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Assessing the risk due to BSE in the cattle population of the Republic of Ireland

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Introduction

- Aims:
  - to estimate BSE infection levels in the ROI cattle population.
  - to estimate exposure to infectivity in the human food supply.
  - to assess the risk from this exposure relative to that posed by BSE in GB cattle.
- Data used.
- Results – the BSE epidemic in ROI.
- Results – human exposure.
- Uncertainties.
- Conclusions.

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Key data

- 824 clinical cases of BSE reported by 1st April 2003.
- Cattle tested from 2001-14/5/2003.

  All over-thirty month (OTM) animals entering the food supply are tested, plus all casualties and fallen stock over 24 months:

  - 1,420,000 apparently healthy OTM cattle tested (75 positive)
  - 3,900 casualty cattle tested (9 positive)
  - 146,000 fallen stock cattle tested (322 positive)
  - [36,000 'BSE eradication' cattle tested (9 positive)]

- No detailed data on all animals tested – only on positives, plus (small) sample of negatives.
- Demographic data: 6.5 million cattle in ROI (2001 figure), compared with ~9 million in GB.
- Detailed farm level demographic data (equivalent to agricultural census or CTS database) was not available.
- Very limited data on age distribution of casualties/fallen stock – crudely estimated to be 15% of all mortality for animals over 3 years of age.
- Unlike in GB, very few casualty animals.

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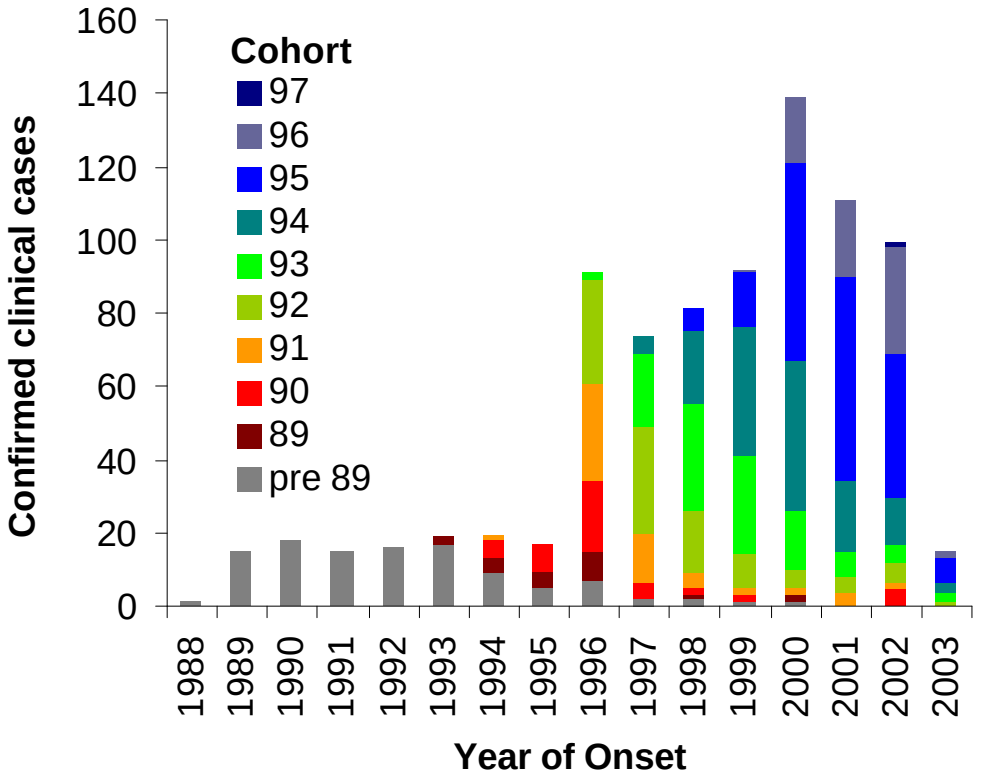
Clinical case data



Birth dates categorised by ‘cohort’, in line with GB analysis.
e.g. 1996 birth cohort corresponds to birth dates from 1/7/95-30/6/96.

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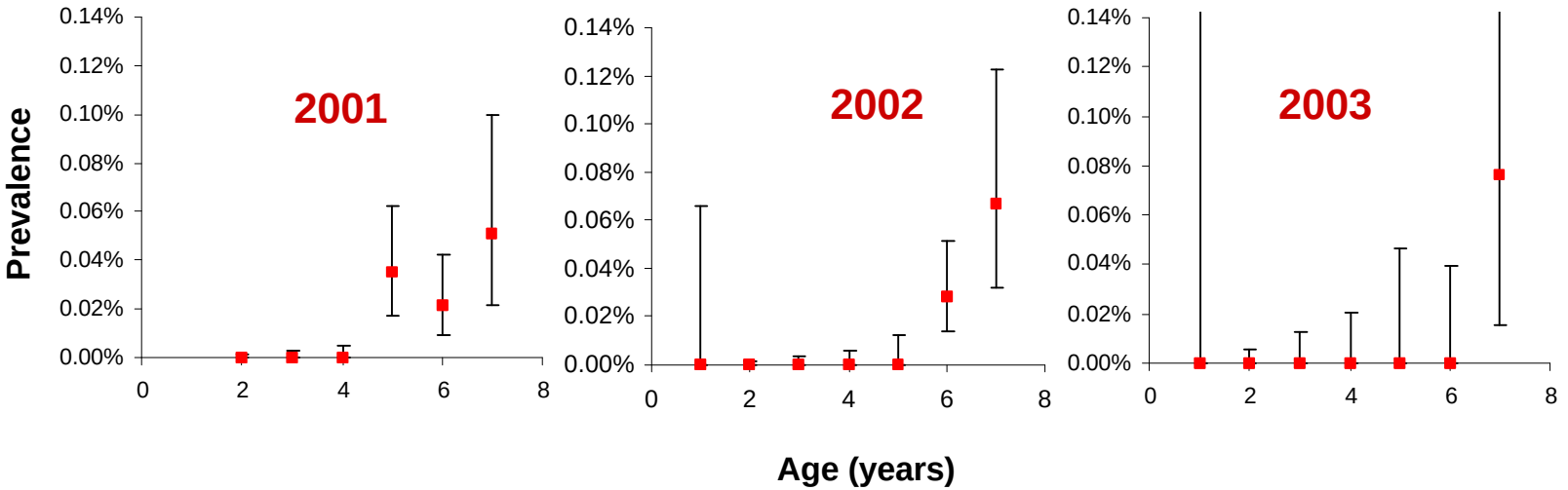
Screening data: apparently healthy OTM animals

Percentage positive by age group (with exact 95% CI)



The age distribution of tested animals is imputed from a small random sample of animals tested for which age information was collected. No age-breakdown was given for animals over 7 years of age, so it is not possible to fit to this category.

