

Scotland's Rural College

Difficulties arising from the variety of testing schemes used for Bovine Viral Diarrhoea Virus (BVDV)

Duncan, AJ; Gunn, GJ; Humphry, RW

Published in:
Veterinary Record

DOI:
[10.1136/vr.103329](https://doi.org/10.1136/vr.103329)

First published: 01/01/2016

Document Version
Peer reviewed version

[Link to publication](#)

Citation for published version (APA):

Duncan, AJ., Gunn, GJ., & Humphry, RW. (2016). Difficulties arising from the variety of testing schemes used for Bovine Viral Diarrhoea Virus (BVDV). *Veterinary Record*, 178(12), 292-300. Advance online publication. <https://doi.org/10.1136/vr.103329>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

Difficulties arising from the variety of testing
schemes used for Bovine Viral Diarrhoea Virus
(BVDV)

A.J. Duncan^{a, b, *} BSc (Hons), PhD;
G.J. Gunn^b BVMS, MSc, Dipl ECVPH, Dipl ECBHM, RCVS Spec. Vet. Epi., MRCVS;
R.W. Humphry^b BA, PhD, Dip. Stat.

^a Inverness College UHI, 1 Inverness Campus, Inverness, IV2 5NA
^b Epidemiology Research Unit. SRUC (Scotland's Rural College), Drummondhill,
Stratherrick Road, Inverness, IV2 4JZ

* Corresponding Author: andrew.duncan.ic@uhi.ac.uk

23 **Abstract (200 words or less)**

24 Globally, the eradication of bovine viral diarrhoea virus (BVDV) is still in its infancy
25 but eradication has been, or is being, adopted by several countries or regions.
26 Comparisons between countries' schemes allow others to assess best practice, and
27 aggregating published results from eradication schemes provides greater statistical
28 power when analysing data. Aggregating data requires that results derived from
29 different testing schemes be calibrated against one another. We aimed to evaluate
30 whether relationships between published BVDV test results could be created and
31 present the outcome of a systematic literature review following the Preferred
32 Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.
33 The results are tabulated, providing a summary of papers where there is potential
34 cross-calibration and a summary of the obstacles preventing such data-aggregation.
35 Although differences in measuring BVDV present barriers to academic progress they
36 may also affect progress within individual eradication schemes. We examined the
37 time taken to retest following an initial antibody BVDV test in the Scottish eradication
38 scheme. We demonstrate that retesting occurred quicker if the initial not negative
39 test was from blood rather than milk samples. Such differences in the response of
40 farmers/veterinarians to tests may be of interest to the design of future schemes.

41

42 Word Count: 199

43

44

45 **Introduction**

46 Programs designed to eradicate bovine viral diarrhoea virus (BVDV) appear, overall,
47 to be making progress, and they exist in various countries (AHI 2014, AHWNI 2014,
48 Barrett and others 2011, Graham and others 2014, Lindberg and others 2006, Presi
49 and others 2011, Sandvik 2004). Other programs are also planned (Farmers Weekly
50 2014, Laurens, 2014). The variation in the design of these existing programs is of
51 use in designing future programs because it allows comparison of different strategies
52 and lessons to be learnt. The publication of results from different programs around
53 the world also provides a potential opportunity for combining data or results to
54 increase the statistical power when testing scientific hypotheses (Egli 2014).

55

56 In Scotland, the eradication of BVDV is on its fourth stage (Scottish Government
57 2014a). The majority of eradication programs attempt to split herds into 'possibly
58 infected' and 'uninfected' (Lindberg and others 2006, Prezi and others 2011). In
59 Scotland the two categories are labelled as 'not negative' and 'negative'. Negative
60 herds continue to be monitored in case their status changes. Not negative herds
61 should initiate further testing, commonly trying to find persistently infected (PI)
62 animals and have their movements restricted (Scottish Government 2014b).

