Simulation of *Trichinella* control scenarios in Belgium

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1 Introduction

The aim of the present exercise is to examine the possibility to perform a scenario analysis concerning the *Trichinella* monitoring.

The risk-based surveillance proposed by Alban et al. (2008) does not actually compute risks, but rather contains a great deal of hypotheses, that are largely untested but that greatly influence the final result.

An alternative approach consists of a scenario and sensitivity analysis (Stirling, 2007).

2 Materials and methods

2.1 Sources of data

Population data were extracted from the national pig population registration database, called SANITEL Varkens, for the period 2005-2008 (Table 1).

Table 1: Pig population in Belgium for the years 2005-2008

	2005	2006	2007	2008
Breeding pigs	653,505	653,385	632,360	615,298
Slaughter pigs	4,973,949	4,850,501	5,007,614	5,123,189
Totaal	5,627,454	5,503,886	5,639,974	5,738,487

Slaughter and test data were obtained from the databases of the Federal Agency for the Safety of the Food Chain (FASFC) for the period 1992-2008. Animals were divided in different categories and type of production (with or without outdoor access), as shown in Table 2.

Table 2: Evolution of proportion of slaughtered domestic pigs that were tested for *Trichinella*

	Number of slaughtered domestic pigs	Number of tested domestic pigs	%	Number of non-tested domestic pigs	%	Number of positive cases
1992	10,455,458	7,142,193	68.31	3,313,265	31.69	0
1993	11,075,172	5,640,335	50.93	5,434,837	49.07	0
1994	10,842,821	4,187,396	38.62	6,655,425	61.38	0
1995	11,262,598	4,622,174	41.04	6,640,424	58.96	0
1996	11,344,930	4,721,866	41.62	6,623,064	58.38	0
1997	10,956,287	3,750,387	34.23	7,205,900	65.77	0
1998	11,587,670	5,047,980	43.56	6,539,690	56.44	0
1999	10,825,407	7,019,134	64.84	3,806,273	35.16	0
2000	11,049,726	9,317,325	84.32	1,732,401	15.68	0
2001	11,319,733	10,207,134	90.17	1,112,599	9.83	0
2002	11,200,914	10,377,363	92.65	823,551	7.35	0
2003	11,609,933	10,226,408	88.08	1,383,525	11.92	0
2004	11,229,149	10,284,186	91.58	944,963	8.42	0
2005	10,861,234	10,549,454	97.13	311,780	2.87	0
2006	10,202,794	10,158,164	99.56	44,630	0.44	0
2007	11,536,172	11,512,504	99.79	23,668	0.21	0
2008	11,588,072	11,547,720	99.65	40,352	0.35	0
Total	188,948,070	136,311,723		52,636,347		0
Mean	11,114,592	8,018,336		3,096,255		0

Import and export data came from the EU-TRACE database for the period 2007-2008 (Table 3). The actual *Trichinella* status of the various member states were obtained from the Trends and Sources for the period 2003-2007 (EFSA, 2007, available at http://efsa.europa.eu/).

Table 3: Import and export of domestic pigs

		Total	France	Netherlands	Luxembourg	Germany	Spain	Other MS
2007	Import	1,307,240	376,885	843,230	40,590	20,391	5,234	20,910
	Export	735,693	114,247	375,131	1,867	58,124	59,450	126,874
2008	Import	1,378,705	434,356	871,239	36,789	11,629	1,084	23,608
	Export	721,187	101,024	424,207	4	76,142	8,160	111,650

2.2 Diagnostic tests

The diagnostic test sensitivity was taken as 40% as proposed by Forbes and Gajadhar (1999). This is a worst case estimate (pool of 100g consisting of sample of 1 gram each from 1 animal with infection of 1LL/100g tissue and 99 uninfected animals). It is understood that Forbes and Gajadhar (1999) dealt with live larvae, whereas ring tests in Belgium involve frozen larvae (i.e. dead and more fragile) because of zoonotic aspects.

Forbes and Gajadhar (1999) give 8/20 positive results when testing 100 1g samples consisting of 1 low-infection sample and 99 non-infected samples. This is translated into a prior beta distribution with respective shape parameters of 9 and 13 ($\beta(9, 13)$), yielding a prior 95% credibility interval of [0.19 – 0.64]. This distribution is shown in Figure 1.