The prevalences above are substantially smaller than seen in GB.

The increasing age of cases from 2001 to 2003 is evidence for a substantial decline in new infections after 1996.

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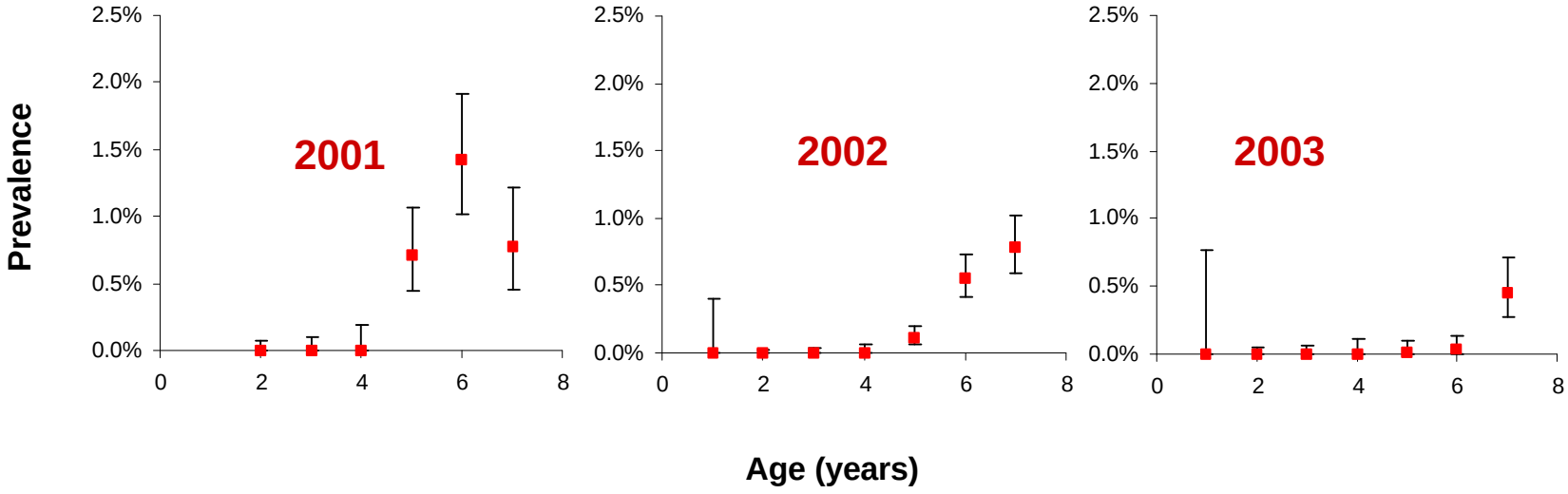
Screening data: risk animals (casualties + fallen stock)

Percentage positive by age group (with exact 95% CI)



As for apparently healthy animals, age distribution estimated from small sample of tested animals, with no information on those over 7 years of age.

Risk group prevalence less than comparable GB figures, but difference less striking than for apparently healthy animals.

Same shifting age distribution as for apparently healthy animals - also indicative of very low levels of new infection post-1996.

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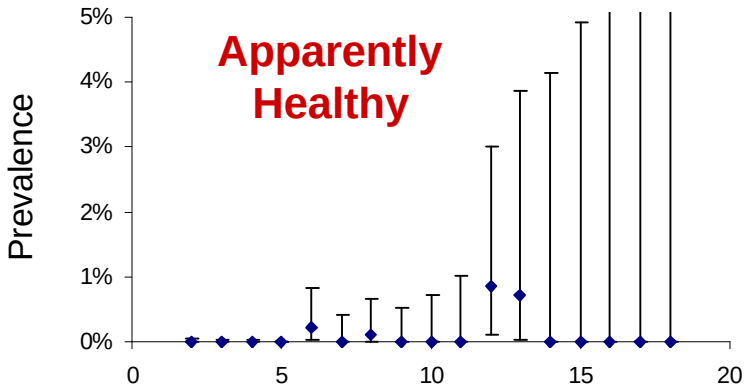
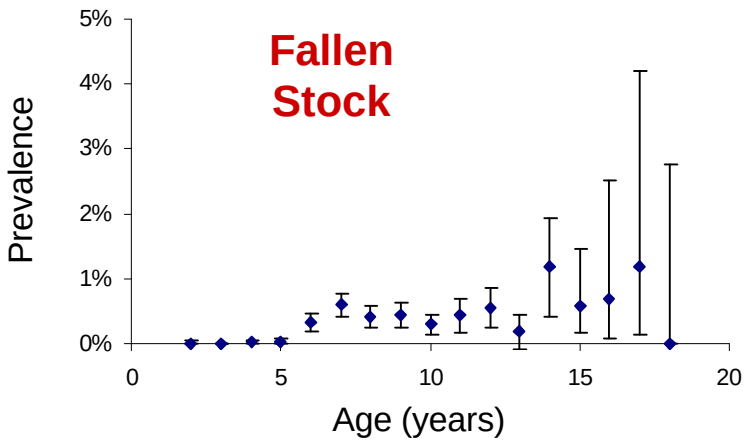
GB 2001/2 screening data for comparison

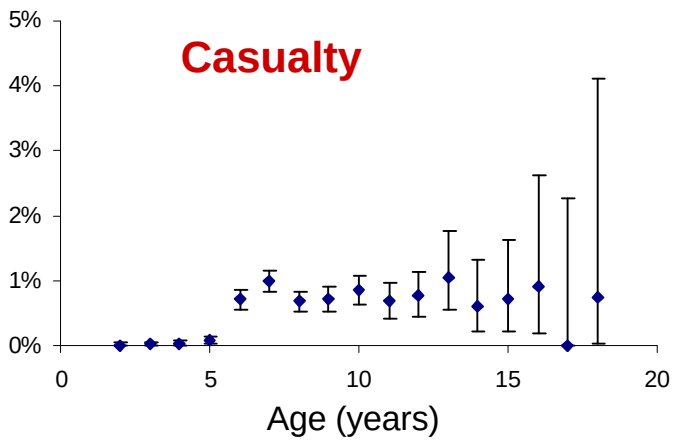


Percentage positive by age group (with exact 95% CI)

The age-group differences are due to a combination of time-varying infection incidence and incubation-stage dependent sensitivity.