63

64 Within the Scottish BVDV eradication scheme there are eight possible testing
65 methods (including three types of calf sampling) and eight groups of laboratories that
66 can process the tests (Scottish Government 2015a, Scottish Government 2015b).
67 Samples may be tissue, semen, blood or milk and can be tested for antigen or
68 antibody (Scottish Government 2014c).

69

70 For dairy herds, bulk milk samples are common in eradication schemes to identify
71 antibody status with antigen blood testing frequently used to establish whether the
72 herd is currently infected and to find PI animals. For beef herds, blood testing
73 predominates. The difference between common types of bulk milk and blood tests
74 provides a useful example of the ramifications of differences in tests.

75

76 Within each sampling method (as described above) there are also many different
77 laboratory tests for BVDV (Lanyon and others 2014a) and a comprehensive list of
78 those available is beyond the scope of this paper. Many of the tests available are
79 based on detection of the virus or the antibody to the virus, and use enzyme-linked
80 immunosorbent assay (ELISA), immunohistochemical tests, reverse transcription
81 polymerase chain reaction (RT-PCR), or neutralization serum antibody tests
82 (Radostits and others 2007). The variation in test regime depends upon a
83 combination of the particular kit manufacturer, the sampling regime and the tissues
84 sampled.

85

86 Between eradication schemes, variety provides a series of “natural experiments” in
87 which different schemes adopt different tests and, thus, the international community
88 has evidence regarding their relative merits. However, this depends on how the tests
89 and their results are reported, and people in business rarely have time to dwell on
90 the complexities of test performance (e.g. sensitivity and specificity). The use of
91 different tests is not only important to the researcher, but also to the farmer,
92 veterinarian and the eradication scheme.

93

94 We set out to try to establish relationships between reported BVDV test results. The
95 first step in this was a systematic literature review using the Preferred Reporting
96 Items for Systematics Reviews and Meta-Analyses (PRISMA) guidelines (Moher and
97 others 2009). We present the results of this review followed by a discussion of the
98 difficulties we had in using the results to establish a relationship between tests. As a
99 consequence of the difficulties we encountered, we also examined the test results
100 from the Scottish BVDV eradication scheme to see if the industry treated results from
101 blood and milk tests differently. We present the results of these tests and a
102 discussion surrounding the differences between blood and milk tests.

103

104 **Materials and Methods**

105 Systematic Review

106 In order to find as many as possible, in a repeatable and documented way, of the
107 papers that have published results that would help us compare test results we
108 conducted a systematic literature review using PRISMA guidelines (Moher and
109 others 2009). Full details of our review process are shown below:

- 110 1. An advanced search was made on Web of
111 Science <http://webofknowledge.com/>
- 112 2. The search we used was:
(TI= ((bovine viral diarr) OR (BVDV) OR(bovine virus diarr*)) AND
113 (TI=(milk OR antibod* OR *prevalence OR eradication OR herd OR elisa)))*
- 114 3. The results were initially filtered on web of science by selecting the document
115 type, research domain and language.
 - 116 i. Document Types: *Article or Review*
 - 117 ii. Research Domain: *Science Technology*
 - 118 iii. Language: *English*
- 119 4. The results were exported in tab delimited format to Windows including their
120 abstracts (where possible). The remaining filtering took place in Microsoft
121 Excel.
- 122 5. The results which didn't have an abstract exported (AB column) were
123 removed.
- 124 6. The results that stemmed from a conference (CT column) were removed.
- 125 7. We then removed any results which we could not access electronically or
126 were not available in paper format from previous work. Double entries were
removed.

- 127 8. Papers were then submitted to two screening questions:
- 128 i. Are numerical results, a statistical model or graphs produced from
- 129 which the reported results can be read?
- 130 ii. Are multiple tests or multiple testing procedures used? Failing that is
- 131 there an equation that can be used to compare with other results?

132 We retained only those publications where quantitative results (e.g. number of

133 animals positive in herd, number of PI, test scores or percentages) were

134 available for comparison from tables or graphs. The exception was where an

135 equation or model governing the relationship between test results, test types

136 or PI animals was reported.