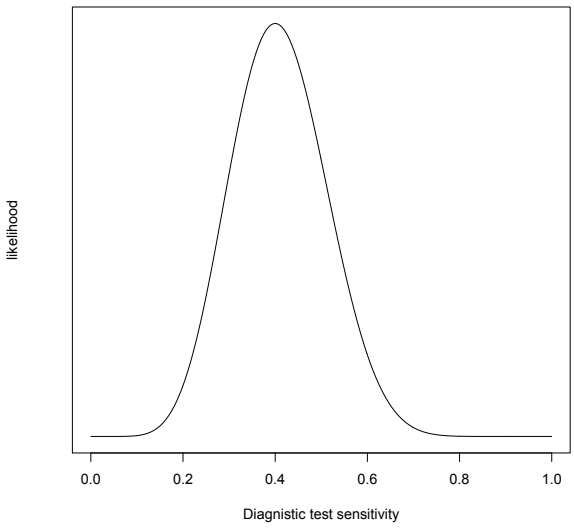

Figure 1: $\beta(9, 13)$

Diagnostic test sensitivity when testing a 100g sample, consisting of one 2g low-infection sample and 49 2g non-infected samples, was estimated by interpolation from Forbes and Gajadhar (1999): the average of 8/20 and 15/20 was taken as 12/20 and this was translated into a prior beta distribution with shape parameters 13 and 9 ($\beta(13, 9)$). This distribution is shown in Figure 2. The prior 95% credibility interval is [0.38–0.78].

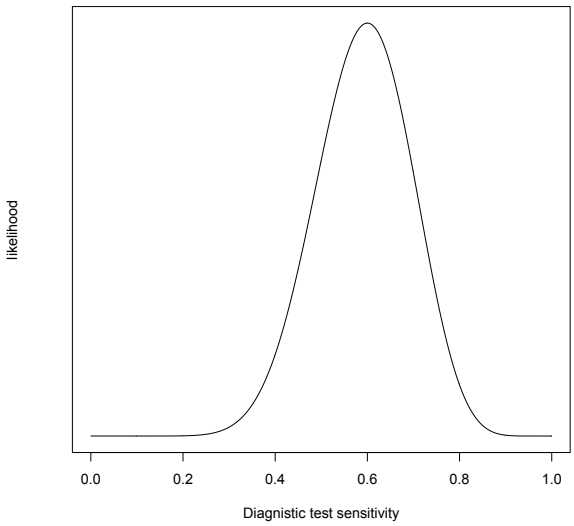

Figure 2: $\beta(13, 9)$

The National Belgian *Trichinella* Reference Laboratory in a ring test organised by the *Trichinella* CRL (http://www.iss.it/crlp/index.php) recovered a 1 live LL/100g tissue infection in three cases out of three in 2009. The 95% confidence interval is [0.36–1].

2.3 Simulations

2.3.1 General

Simulations were performed in R 2.9.2 (http://www.r-project.org/).

2.3.2 Hypotheses and scenarios

- Diagnostic test sensibility: $\beta(9, 13)$ and $\beta(13, 9)$ see Sec. 2.2.
- Design prevalence: the EFSA design prevalence of 10^{-6} is adopted (EFSA-Q-2004-017A, 2005). In addition, two other scenarios were tested, namely one with a design prevalence of 10^{-5} and one with a design prevalence of 10^{-4}.

3 Results

3.1 Probability that Belgium is currently free from *Trichinella*

The probability that Belgium is currently (beginning of 2009) free from *Trichinella* was calculated using the following R programme, using the number of pools of 100g tissue that were tested in Belgium in 2008.

```
n <- 115477
k <- 0
mn <- 0; mx <- 0.0001; dr <- 12
mn <- mn - 5*10^-(dr+1); mx <- mx + 5*10^-(dr+1)
prob <- .95
sw <- 10000; sd <- sw*10
ss <- 0
probsDoingIt <- NULL
while(ss < sw)
{
        a <- array(0, c(sd, 2))
        a[,1] <- round(runif(sd, mn, mx), dr)
        a[,2] <- rbinom(sd, n*100, a[,1])
        a[,2] <- rbinom(sd, a[,2], rbeta(sd,9,13))
        probsDoingIt <- c(probsDoingIt, a[a[,2]==k,1])
        ss <- length(probsDoingIt)
        }
plot(density(probsDoingIt),yaxt="n",xlab="Probability of
    introduction",ylab="Likelihood")
```

The results of this simulation shows that the said probability is 0.985 with an upper 95% credibility limit for the probability of infection of $7.6 \cdot 10^{-07}$.

