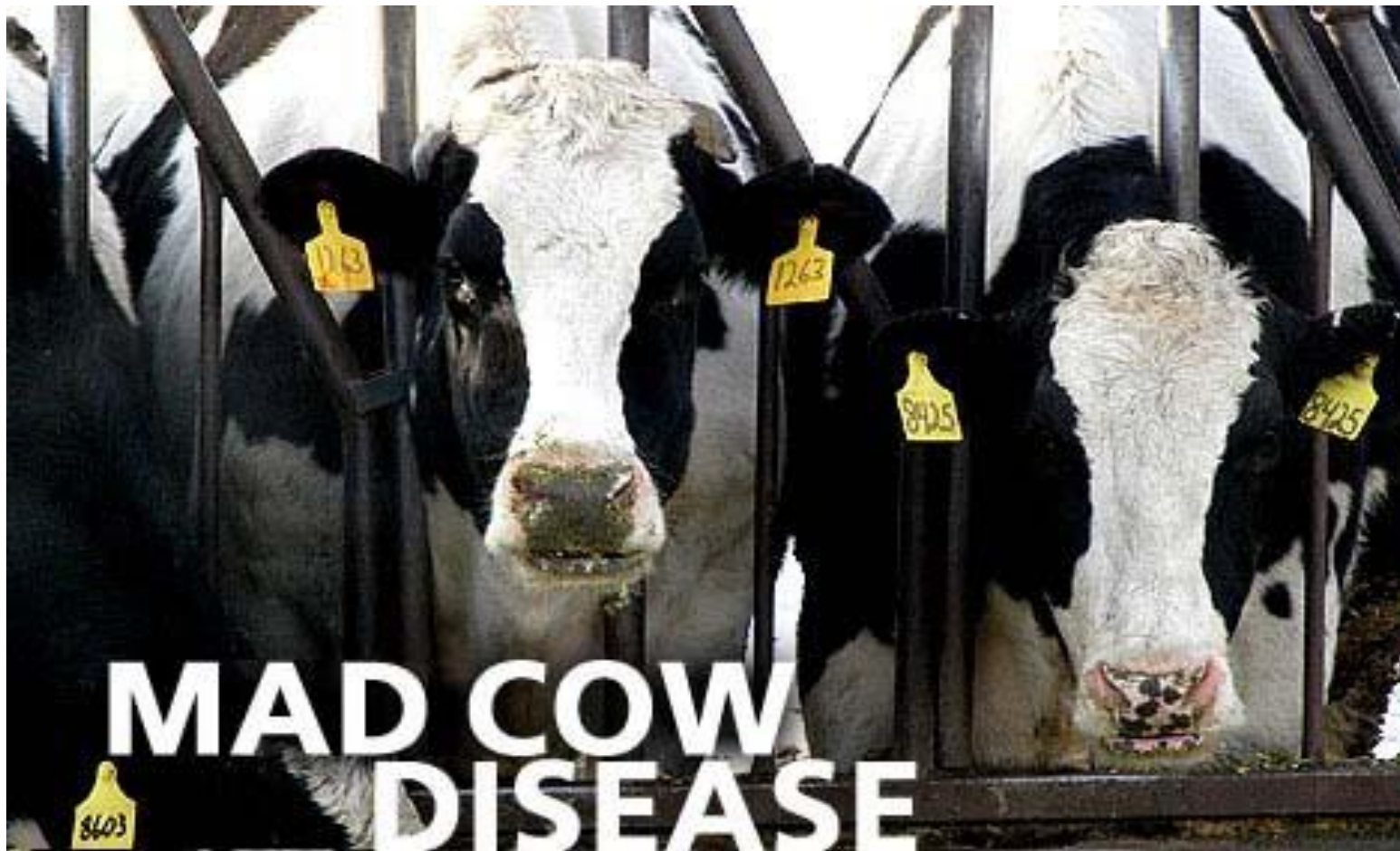


Ireland: four area badger removal project, 1997 – 2002.