137

138 For each paper we extracted the following information into tabular form: the sample

139 types (blood/bulk milk), the tests used, how the results are presented, whether

140 individual PI animal status was reported, whether the animals/herds tests were

141 vaccinated, and an explanation of why we think the result can or cannot be used to

142 link to another paper/test. As the papers were subjectively assessed there is a risk of

143 bias across the studies from step 8 above and in extracting the results from the

144 publication. Where the lead author was in any doubt, one of the other authors acted

145 as a secondary reviewer.

146

147 Retesting Analysis of the Scottish BVDV Eradication Scheme

148 To establish whether the results from blood and milk antibody tests are treated

149 differently we used the results of the BVD eradication scheme in Scotland. Results

150 were collated and matched by the County, Parish, Holding (CPH) unique identifier.

151 For each CPH we identified the first blood or milk antibody test and then established

152 the number of days for the same CPH to conduct an antigen test. Those antigen
153 tests taking place less than nine days after the antibody test were counted as part of
154 the same testing due to the length of time needed to return test results to the CPH in
155 question. These resampling results are presented as a proportion of those CPHs
156 within each class of the same initial test (milk or blood) and initial test result
157 (negative or not negative). Only the test results recorded as “Negative” or “Not
158 Negative” were used. To use other values would have necessitated a subjective
159 interpretation of the overall test result.

160

161 To establish if there was a statistical significant difference in the proportions of
162 holdings retesting within 90 days (AFBI 2015, DEFRA 2015) based on the type of
163 initial antibody test, we carried out a two-sided proportion test and a survival
164 analysis. We selected a 90 day threshold for our analyses because this is the period
165 within which retesting is normally recommended or required for bulk milk tests,
166 regardless of herd status (AFBI 2015, DEFRA 2015). The CPHs were split by initial
167 test type (milk or blood). Those CPHs that did not retest within 90 days, regardless of
168 whether they later retested, were treated as “not retesting”.

169

170 For the proportion test (Newcombe 1998) a two by two table of counts (resample
171 before 90 days yes/no versus initial antibody test blood/milk) was constructed before
172 we used the *prop.test* function in the statistical software R (R Core Team 2015) to
173 carry out the test. The survival analysis was carried out using the survival package
174 (Therneau 2015, Therneau and Grambsch 2000).

175

176

177 **Results**

178 Systematic Review

179 Table 1 shows the papers that completed the PRISMA systematic review process.
180 For each paper we show: the sample types (blood/bulk milk), tests used, result
181 format, whether individual PI animal status was reported, the vaccination status of
182 the animals/herds (if reported) and description of whether the result can be used to
183 link to another paper/test. The number of papers that remained after each stage of
184 our process described above are shown in table 2.

185

186 The papers in table 1 should allow us to compare results from different tests and
187 different testing methods. However, we encountered significant difficulties in doing
188 so. The most common difficulties surrounded vaccination and test variety.

189

190 Retesting Analysis of the Scottish BVDV Eradication Scheme

191 Figure 1 shows the proportion of farms (in the Scottish BVDV eradication scheme
192 2013-2014) retesting over the year, split by the type of initial test. (Red, solid: initial
193 negative blood test. Green, short dashed: initial not-negative blood test. Blue,
194 dashed: initial negative milk test. Purple, long-dashed: initial not-negative milk test.)
195 There is a clear difference between the time taken to retest. Within the first 90 days,
196 farms are more likely ($p = 0.05139$ from the two-sided test of proportions) to retest
197 following a not-negative result if the initial test was using blood testing rather than
198 bulk milk. This is confirmed by the survival analysis which provides a relative risk of
199 0.73 with a 95% confidence interval of (0.54, 0.98) and a rejection of the null
200 hypothesis that the relative risk is one, based on a p-value of 0.037.

