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Extension of 2003 OTM risk assessment

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Introduction

- Aim is to assess impact of changes to OTM rule on human exposure in period 2004-2009.
- Previous assessment used 5,000 future vCJD deaths as pessimistic scenario (published in Ferguson & Donnelly etc)
- Used “worst-case” scenario approach
- Predictions from clinical cases suggest much lower risk
- Results from survey of lymphoreticular tissues suggest higher risk
- Extended work integrates BSE modelling and vCJD data to estimate the probabilities associated with numbers of vCJD cases arising from infection in the period 2004-2009.

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Survey of human lymphoreticular tissues

- 12,674 samples – majority appendix
- 83% of samples from 10-30 age group
- Removed between 1995 and 2000
- 3 samples positive according to study protocol, although patterns of staining for 2 samples were different from those previously observed in vCJD cases
- Estimated detectable prevalence of 237 per million with wide confidence limits (49-692 per million)
- Applied to 10-30 age-group, estimate 3,800 individuals may be infected (95% CI: 780-11,100)
- If the test is 50% sensitive, the estimate is 7,600 (95% CI 1,900 -19,800)

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Simple extrapolation to the whole population

Assume age distribution of cases due to age-dependent susceptibility/exposure

Age-group	Cases (to end 2003)	N (millions in year 2000)	Incidence (per million)	Ratio
<10	0	7.4	0	0
10-29	94	15.2	6.2	1
30-49	43	16.6	2.6	0.4
50+	8	19.6	0.4	0.07

Effective population size is 23.5 million. This increases the estimates on the previous slide by approximately 50%.

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Combined BSE/vCJD analyses

- BSE model reprogrammed to produce likelihood profile for proportion of total infectious material entering the food supply that occurs between 2004 and 2009 with change to OTM
  - ➢Based on healthy animals only entering food supply
  - ➢Based on healthy + casualty (but conservative since denominator only contains healthy animals)
- Likelihood profiles for future numbers of vCJD cases considered
  - ➢Age-weighted extrapolation of tonsil/appendix survey
  - ➢Non-age weighted extrapolation of tonsil/appendix survey
  - ➢Estimates of vCJD cases based on deaths to end 2003
- Likelihood profiles combined assuming independence – this assumption is being tested

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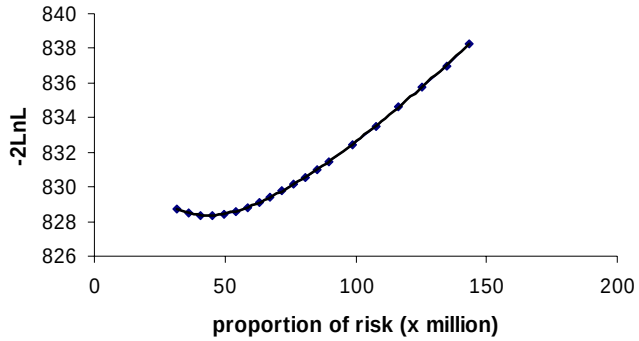
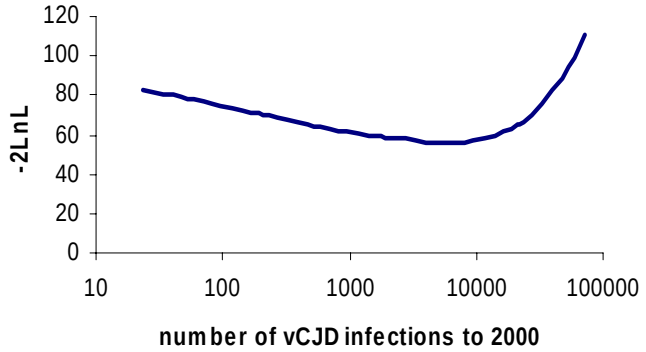
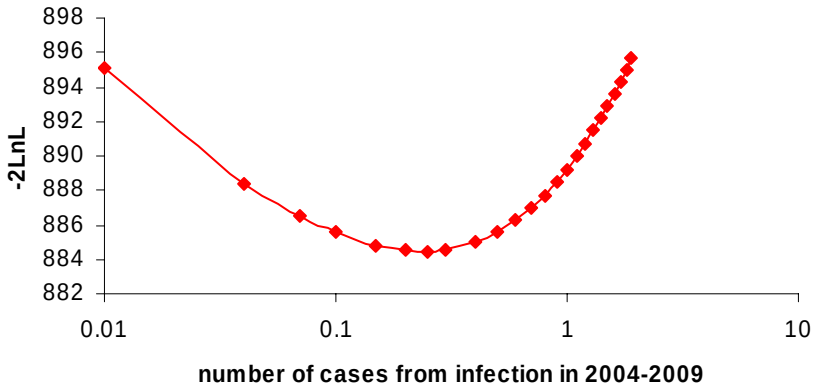
Example