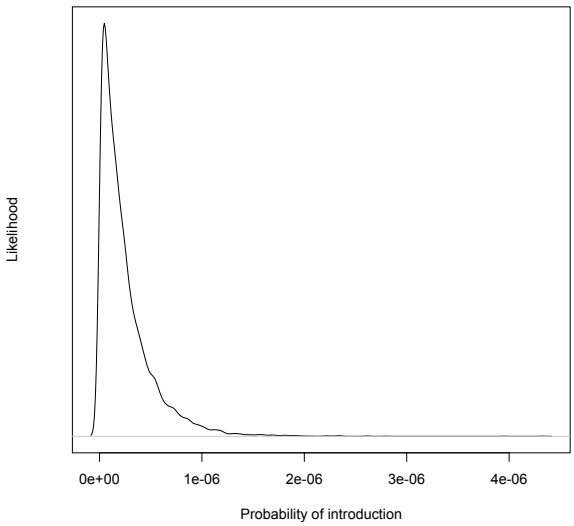

Figure 3: Likelihood of probability of freedom on 1 January 2009

3.2 Probability to find infection in function of number of pigs tested

A scenario analysis taking into account various testing strategies and different values of relative risks is examined in the following R programme.

Relative risk (RR) is defined as:

$$RR = \frac{\text{Probability of introduction of infection in risk group}}{\text{Probability of introduction of infection in indoor pigs}}$$

The following six scenarios were considered:

1. Sample tested $= 100 \times 1g; RR = 1$
2. Sample tested $= 100 \times 1g; RR = 10$
3. Sample tested $= 100 \times 1g; RR = 100$
4. Sample tested $= 50 \times 2g; RR = 1$
5. Sample tested $= 50 \times 2g; RR = 10$
6. Sample tested $= 50 \times 2g; RR = 100$

The proportion of tested domestic indoor slaughtered pigs was varied between zero and one in each of the above six scenarios. The simulations were carried out using the following programme. The effect of the sample size submitted for testing ($100 \times 1g$ or $50 \times 2g$) is reflected in the diagnostic test sensitivity (respectively $\beta(9, 13)$ and $\beta(13, 9)$).

```
req <- 10000
par(mfrow=c(2,3))
p_min <- 1e-6; p_max <- 2e-6
pop <- 11547700; pop_risk <- 338000; pop_inside <- pop - pop_
    risk
se <- array(c(8,13,13,8),c(2,2))
rrel <- array(c(1,10,100), c(3,1))
psize <- c(100,50)
for (ps in 1:2)
{
  for (rr in 1:3)
  {
    num_inf <- NULL
    rrel2 <- rrel[rr,1]
    for (prop_tested in seq(0, 1, .01))
    {
      a <- array(0, c(req, 6))
      a[,1] <- runif(req, p_min, p_max)
      a[,1] <- a[,1]*pop/(pop_inside+rrel2*pop_risk)
      a[,2] <- rbinom(req, pop_inside, a[,1])
      a[,3] <- rbinom(req, pop_risk, a[,1]*rrel2)
      a[,4] <- a[,3] + rhyper(req, a[,2], pop_inside-a[,2], pop_
          inside*prop_tested)
```

```
        a[,5] <- rbinom(req, a[,4], rbeta(req, se[1,ps], se[2,ps])
            )
        a[,6]  <- a[,2] + a[,3]
        num_now <- length(a[a[,5]>0,1])/length(a[a[,6]>0,1])
        num_inf <- c(num_inf, num_now)
        }
      ttt <- paste("poolsize =", psize[ps],"; RR =", rrel2)
      plot(seq(0,1,.01), num_inf, type="l", ylim=c(0,1), xlab="
          proportion indoor slaughter pigs tested", ylab="
          probability to detect infection", main=ttt)
      abline(h=.99)
      abline(v=seq(0,1,.01)[min(which(num_inf>=.99))])
      }
    }
```

The results are shown in Figures 4–5–6. In each of the sub-graphs the probability to detect an introduction of an infection affecting one in a million animals (Figure 4), one in a hundred thousand animals (Figure 5) and one in ten thousand animals (Figure 6) is shown in function of the proportion of indoor-raised slaughter pigs tested. In each sub-graph, the minimum proportion of indoor slaughter animals needed to be tested to achieve the minimum of 99% probability to detect infection is shown by the vertical line. Of the scenarios tested for a probability of introduciton of infection of 10^{-6}, only scenario 6 (test sample size $= 50 \times 2g$ and $RR = 100$) guarantees 99% probability to detect infection when none of the indoor-raised slaughtered animals are tested. A higher probability of introduction of infection decreases the need to test indoor-bred animals, as expected.