Prevalence greatest in casualties and lowest in apparently healthy animals.





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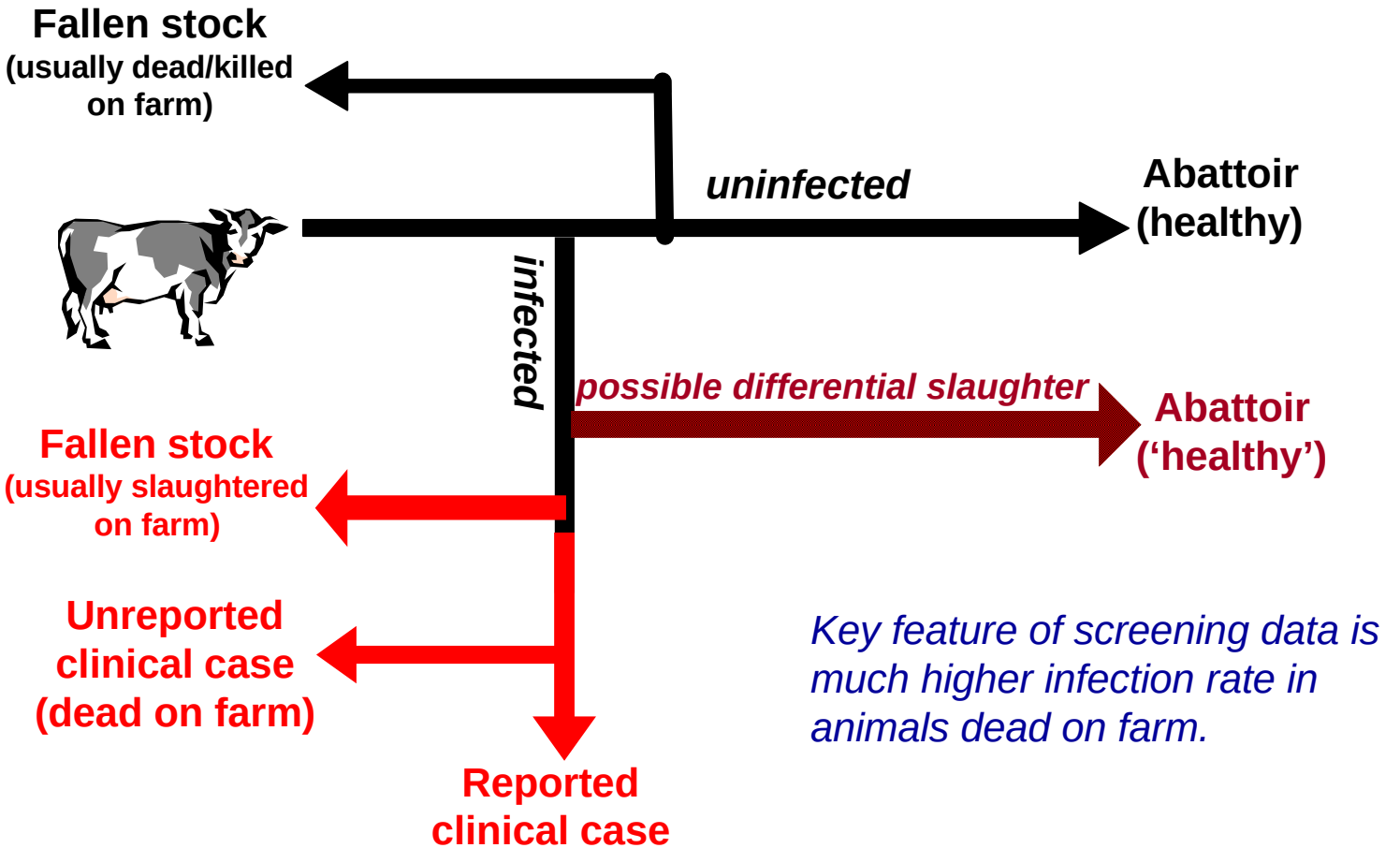
What happens to a BSE-infected cow?

Multiple possible life histories for infected animal:



Key feature of screening data is much higher infection rate in animals dead on farm.

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Analysis method: back-calculation

- Basic approach
  - If animals are infected when young, and only a fraction survive to the age when clinical signs develop, then there will have been many times more animals infected than were diagnosed.
- With information on
  - Incubation period distribution
  - Demography of GB herd (survivorship)
  - Exposure/susceptibility with age

…it is possible to estimate the total number of animals infected through time, and the proportion of these entering the human food supply.

- Methods extended to also analyse screening data.

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Estimating under-ascertainment

- The number of apparently healthy OTM animals testing positive in GB is higher than would be expected based on the number of clinical cases.
- These animals do not show any (obvious) clinical signs of BSE.
- Previous modelling work has shown that this data can best be explained by 'differential mortality' – at some point before clinical onset, infected animals become more likely to be sent for slaughter or to die on farm than uninfected animals (due to loss of milk yield or non-specific clinical disease). See Ferguson, N.M. & Donnelly, C.A. Assessment of the risk posed by bovine spongiform encephalopathy in cattle in Great Britain and the impact of potential changes to current control measures. *Proceedings of the Royal Society B* (2003) [http://www.pubs.royalsoc.ac.uk/proc_bio/proc_bio.html].
- The level of differential mortality for ROI is estimated from the ROI data.
- Results shown here examine the effect of allowing for step changes in degree of differential mortality from 1996 onwards.
- It is important to note that under-ascertainment of cases does not imply deliberate non-reporting – in many cases animals may exhibit non-specific signs or die from other causes prior to the onset of obvious clinical signs of BSE.
- Varying assumptions about historical levels of under-ascertainment has little effect on estimates of current risk, which are only sensitive to current under-ascertainment levels.