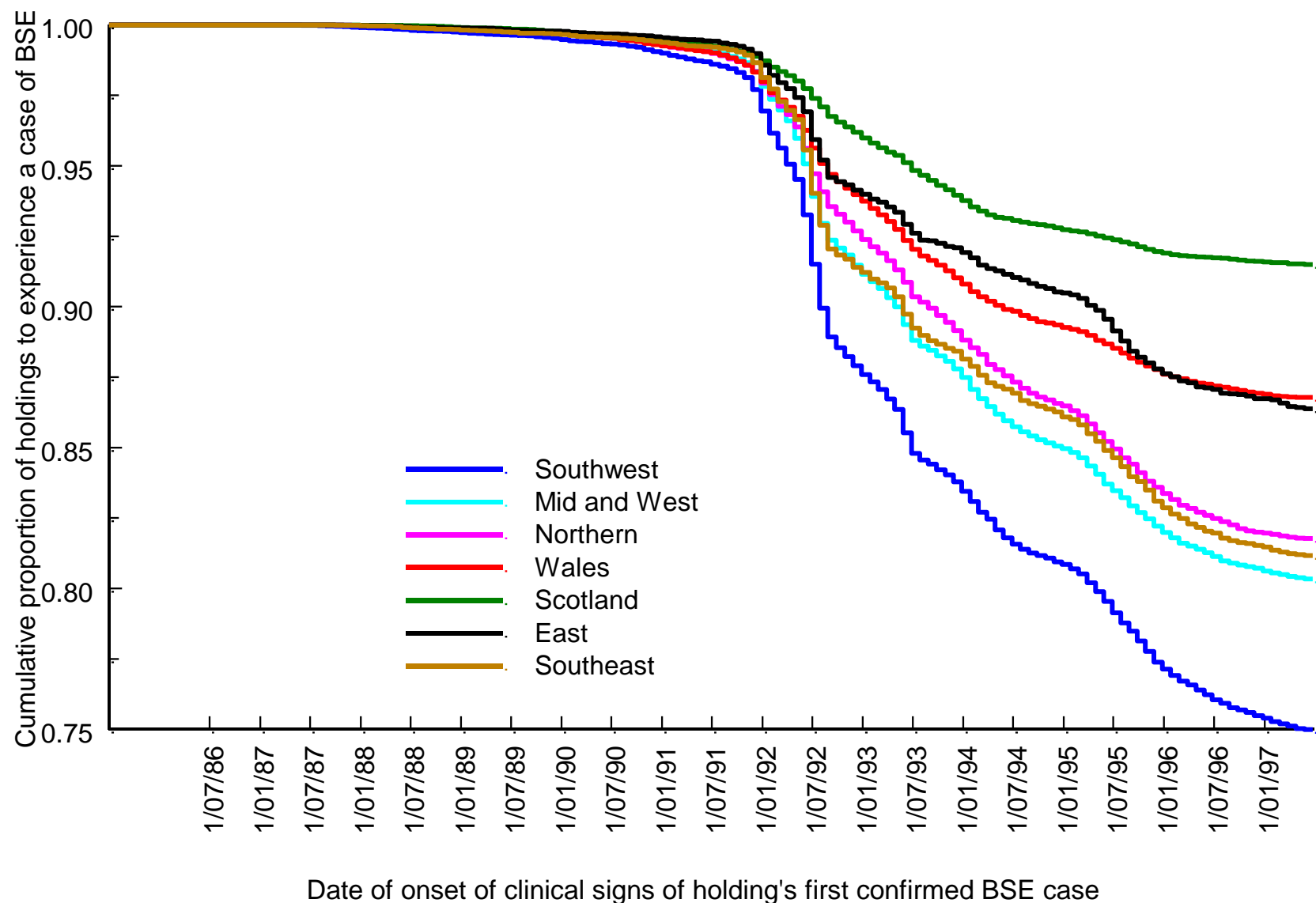


Ireland: four area badger removal project, 1997 – 2002.





Days to index BSE case - British cattle holdings.



Stevenson, M., Wilesmith, J., Ryan, J., Morris, R., Lockhart, J., Lin, D., Jackson, R., 2000a. Temporal aspects of the bovine spongiform encephalopathy epidemic in Great Britain: Individual animal-associated risk factors for disease. Veterinary Record 147, 349 - 354.

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Censoring

- Censoring
 - in a follow-up study, the exact survival time is only known for those individuals that show the event of interest during the study period
 - other individuals (that were observed until the end of the study) might have shown the event of interest after the study finished
 - these individuals are said to have censored observations
 - types \equiv *right, left, interval*
 - usual to code censored observations as '0' and events as '1'

Censoring

- Right censoring
 - animal is 'lost' to follow-up after the study starts
 - implies that event was able to occur sometime after the date of right censoring
 - most common form of censoring