3.3 Deterministic calculation of minimum proportion of indoor-reared slaughter pigs to be tested

Using point estimates for all parameters, the following equation can be used to calculate the minimum proportion of indoor-reared slaughter pigs that need to be tested to guarantee a 99% probability to detect an infection with a predetermined design prevalence.

Parameters:

- Total number of animals in population: N
  - Number of indoor-reared slaughter pigs: N_i
  - Number of pigs-at-risk: N_r
- Design prevalence: p_d
  - Relative risk (defined as above): RR
  - Prevalence in indoor group:

$$p_i = \frac{p_d \times N}{N_i + RR \times N_r}$$

– Prevalence in group-at-risk:

$$p_r = RR \times p_i = \frac{RR \times p_d \times N}{N_i + RR \times N_r}$$

- Number of infected animals: $p_i \times N_i + p_r \times N_r = p_d \times N$
- Diagnostic test sensitivity: se
- Proportion indoor-reared slaughter pigs tested: t_i

Assuming a random distribution of the infected animals, we can assume that there is each time only one infected animal per pool, i.e. there are $p_d \times N$ infected pools.

The probability to detect at least one infected pool must be 99%. This probability is given by:

$$\begin{aligned} 1 - (1 - se)^{p_r \times N_r} (1 - se)^{t_i \times p_i \times N_i} &= 0.99 \\ 1 - (1 - se)^{RR \times p_i \times N_r + t_i \times p_i \times N_i} &= 0.99 \end{aligned}$$

The idea now is to isolate t_i.

$$\begin{aligned} 0.01 &= (1 - se)^{RR \times p_i \times N_r + t_i \times p_i \times N_i} \\ log(0.01) &= log\left((1 - se)^{RR \times p_i \times N_r + t_i \times p_i \times N_i}\right) \\ log(0.01) &= (RR \times p_i \times N_r + t_i \times p_i \times N_i) \times log(1 - se) \\ t_i \times p_i \times N_i \times log(1 - se) &= log(0.01) - RR \times p_i \times N_r \times log(1 - se) \end{aligned} \tag{1}$$

$$\begin{aligned} t_i &= \frac{log(0.01) - RR \times p_i \times N_r \times log(1 - se)}{p_i \times N_i \times log(1 - se)} \\ &= \frac{log(0.01)}{p_i \times N_i \times log(1 - se)} - \frac{RR \times N_r}{N_i} \end{aligned}$$

$$t_i = max\left[min\left(\frac{log(0.01)}{\frac{p_d \times N}{N_i + RR \times N_r} \times N_i \times log(1 - se)} - \frac{RR \times N_r}{N_i}, 1\right), 0\right] \tag{2}$$

The evaluation of Eq. 2 is shown in Figure 7.

3.4 Minimum relative risk required to abandon testing indoor-reared slaughter pigs

Alternatively, the minimum value for RR needed to permit no testing of indoor-reared slaughter pigs can be calculated from the above equations, i.e. determine the minimum value of RR when $t_i = 0$.

Equating t_i to zero in Eq. 1 yields:

$$log(0.01) = RR \times \frac{p_d \times N}{N_i + RR \times N_r} \times N_r \times log(1 - se)$$

$$log(0.01) = \frac{RR \times p_d \times N \times N_r \times log(1 - se)}{N_i + RR \times N_r}$$

$$RR \times p_d \times N \times N_r \times log(1 - se) = log(0.01) \times (N_i + RR \times N_r)$$
$$RR \times p_d \times N \times N_r \times log(1 - se) = log(0.01) \times N_i + log(0.01) \times RR \times N_r$$
$$RR \times (p_d \times N \times N_r \times log(1 - se) - log(0.01) \times N_r) = log(0.01) \times N_i$$

$$RR = \frac{N_i \times log(0.01)}{N_r \times (p_d \times N \times log(1 - se) - log(0.01))} \quad (3)$$

The minimum RR required to abandon testing of indoor-reared slaughter pigs in function of the design prevalence and the test sensitivity is shown in Table 4 (rounded up to next integer).