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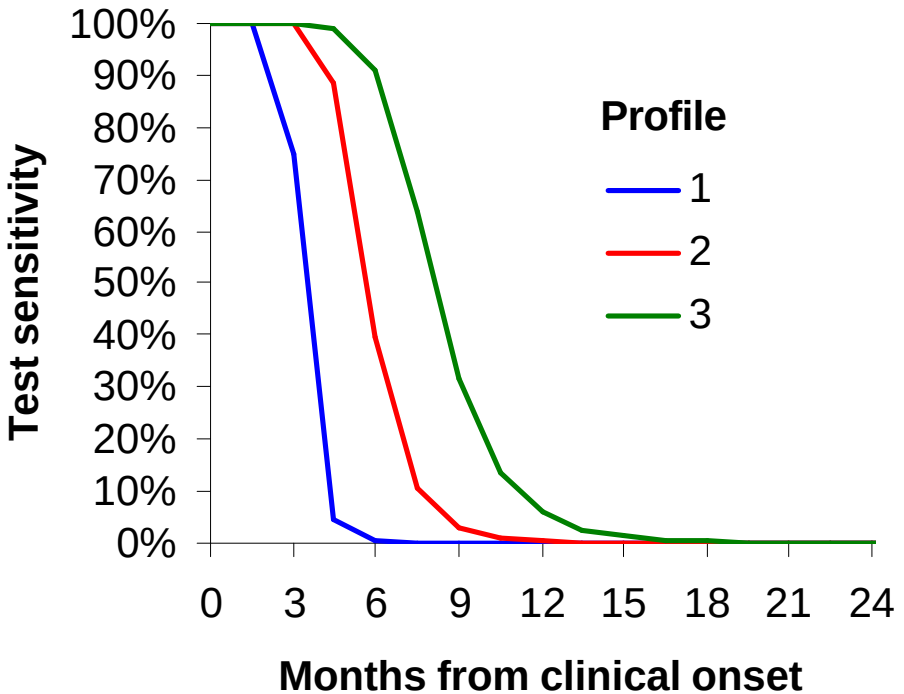
Test sensitivity scenarios examined

Same 3 profiles examined as for GB, since precise form unknown.



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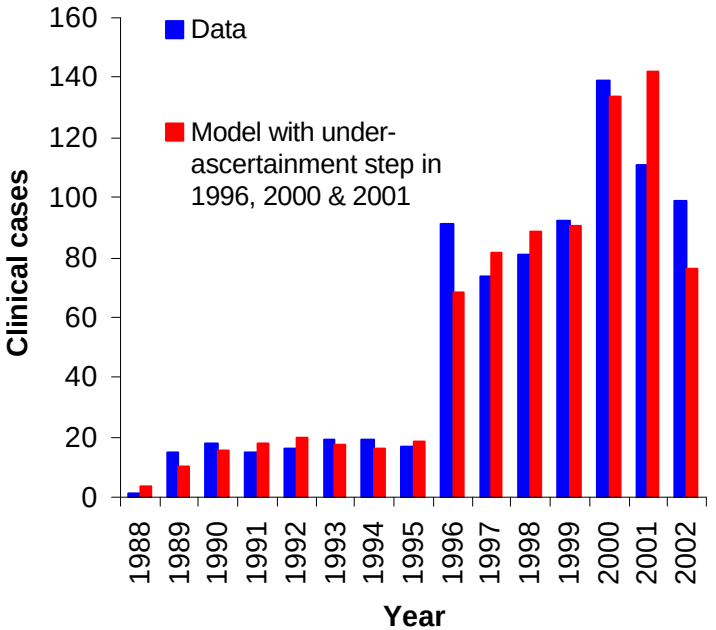
Results: model fit (1)

3 month sensitivity, 3 month differential survivorship baseline scenario shown.



- Best fit achieved using model which estimates decreases in differential mortality at the start of 1996, 2000 and 2001, from 97% prior to 1996, to 89%, 81% and then 68%.
- There is an estimated 6-fold higher than normal risk that this mortality will occur on farm rather than in an abattoir.
- This suggests case ascertainment improved dramatically from 1996 – from 3% prior to that date, to 32% at the current time.

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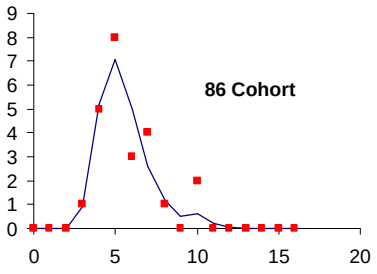
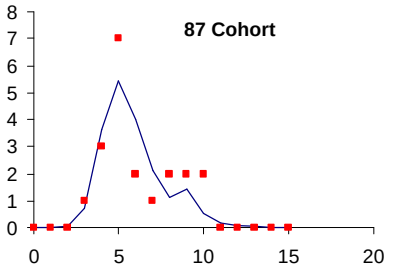
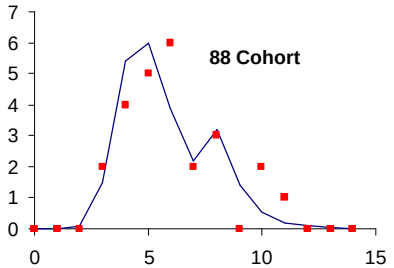
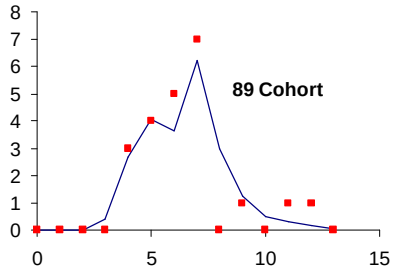
Results: model fit (2)

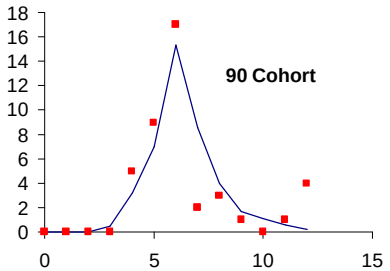
Generally good fit to age-stratified clinical case data.