201

202 **Discussion**

203 Whilst progress appears to be being made in the uptake of eradication schemes for
204 BVDV around the world, it is still in its infancy, with more countries **not** yet planning
205 such a scheme than there are countries planning, in the process of, or having
206 achieved, eradication (Moennig and Becher 2015). We are therefore at a useful
207 stage in the global eradication trend, because we can make use of data being
208 reported from the different schemes from around the world. Results from schemes
209 can be used either by aggregating data in order to achieve increased statistical
210 power when asking epidemiological questions (e.g. does herd size affect the
211 probability of a herd containing a PI and by how much?) or, qualitatively, by heeding
212 the lessons learnt from the reports of successful and unsuccessful strategies. Here
213 we describe the difficulties we had in aggregating data and present evidence from
214 one particular scheme in which the differences in farmers'/veterinarians' perception
215 of the test may be influencing the time taken to retest. Comparative studies of
216 strategies **within** a scheme may be even more powerful than between schemes
217 because unknown confounders (at the scheme level) should be effectively controlled
218 for.

219

220 Aggregating data requires that data be “calibrated” into common and genuinely
221 equivalent units (e.g. within herd seroprevalence) and therefore is dependent on
222 comparing results from different schemes with different methods. The difficulties
223 encountered in comparing results from different papers were mainly due to:
224 vaccination, the variety of tests used and how their results were reported. It is clear
225 from table 1 that some papers have vaccinated animals whilst other are
226 unvaccinated or vaccination status is not reported. Some eradication schemes have

227 banned vaccination (Lindberg and others 2006) and comparing antibody results
228 across studies without accounting for differences in vaccination regimes risks
229 ignoring vaccination as a clear confounder (Bauermann and others 2013, Gonzalez
230 and others 2014a, 2014b, Humphry and others 2012, Stevens and others 2011).

231

232 Whilst vaccine usage might possibly be dictated by an eradication scheme,
233 (Lindberg and others 2006) the particular laboratory tests used could be more
234 difficult to control. For example, within the Scottish BVDV eradication scheme the
235 testing methods and the laboratories analysing them are controlled but not the
236 manufacturer of the tests they use (Scottish Government 2015a). Table 1 gives an
237 example of the variety of tests for both blood and milk that are reported in the
238 literature. Tests range from those used by specific laboratories to bespoke (Houe
239 1994, Houe and Meyling 1991, Rüfenacht and others 2000). Some results are
240 reported with insufficient detail to allow comparison. For example, the percentage
241 inhibition results from Booth and others (2013) are reported without the control
242 values needed to replicate them. However, in Niskanen and others (1991) and
243 Niskanen (1993), the control values are reported. Incomplete reporting of results
244 may not be the authors' choice - it may arise from the laboratory or test used.
245 However, where full details can be made available, doing so would assist other
246 researchers and, possibly, those in charge of eradication schemes.

247

248 The accuracy and reliability of the type of test should also be considered as this can
249 be used to estimate confidence ranges around any calibrated result from one
250 scheme in comparison to another. For example there is good evidence (Brülisauer
251 and others 2010, Humphry and others 2012) that using the proportion of seropositive

252 young-stock gives better classification of herds into distinct antibody-level groups
253 than bulk milk antibody scores. Figure 2 shows the frequency distribution for
254 percentage positivity (PP) scores of bulk milk tests for 220 Scottish farms whilst
255 figure 3 shows the frequency of 10 young stock that were BVDV seropositive in 274
256 Scottish herds. Even with the complicating observation of a small spike at about 5
257 seropositive animals in figure 2 (see Brülisauer and others (2010) for a full
258 discussion) the bloods have a very clear second maximum for 9 and 10 seropositive
259 animals, whereas the bulk milk results have no clear separation.