Table 4: Minimum value for RR to abandon testing of indoor-reared slaughter pigs

p_d	$se = 0.4$	$se = 0.6$
10^{-6}	119	26
10^{-5}	3	2
10^{-4}	1	1

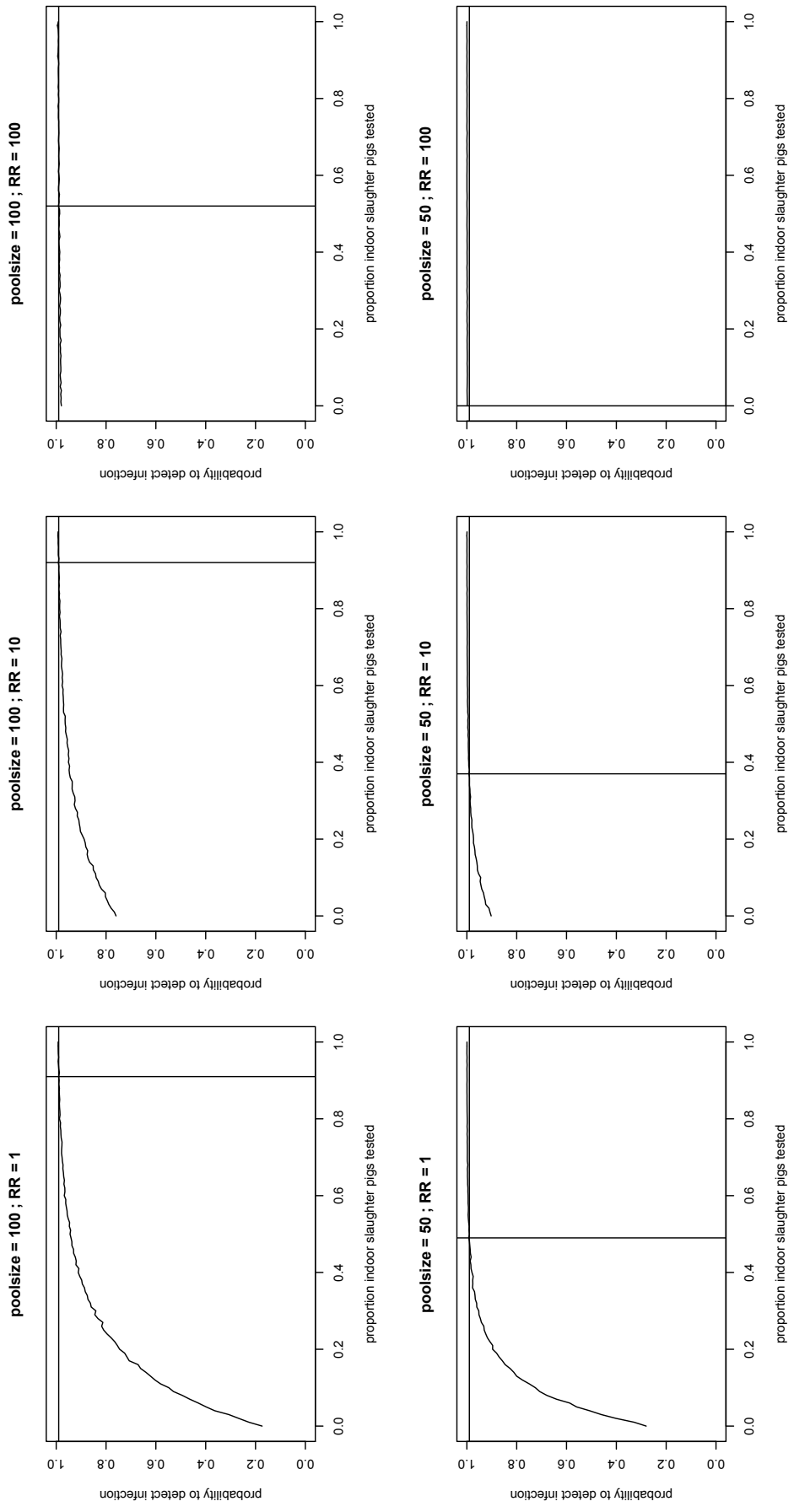

Figure 4: Probability to detect introduction of infection in function of test sample size ($100 \times 1g$ and $50 \times 2g$), relative risk (RR = 1; RR = 10; RR = 100) and proportion of indoor slaughter pigs tested (shown in abscissa, 0 - 1). Design prevalence = 10^{-6}. The horizontal line is the 99% probability to detect introduction. The vertical line represents the minimum proportion of indoor slaughter pigs to be tested to achieve a 99% probability to detect.