% BSE infection 2004-2009 (healthy + casualty)



Age-weighted tonsil/appendix survey





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Baseline Results

- Using data from the tonsil/appendix survey (assuming 50% test sensitivity)
- Baseline BSE assumptions: differential mortality in last 3 months of incubation period

	Estimate	Upper 95%	Upper 99%	Upper 99.9%
Mean number of vCJD cases arising from consumption of apparently healthy animals in 2004-2009	0.06	0.24	0.34	0.49
Mean number of vCJD cases arising from consumption of apparently healthy and casualty animals in 2004-2009	0.07	0.27	0.39	0.57

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Baseline Results allowing for Poisson sampling

Note: *the work presented on this slide was completed too late to be considered by SEAC in June 2004 or to be presented to the FSA board in July 2004. The work on this slide is being presented here since it represents a simple way of interpreting the mean risk estimates presented on the previous slide.*

• The results on the previous slide present mean estimates. In reality fractions of cases cannot be observed. Incorporating a Poisson sampling process into the model translates these mean estimates into integer numbers.

	Best estimate	Upper 95%	Upper 99%	Upper 99.9%
Number of vCJD cases arising from consumption of apparently healthy animals in 2004-2009	0	1	2	2
Number of vCJD cases arising from consumption of apparently healthy and casualty animals in 2004-2009	0	1	2	2

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Worst-case scenario

- Using data from the tonsil/appendix survey (50% sensitive)
- Only examine total risk from casualty plus 'apparently healthy' animals.
- Worst-case BSE assumptions: differential mortality in last 12 months of incubation period.
- 99% upper confidence bound chosen as suitably pessimistic measure of worst-case risk – here 2.5 cases.
- If risk were at the levels predicted below, then we would be expecting somewhere between 5,000 and 20,000 vCJD cases in total – *i.e*. many fold more than seen so far (or predicted to occur from analyses of trends in vCJD case numbers alone).

	Best estimate	Upper 95%	Upper 99%	Upper 99.9%
Mean number of vCJD cases arising from consumption of apparently healthy animals in 2004-2009	0.3	1.0	1.4	2.0
Mean number of vCJD cases arising from consumption of apparently healthy and casualty animals in 2004-2009	0.5	1.8	2.5	3.7

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Worst-case scenario allowing for Poisson sampling

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- The results on the previous slide present mean estimates. In reality fractions of cases cannot be observed. Incorporating a Poisson sampling process into the model translates these mean estimates into integer numbers.
- This modification leads to a slight increase in upper bounds, but predicts there is a 80%+ chance of seeing no extra cases as a result of any increase in risk from changing the OTM rule.

	Best estimate	Upper 95%	Upper 99%	Upper 99.9%
Number of vCJD cases arising from consumption of apparently healthy animals in 2004-2009	0	2	3	4
Number of vCJD cases arising from consumption of apparently healthy and casualty animals in 2004-2009	0	3	4	5

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Summary

- Current exposure (under OTM rule) at *very* low levels compared with the past.
- Any policy change which allows more older animals into the food supply will increase current human exposure, even if those animals are screened.
- However resulting levels of exposure are still very low compared with the past – best estimate for worst-case scenario (making pessimistic assumptions) is that additional exposure in 2004-9 from changing to testing regime for animals born after 7/96 would be 0.045% of past risk.
- This analysis translates these relative estimates into absolute risk (excess vCJD cases) using the most conservative approach possible – namely extrapolating results from tonsil/appendix survey to the whole population without taking into account the very small case numbers being seen at the current time.
- Doing this extrapolation gives upper 99% confidence bounds on the mean number of vCJD cases arising from additional exposure in 2004-9 for the worst-case scenario of <2.5. Even allowing for random variation around this mean figure, the 99% confidence bound is <4 future cases arising in the next 60 years.
- If testing of cattle for BSE were only 90% sensitive at detecting infection in cattle at clinical onset (i.e. if 10% of cattle were to be incorrectly tested or not tested at all), the worst case figures above would increase by approximately 20%.
- Note all these figures assume the OTM rule was replaced by testing on 1/1/04 – in reality the ongoing delay to any change means the figures above over-estimate the likely true risk which will be experienced if the rule is changed.