260

261 This suggests that at herd-level, bulk milk results are more likely to produce false
262 positives, or false negatives than is the serum screening of young-stock. Bulk milk
263 antibody scores are not only an average of contributing animals but they also
264 represent an average over time, reflecting historic as well as current BVDV status.
265 The removal of PI animals will not necessarily produce an immediate change in bulk
266 milk results (figure 4 - reproduced from Houe 1999). It is clear that even three years
267 after the removal of the final PI animal, the bulk milk results had not changed greatly.

268

269 Differences in the “performance” of a test are not just of importance to academic
270 researchers when trying to make use of reported results from around the world.
271 These differences, whilst appearing highly epidemiological and quantitatively
272 technical, are also of great importance to the individual scheme itself and to the
273 farmers and practitioners within the scheme. How farmers and their veterinarians
274 respond to any difference in test performance (sensitivity and specificity) is hard to
275 predict. A precautionary approach may be adopted – i.e. any bulk milk score which is
276 just negative might be followed up with additional tests lest it be a false negative.

277 Conversely, a riskier approach might be that any not-negative test be considered a
278 probable false positive. The Scottish Eradication data provides evidence that may
279 be, in part, an example of scheme members responding to different tests according
280 to the different test performance.

281

282 Figure 1 shows that the length of time taken to retest from an initial not negative
283 antibody test result is dependent on whether that initial test was a blood or a milk
284 test. It is possible that farmers take a not-negative result from blood more seriously
285 and hence retest quicker. Farmers may be taking the riskier approach with the not
286 negative milk result which we suggested above. We should also consider whether
287 dairy farms treat PI calves with less concern than beef farms as calves are removed
288 from dairy herds at a younger age than in beef herds. Other explanations include the
289 availability of follow up tests depending on whether the farm is beef or dairy, if the
290 financial impact of a movement ban of animals is greater for beef farms or if there is
291 more pressure within the beef sector for retesting.

292

293 We do not know why those receiving not negative blood test results retest quicker
294 but the discussion about bulk milk results is pertinent not least because the Scottish
295 Government have removed the option for bulk milk tests from June 1st, 2015
296 (Scottish Government 2015c). This seems understandable as eradication enters its
297 next phase, given the importance of successful detection of the virus and the relative
298 imperfection of the bulk milk antibody test but this policy differs from some other
299 schemes (Hult and Lindberg 2005).

300

301 Whilst we have acknowledged the limitations of bulk milk testing, this is not to
302 dismiss the value of testing milk from all or some cows in a herd. Milk sampling from
303 a sub-group of milking animals can be particularly useful for testing new heifers
304 whose antibodies provide a “signal” of recent rather than historic infection (Brownlie
305 and Booth 2014, Houe and others 2006, Ohlson and others 2013). It is therefore
306 reasonable that, after a scheme has effectively eradicated BVDV (and depending on
307 vaccination regimes), the relatively convenient and cheap test that is bulk milk
308 testing may come into its own as a first line of screening for sporadic breakdown
309 (Booth and others 2013).

310

311 There are many different tests available for BVDV and a lot of research has been
312 published detailing test results and progress in eradication schemes (Laurens 2014,
313 Lindberg and others 2006, Sandvik 2004). Whilst not of immediate concern to the
314 design of a scheme, taking into account how transferable the results of that scheme
315 are with data from other schemes has the added benefit of facilitating research
316 based on aggregating results. When designing an eradication scheme the testing
317 methods and individual tests available should be considered to ensure that a variety
318 of tests within the scheme does not discombobulate the scheme itself. If the scheme
319 is too complicated, this will only hinder the eradication.

320 **Acknowledgements**

321 The SRUC receives financial support from the Scottish Government within WP6.1 of
322 the RESAS 2011–2016 research programme. The Scottish Government had no
323 involvement in the analysis and interpretation of the data; in the writing of the report;
324 and in the decision to submit. The authors would like to acknowledge the link
325 between Inverness College UHI and the SRUC thus enabling this work to be carried
326 out.

327

328 **References**

329

330 AFBI (2015) Milk Testing. <http://www.afbini.gov.uk/bulk-tank-milk-testing.pdf>. Last
331 accessed November 10, 2015.