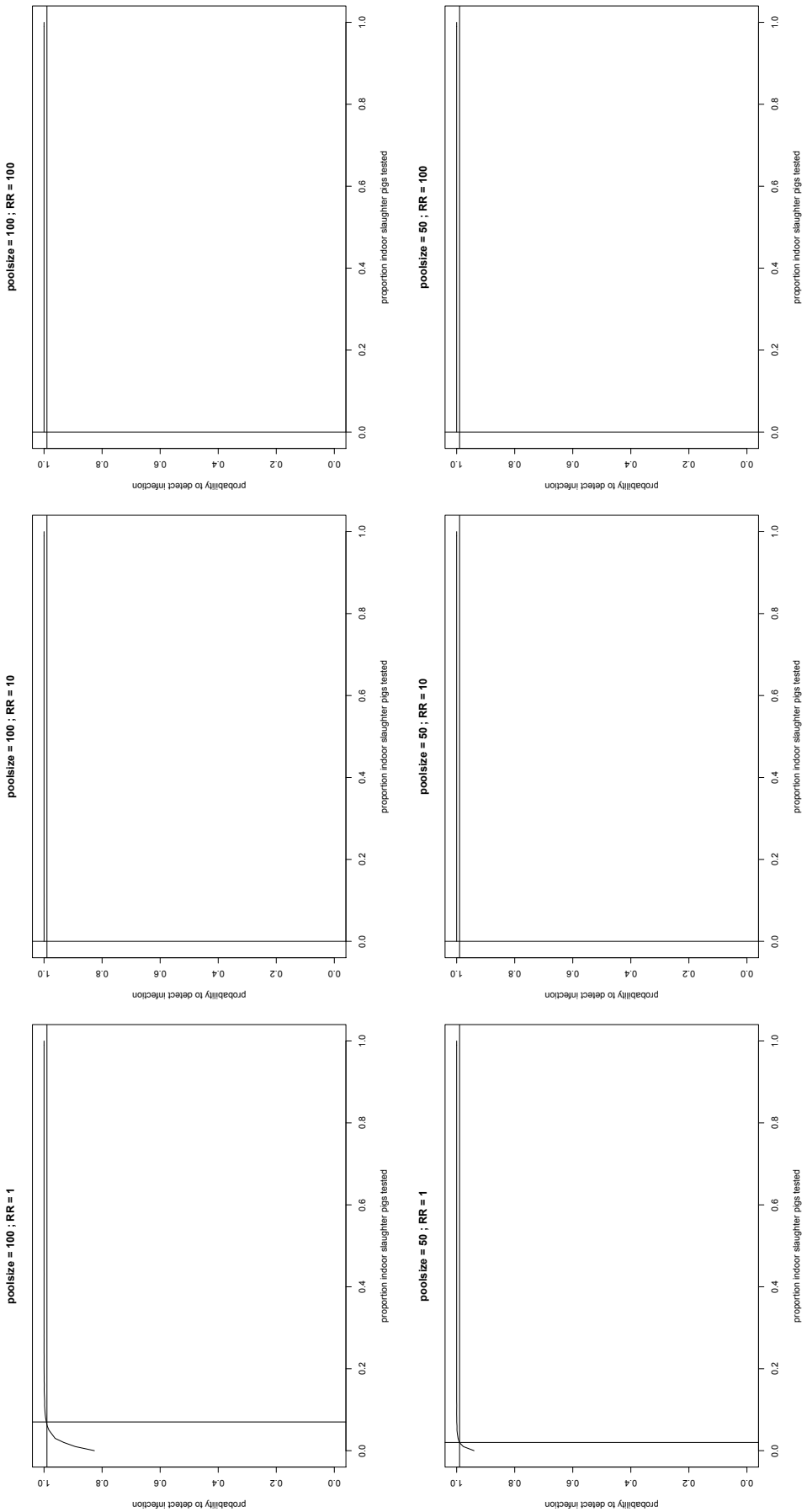

Figure 5: Probability to detect introduction of infection in function of test sample size ($100 \times 1g$ and $50 \times 2g$), relative risk (RR = 1; RR = 10; RR = 100) and proportion of indoor slaughter pigs tested (shown in abscissa, 0 - 1). Design prevalence = 10^{-5}. The horizontal line is the 99% probability to detect introduction. The vertical line represents the minimum proportion of indoor slaughter pigs to be tested to achieve a 99% probability to detect.