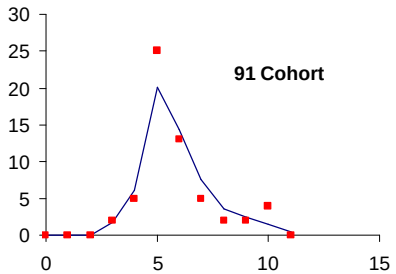


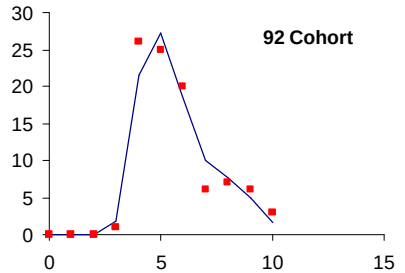


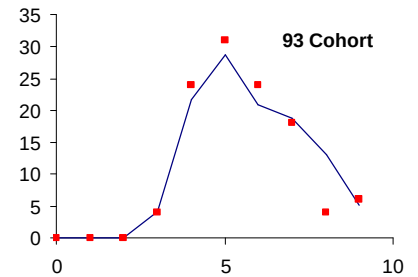


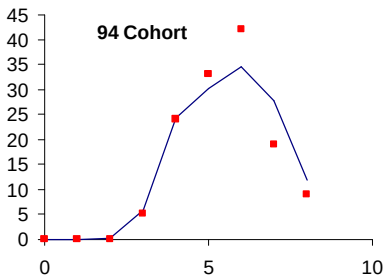


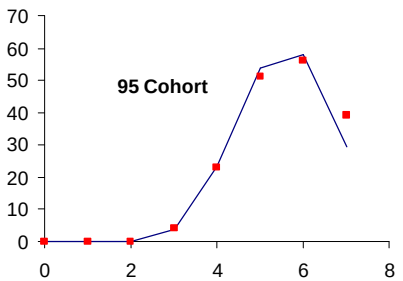


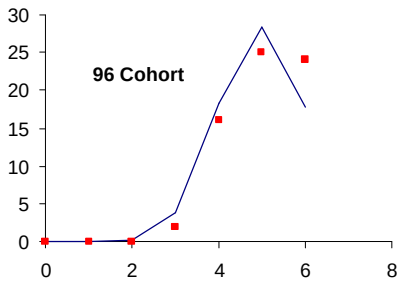


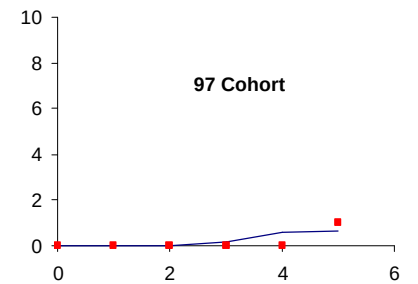












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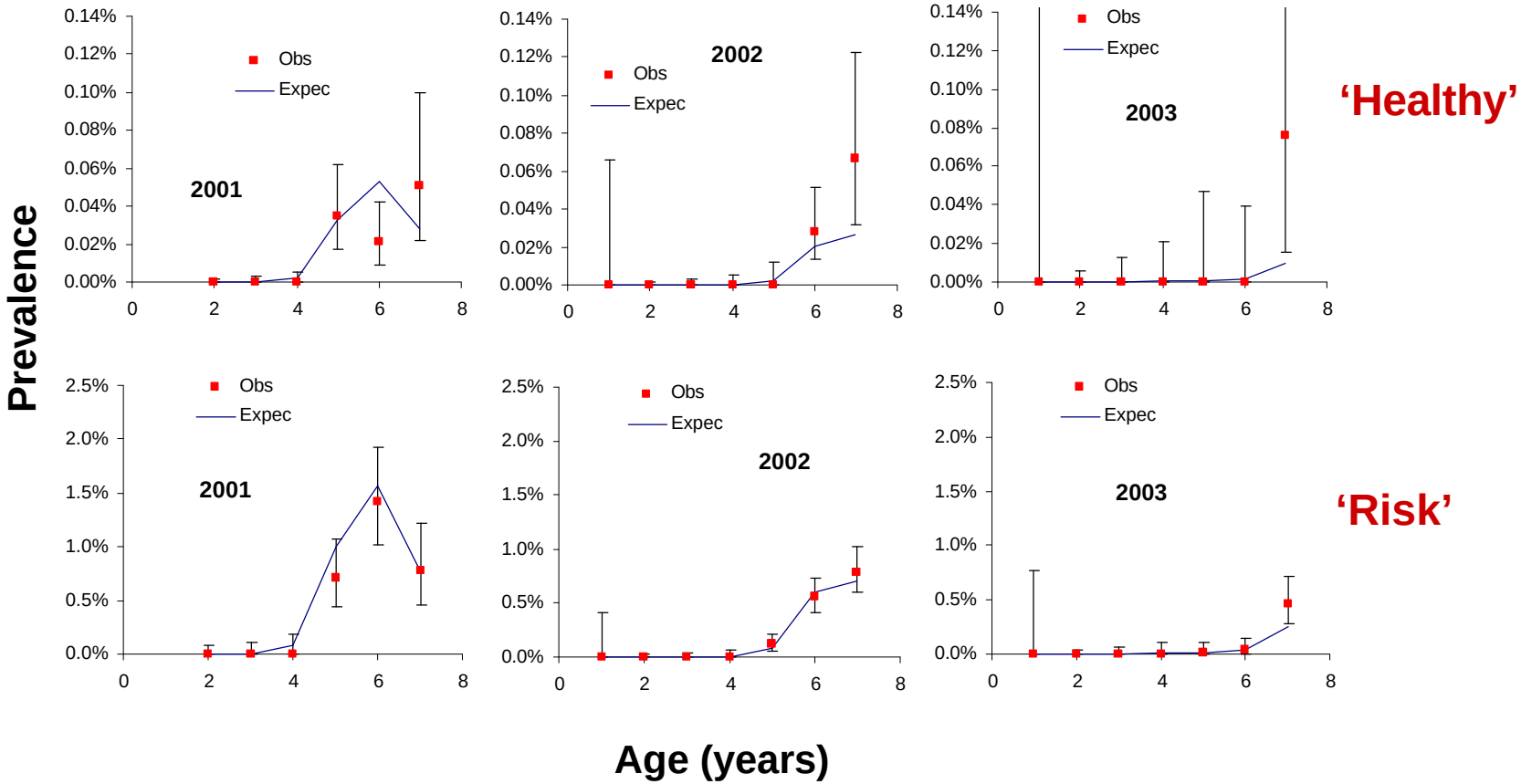
Results: model fit (3)

Good fit to screening data.