332

333 AHI (2014) BVD National Eradication Programme in Ireland.

334 <http://www.animalhealthireland.ie/page.php?id=3>. Last accessed August 5, 2014.

335

336 AHMAD, A., RABBANI, M, MUHAMMAD, K., YOUNUS, M., SHABBIR, M.Z.,
337 GHAFOR, A., ANJUM, A.A., NAZIR, J., SALEEMI, M.K., MUHAMMAD, J., ALI,
338 A.A. & CEPICA, A. (2014) Comparative diagnostic applications of antigen capture
339 elisa and immunochemistry for detection of bovine viral diarrhoea persistent infection.
340 *Journal of Animal and Plant Science* **24**, 1019-1025.

341

342 AHWNI (2014) BVD Eradication in Northern Ireland.

343 <http://www.animalhealthni.com/BVD.aspx>. Last accessed August 4, 2014.

344

345 BARRETT, D.J., MORE, S.J., GRAHAM, D.A., O'FLAHERTY, J., DOHERTY, M.L. &
346 GUNN, H.M. (2011) Considerations on BVD eradication for the Irish livestock
347 industry. *Irish Veterinary Journal* **64**, 12-21.

348

349 BAUERMAN, F.V., HARMON, A., FLORES, E.F., FALKENBERG, S.M., REECY,
350 J.M. & RIDPATH, J.F. (2013) In vitro neutralization of HoBi-like viruses by antibodies
351 in serum of cattle immunized with inactivated or modified live vaccines of bovine viral
352 diarrhoea viruses 1 and 2. *Veterinary Microbiology* **166**, 242-245.

353

354 BEAUDEAU, F., ASSIE, S., SEEGER, H., BELLOC, C., SELLAL, E. & JOLY,
355 A.(2001a) Assessing the within-herd prevalence of cows antibody-positive to bovine
356 viral diarrhoea virus with a blocking ELISA on bulk tank milk. *Veterinary Record* **149**,
357 236–240.

358

359 BEAUDEAU, F., BELLOC, C., SEEGER, H., ASSIÉ, S., POURQUIER, P. & JOLY,
360 A. (2001b) Informative Value of an Indirect Enzyme-Linked Immunosorbent Assay
361 (ELISA) for the Detection of Bovine Viral Diarrhoea Virus (BVDV). *Journal Veterinary*
362 *Medicine B* **48**, 705-712.

363

364 BEAUDEAU, F., BELLOC, C., SEEGER, H., ASSIÉ, S., SELLAL, E. & JOLY, A.
365 (2001c) Evaluation of a blocking ELISA for the detection of bovine viral diarrhoea
366 virus (BVDV) antibodies in serum and milk. *Veterinary Microbiology* **80**, 329-337.

367

368 BOOTH, R.E. & BROWNLIE, J. (2011) Establishing a pilot bovine viral diarrhoea
369 virus eradication scheme in Somerset. *Veterinary Record* **170**, 73-79.

370

371 BOOTH, R.E., CRANWELL, M.P. & BROWNLIE, J. (2013) Monitoring the bulk milk
372 antibody response to BVDV: the effects of vaccination and herd infection status.
373 *Veterinary Record* **172**, 449-456.

374

375 BOSCO COWLEY, D.J., CLEGG, T.A., DOHERTY, M.L. & MORE, S.J. (2012)
376 Bovine viral diarrhoea virus seroprevalence and vaccination usage in dairy and beef
377 herds in the Republic of Ireland. *Irish Veterinary Journal* **65**, 16-24.