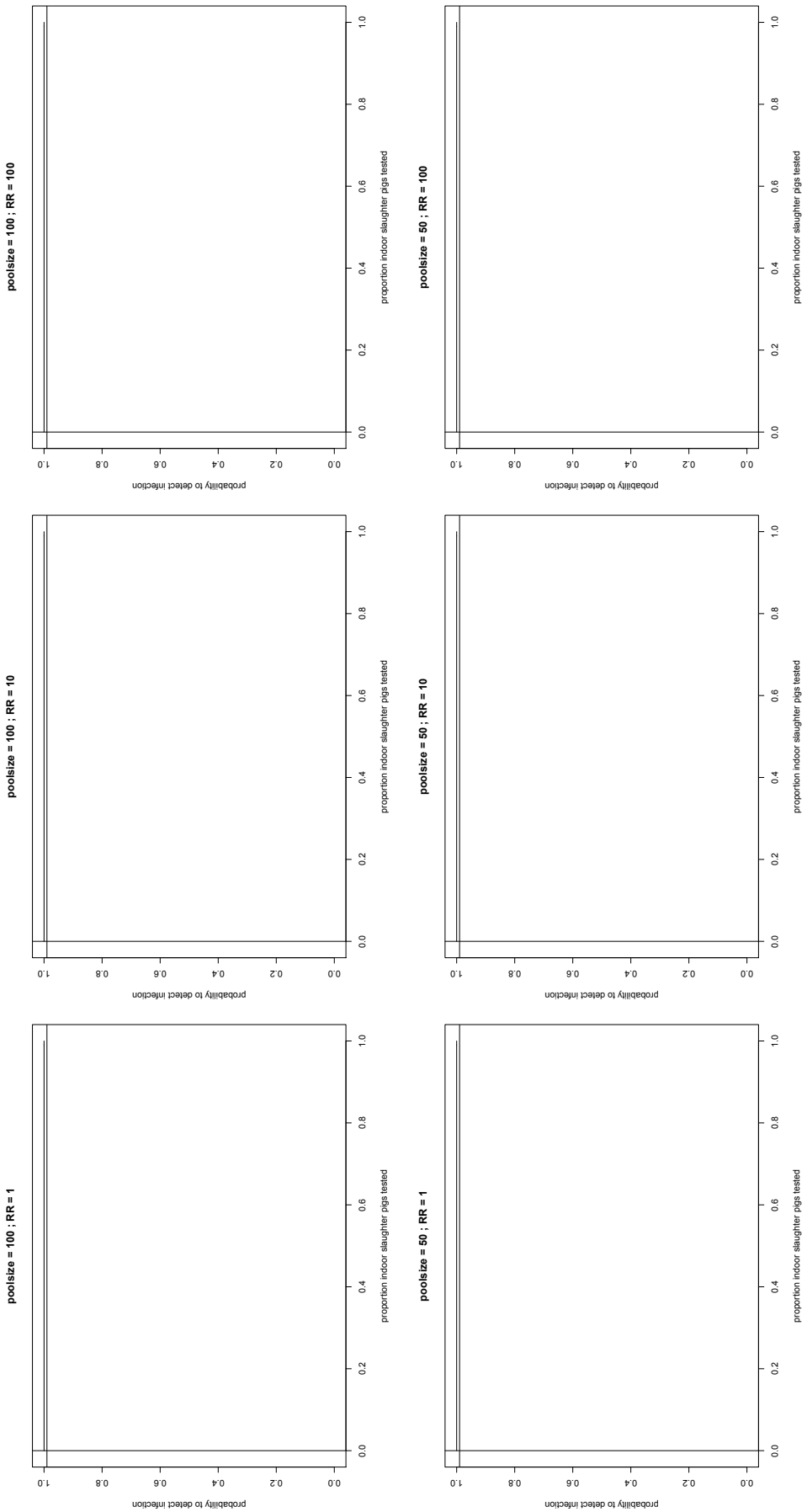

Figure 6: Probability to detect introduction of infection in function of test sample size ($100 \times 1g$ and $50 \times 2g$), relative risk (RR = 1; RR = 10; RR = 100) and proportion of indoor slaughter pigs tested (shown in abscissa, 0 - 1). Design prevalence = 10^{-4}. The horizontal line is the 99% probability to detect introduction. The vertical line represents the minimum proportion of indoor slaughter pigs to be tested to achieve a 99% probability to detect.