Censoring

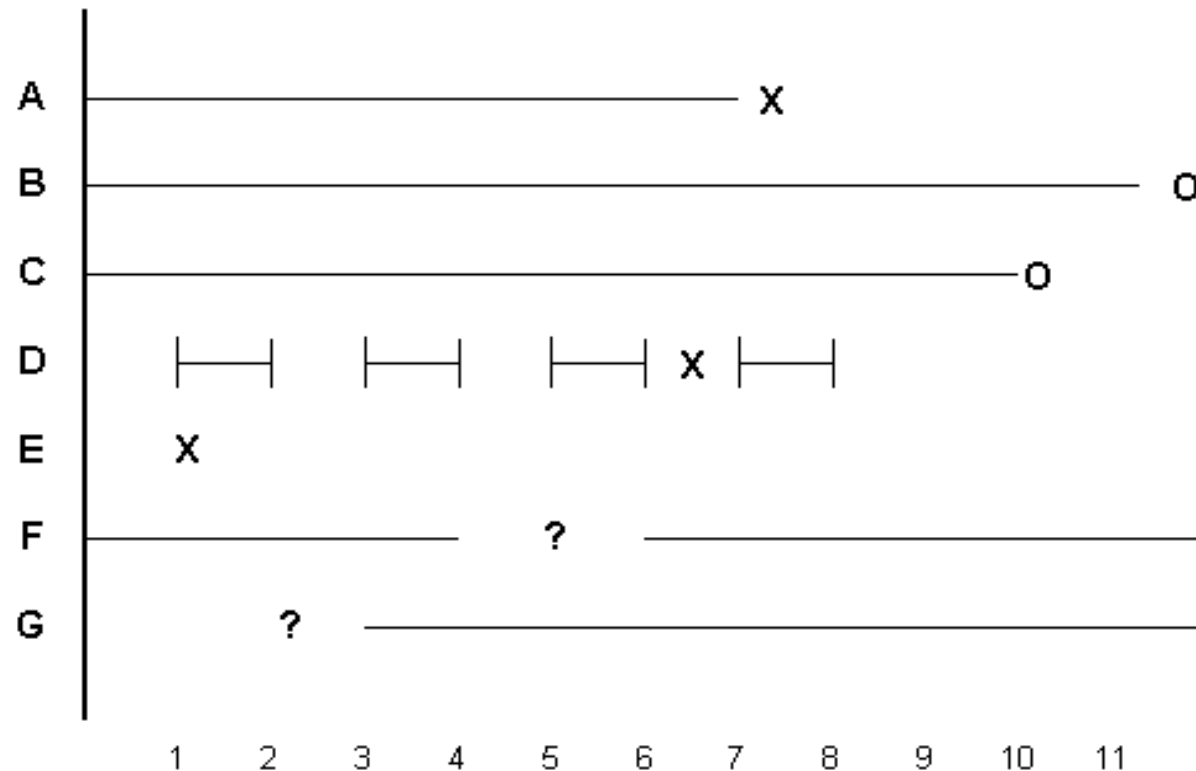
- Left censoring
 - event of interest occurred before the start of the study
 - implies that event occurred sometime before the date of left censoring
 - example:
 - you plan to investigate time to onset of first oestrus in dairy cattle
 - the observation period starts at day 30 after calving date and finishes on day 100
 - you examine all animals entering the study (at DSC = 30) and find that some have already cycled – these animals would be left censored at day 30

Censoring

- Interval censoring
 - event of interest is known to be occur sometime between times a and b but we don't know exactly when
 - useful when animals are periodically monitored
 - outcome of interest = date of seroconversion
 - animals sampled every 4 months

Censoring

- Truncated data
 - a separate issue from censoring
 - can be left or right
 - required to account for periods when the subject is not at risk
 - that is, there is no way possible that the event could have occurred
 - outcome of interest = date of herd index case;
 - herds that came into existence after the start of the study are left-truncated up until their first day of existence



Event of interest on day 7.

Right censored on day 12.

Right censored on day 10.

Interval censored on day 6.5.

Left censored on day 1.

Interval truncated data.

Left truncated data.

x = event of interest; o = censored; ? = absent from data set

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Ties

- Tied events
 - survival analyses assume that time is *continuous*
 - sometimes outcome of interest not measured on continuous scale
 - service number when conception occurred
 - means that many events occur at the same time (producing ‘tied’ event times)
 - analytical methods to deal with this: Breslow approximation and Efron approximation
 - when the number of ties is large, approximate methods yield coefficients biased towards zero

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Data structure

End of study period = 30 November 2001

ID	Enter date	First service	Comments
001	20 Oct 2001	31 Oct 2001	
002	20 Oct 2001	-	Sold 1 Nov 2001
003	10 Oct 2001	31 Oct 2001	
004	-	10 Nov 2001	Purchased 1 Nov 2001
005	20 Oct 2001	-	
006	20 Oct 2001	22 Oct 2001	

Data structure

ID	Days	Status
001	11	1
002	12	0
003	21	1
004	10	1
005	41	0
006	2	1

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