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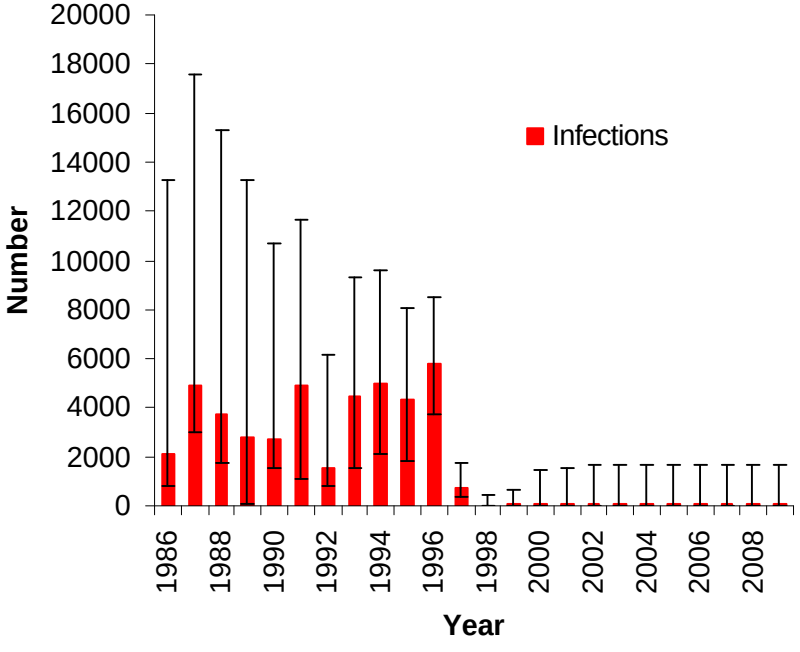
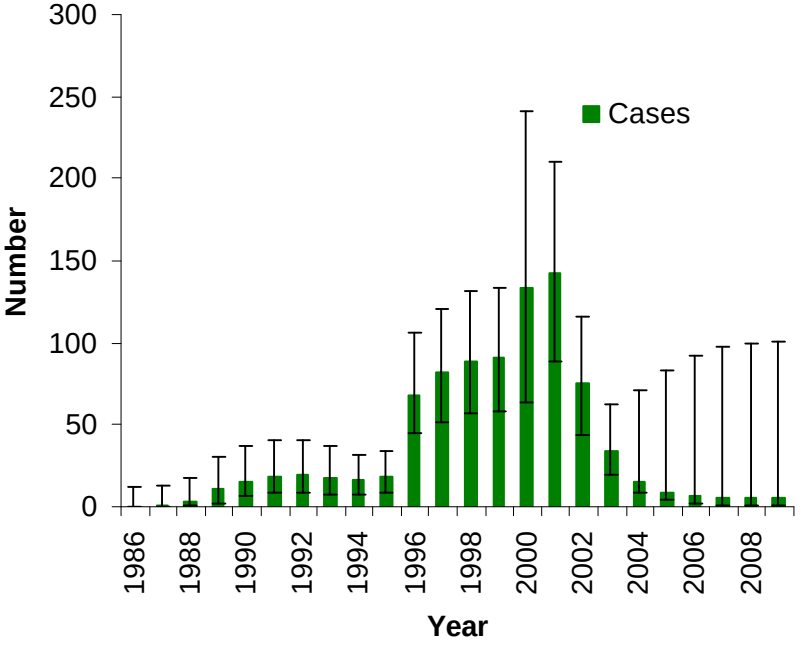
Results: past epidemic

- Between 19,000 and 50,000 cattle estimated to have been infected in ROI.
- High level of uncertainty in past infection incidence estimates due to historical case under-ascertainment.
- This uncertainty has little effect on estimates of current and future risk to human health.
- Dramatic drop in infection rates estimated to have occurred after 1996.





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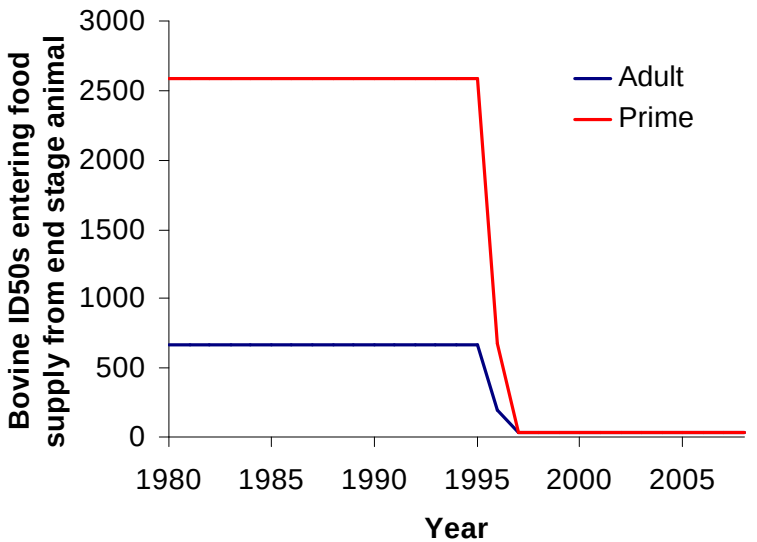
Translating exposure into risk: the effect of SRM controls

- Historical exposure estimates derived from weighted average over multiple body tissues, incorporating data on consumption and infectivity.
- Substantial uncertainty.
- Profile based on that for GB – but due to later (1996) SRM ban, GB values for 1988 are assumed for all years before 1996. Post 1996, values are assumed to take GB 1998 values (*i.e.* excluding vertebral column).
- 2 month doubling time assumed for results shown here.