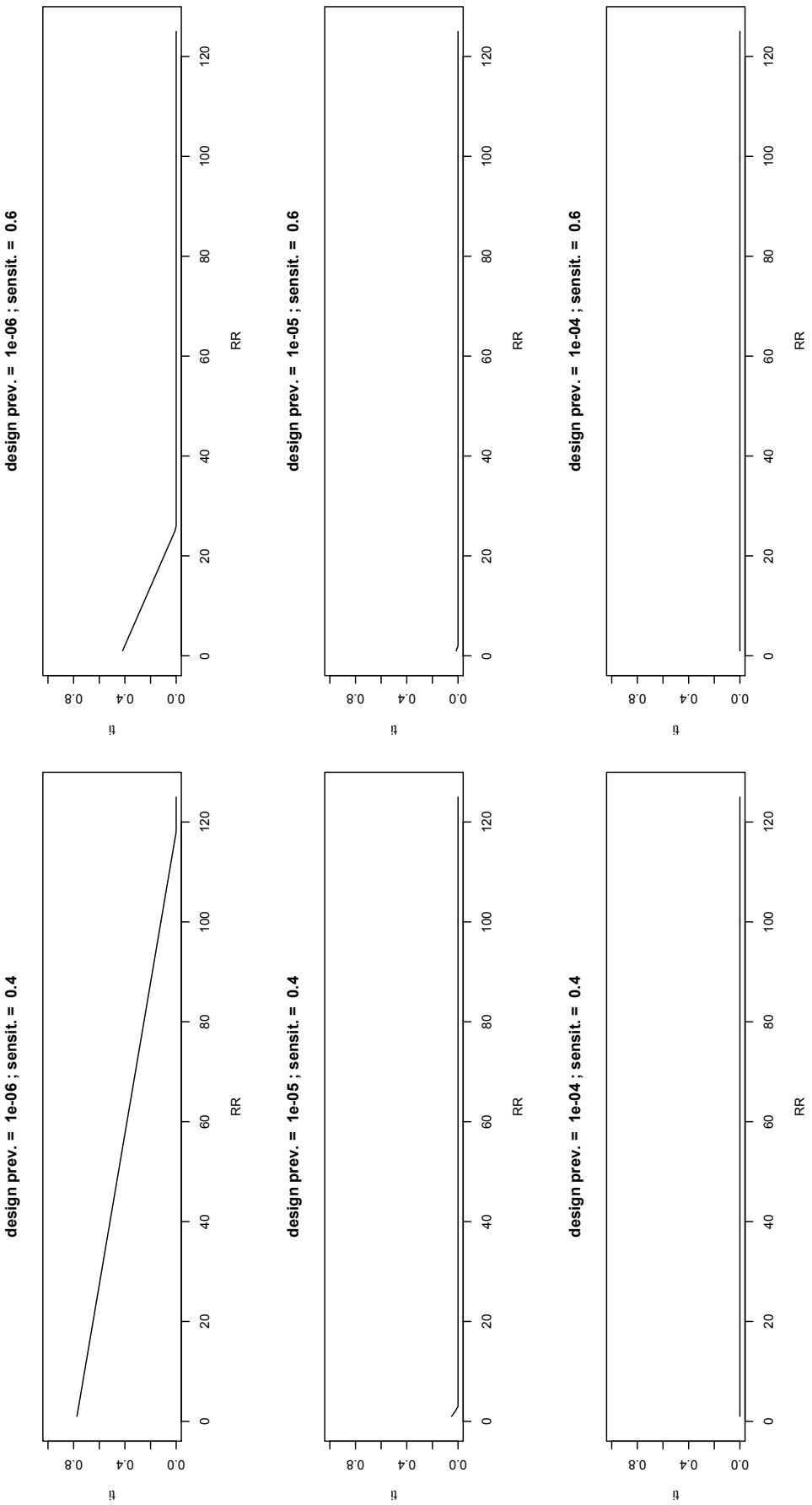

Figure 7: Minimum proportion of indoor-reared slaughter pigs that need to be tested in function of relative risk (abscissa) and design prevalence (from top to bottom 10^{-6}, 10^{-5} and 10^{-4}) and test sensitivity (from left to right 0.40 and 0.60)

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