378 BROWNLIE, J. & BOOTH, R. (2014) Diagnostic Tests to Detect and Eradicate BVDV
379 in Herds. *Veterinary Times* **25**, 8-10.
380
381 BRÜLISAUER, F., LEWIS, F.I., GANSER, A.G., McKENDRICK, I.J., GUNN, G.J.
382 (2010) The prevalence of bovine viral diarrhoea virus infection in beef suckler herds
383 in Scotland. *The Veterinary Journal* **186**, 226-231.
384
385 CORNISH, T.E., VAN OLPHEN, A.L., CAVENDER, J.L., EDWARDS, J.M., JAEGER,
386 P.T., VIEYRA, L.L., WOODARD, L.F., MILLER, D.R. & O'TOOLE, D. (2005)
387 Comparison of ear notch immunohistochemistry, ear notch antigen-capture ELISA,
388 and buffy coat virus isolation for detection of calves persistently infected with bovine
389 viral diarrhoea virus. *Journal of Veterinary Diagnostic Investigation* **17**, 110-117.
390
391 DEFRA (2015) Herdsure protocol for bovine viral diarrhoea (BVD) in cattle herds.
392 ahvla.defra.gov.uk/apha-scientific/documents/herdsure/herdsure-vethdbk-bvd.pdf.
393 Last accessed November 10, 2015.
394
395 DIÉGUEZ, F.J., YUS, E., SANJUÁN, M.L., VILAR, M.J. & ARNAIZ, I. (2008)
396 Monitoring bovine viral diarrhoea virus (BVDV) infection status in dairy herds.
397 *Pesquisa Veterinária Brasileira* **28**, 588-592.
398
399 EGLI, C. (2014) What Can We Learn From International BVD Experience? IDEXX
400 Bovine
401 Diagnostics <http://www.nationalmilklabs.co.uk/downloads/ChrisEgliIntBVDExper.pdf>.
402 Last accessed November 10, 2015.
403
404 EIRAS, C., ARNAIZ, I., SANJUÁN, M.L., YUS, E. & DIÉGUEZ, F.J. (2012) Bovine
405 viral diarrhoea virus: Correlation between herd seroprevalence and bulk tank milk
406 antibody levels using 4 commercial immunoassays. *Journal of Veterinary Diagnostic*
407 *Investigation* **24**, 549-553.
408
409 FARMERS WEEKLY (2014) Government chief vets plan to tackle
410 BVD. <http://www.fwi.co.uk/livestock/government-chief-vets-plan-to-tackle-bvd.htm>.
411 Last accessed January 27, 2014.
412
413 FODDAI, A., ENØE, C., STOCKMARR, A., KROGH, K. & UTTENTHAL, A. (2015)
414 Challenges for bovine viral diarrhoea virus antibody detection in bulk milk by
415 antibody enzyme-linked immunosorbent assays due to changes in milk production
416 levels. *Acta Veterinaria Scandinavica* **57**, 32.
417
418 GONZALEZ, A.M., ARNAIZ, I., EIRAS, C., CAMINO, F., SANJUÁN M.L., YUS, E. &
419 DIÉGUEZ, F.J. (2014a) Monitoring the bulk milk antibody response to bovine viral
420 diarrhoea in dairy herds vaccinated with inactivated vaccines. *Journal Dairy Science*
421 **97**, 3684-3688.
422
423 GONZALEZ, A.M., ARNAIZ, I., YUS, E., EIRAS, C., SANJUÁN M.L., & DIÉGUEZ,
424 F.J. (2014b) Evaluation of long-term antibody responses to two inactivated bovine
425 viral diarrhoea virus (BVDV) vaccines. *The Veterinary Journal* **199**, 424-428.
426