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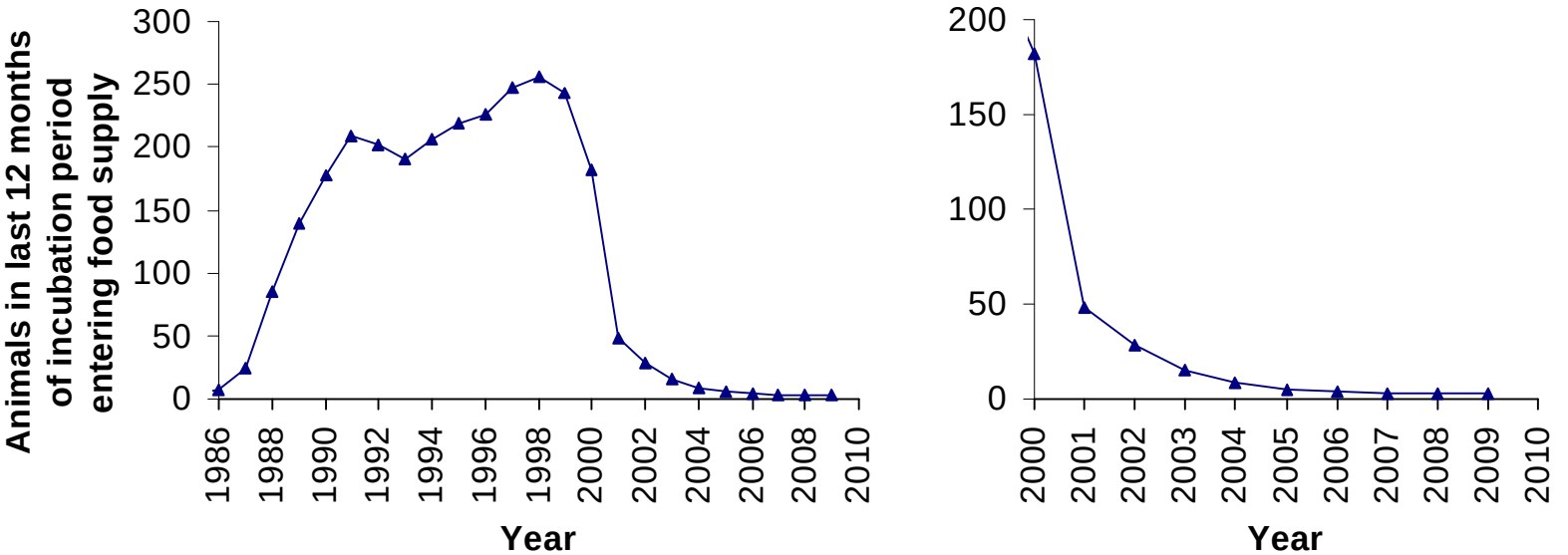
Results for baseline scenario: infected animals in last 12 months

- Exposure peaked in 1998, but at much lower level than seen in GB.
- Estimates of historical exposure levels sensitive to uncertainty in historical under-ascertainment – but this uncertainty has little effect on estimates of current and future risk.
- Testing substantially reduced exposure from 2001.



Test sensitivity windows > 3 months give lower risk estimates.
Diff. mortality periods > 3 months give higher risk estimates.

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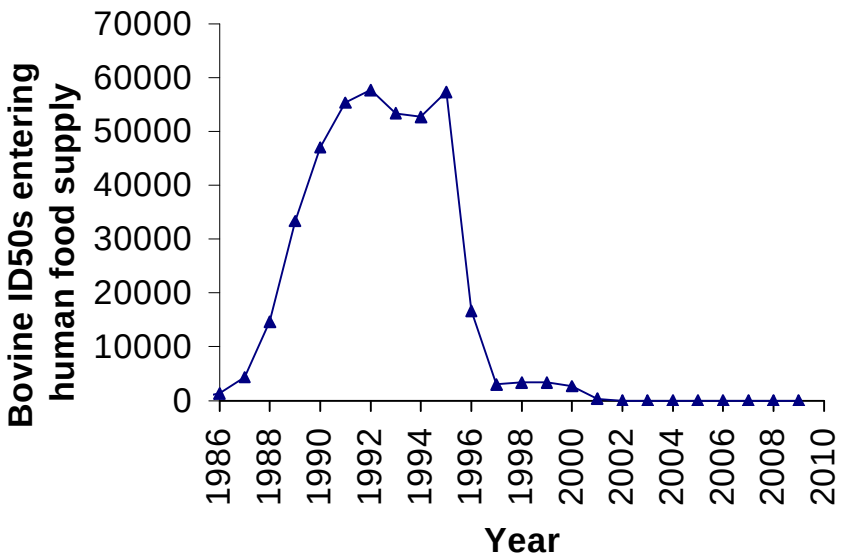
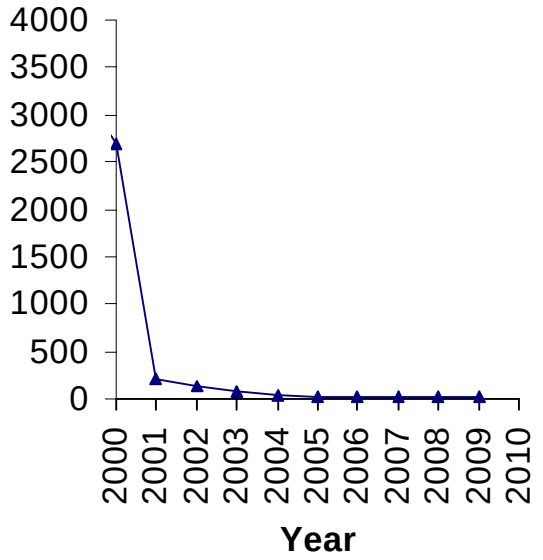
Results for baseline scenario: Bovine ID50s

- Model produces estimates of numbers of infected animals entering food supply through time by age of animal and stage of incubation.
- Weighting this by the previous infectivity estimates gives an estimate of the total amount of infectivity entering the food supply through time.
- Results for 3 month sensitivity, 3 month differential survivorship (with screening), in bovine ID50 units:





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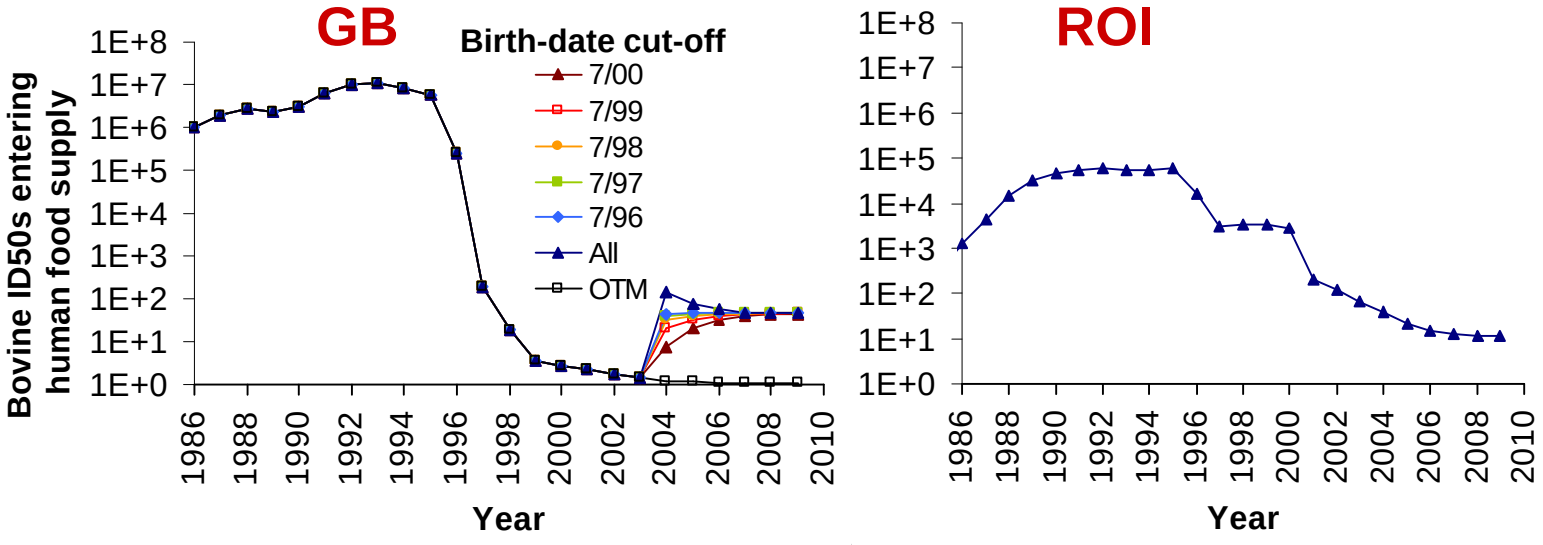
GB vs ROI

- Historical risk in GB over 100-fold higher than in ROI.
- Best estimate of current risk in GB lower than in ROI, due to OTM rule in GB.
- Best estimate of future risk in GB higher than in ROI under any of the birth-date cut-off options examined – though still very low by historical standards.
- Key factors giving lower ROI risk is very low positive rate in healthy cattle – nearly all BSE positives end up as fallen stock – and infection levels post 96.
- Necessary to use logarithmic scale to compare past & present risk levels or those from GB and ROI:



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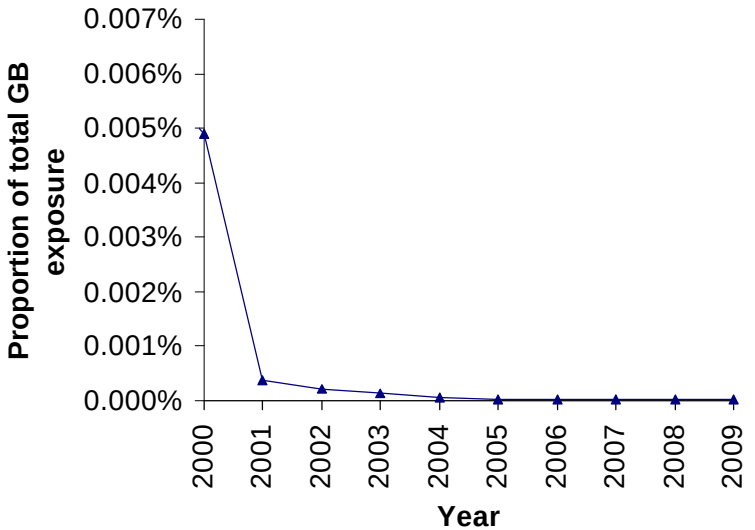
Using relative risk measures

Quantify risk in terms of proportion of exposure during whole epidemic:



- Taking a *very* pessimistic scenario of 5,000 vCJD deaths in total resulting from past exposure in GB, comparison of future exposure from ROI with past GB exposure gives 0.01 extra deaths over the next 60 years from infections occurring over the period 2004-9.

- This figure is 3.8 times less than predicted GB risk given complete removal of the OTM rule and replacement with testing (2.7 times less on an animal for animal basis, given national herd size differences).

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Uncertainty & worst case scenario

- Worst case scenario assumes 3 month test sensitivity but differential mortality over last 12 months of incubation period in cattle. Central estimates for this scenario give 3-fold higher risk than baseline scenario (0.028 vCJD deaths from exposure in 2004-9) – but 5-fold less than equivalent GB figure.
- Much uncertainty in current and future levels of infection in cattle. Allowing for this gives worst case (upper 95% bound) cattle infection level ~20 fold higher than best estimate.
- 20 fold uncertainty in future cattle infection levels translates into approximately 10-fold uncertainty in exposure during 2004-9.
- Combined, these give worst case risk estimates ~30 fold greater than the baseline results: *i.e.* 0.3 vCJD deaths – still 5-fold less than the equivalent figure for GB worst-case risk.
- Estimates of future risk levels are not highly sensitive to assumptions about step changes in under-reporting – near identical results are obtained assuming a constant level of differential mortality during epidemic.

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Assessing the risk from exports to GB

- Current data do not permit this to be easily assessed.
- Need to know proportion of all ROI cattle products imported into GB, correcting for age and type of product.
- This quite complex analysis is less critical, given the predicted lower risk levels for ROI compared with GB under any likely replacement to OTM rule.

Ongoing work

- Additional sensitivity analyses and investigation of temporal changes in case ascertainment.
- Preparation of scientific paper.

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Summary

- Demographic data available not as detailed as for GB. Limited denominator information for testing data.
- Clinical case data for ROI shows evidence of substantial and changing under-ascertainment.
- Best estimates indicate 15,000-50,000 animals infected with BSE in ROI over last 20 years. Wide bounds due to uncertain historical case ascertainment, but this uncertainty has little effect on estimates of current and future risk.
- Infection rates estimated to have peaked in 1996, then fallen dramatically.
- Current infectivity levels entering food supply greater than in GB, due to presence of OTM rule in GB.
- Under any birth-date based replacement to OTM rule in GB, central estimates of GB risk levels are substantially (2-4 fold) more than central estimates of current or future ROI levels.
- This conclusion appears to be robust to uncertainties in the duration of test sensitivity, differential mortality or historical under-reporting levels.
- There is +/- 10-fold uncertainty in risk levels due to uncertainty in ongoing BSE infection rates – so prediction intervals for future risk overlap for GB and ROI.