427 GRAHAM, D.A., GERMAN, A., MAWHINNEY, E.A. & GOODALL, E.A. (2003)
428 Antibody responses of naive cattle to two inactivated bovine viral diarrhoea virus
429 vaccines, measured by indirect and blocking ELISAs and virus neutralisation.
430 Veterinary Record **152**, 795-800.
431
432 GRAHAM, D.A., LYNCH, M., COUGHLAN, S., DOHERTY, M.L., O'NEILL, R.,
433 SAMMIN, D. & O'FLAHERTY, J. (2014) Development and review of the voluntary
434 phase of a national BVD eradication programme in Ireland. Veterinary Record **174**,
435 67.
436
437 HANON, J.B., VAN DER STEDE, Y., ANTONISSEN, A., MULLENDER, C., TIGNON,
438 M., VAN DEN BERG, T. & CAIJ, B. (2014) Distinction Between Persistent and
439 Transient Infection in a Bovine Viral Diarrhoea (BVD) Control Programme:
440 Appropriate Interpretation of Real-Time RT-PCR and Antigen-ELISA Test Results.
441 Transboundary and Emerging Diseases **61**, 156-162.
442
443 HOUE, H. (1994) Bovine virus diarrhoea virus: detection of Danish dairy herds with
444 persistently infected animals by means of a screening test of ten young stock.
445 Preventative Veterinary Medicine **19**, 241-248.
446
447 HOUE, H. (1999) Epidemiological features and economical importance of bovine
448 virus diarrhoea virus (BVDV) infections. Veterinary Microbiology **64**, 89–107
449
450 HOUE, H., BAKER, J.C., MAES, R.K., WURYASTUTI, H., WASITO, R., RUEGG,
451 P.L. & LLOYD, J.W. (1995) Prevalence of cattle persistently infected with bovine viral
452 diarrhoea virus in 20 dairy herds in two countries on central Michigan and comparison
453 of prevalence of antibody-positive cattle herds among herds with different infection
454 and vaccination status. Journal of Veterinary Diagnostic Investigation **7**, 321-326.
455
456 HOUE, H., LINDBERG, A. & MOENNIG, V. (2006) Test strategies in bovine viral
457 diarrhoea virus control and eradication campaigns in Europe. Journal of Veterinary
458 Diagnostic Investigation **18**, 427-436.
459
460 HOUE, H. & MEYLING, A. (1991) Prevalence of Bovine Virus Diarrhoea (Bvd) in 19
461 Danish dairy herds and estimation of incidence of infection in early-pregnancy.
462 Preventive Veterinary Medicine **11**, 9–16.
463
464 HULT, L. & LINDBERG, A. (2005) Experiences from BVDV control in Sweden.
465 Preventative Veterinary Medicine **72**, 143–148.
466
467 HUMPHRY, R., BRÜLISAUER, F., MCKENDRICK, I., NETTLETON, P. & GUNN, G.
468 (2012) Prevalence of antibodies to bovine viral diarrhoea virus in bulk tank milk &
469 associated risk factors in Scottish Dairy Herds. Veterinary Record **171**, 445-454.
470
471 KUTA, A., POLAK, M.P., LARSKA, M. & ŻMUDZIŃSKI, J.F. (2013) Monitoring of
472 bovine viral diarrhoea virus (BVDV) infection in Polish dairy herds using bulk tank
473 milk samples. Bulletin of the Veterinary Institute in Pulawy **57**, 149-156.
474
475

476 LANYON, S.R., ANDERSON, M.L., BERGMAN, E. & REICHEL, M.P. (2013)
477 Validation and evaluation of a commercially available ELISA for detection of
478 antibodies specific to bovine viral diarrhoea virus (bovine pestivirus). Australian
479 Veterinary Journal **91**, 51-56.
480
481 LANYON, S.R., HILL, F.I., REICHEL, M.P. & BROWNLIE, J. (2014a) Bovine viral
482 diarrhoea: Pathogenesis and diagnosis. Veterinary Journal **199**, 201-209.
483
484 LANYON, S.R., MCCOY, R., BERGMAN, E. & REICHEL, M.P. (2014b) Milk as a
485 diagnostic sample for a commercially available ELISA to identify bovine viral
486 diarrhoea (BVD) antibodies in dairy herds. Australian Veterinary Journal **92**, 269-
487 273.
488 LAUREYNS, J. (2014) Challenges in the control of bovine viral diarrhoea virus –
489 implications for a Belgian eradication programme, PhD thesis, Ghent University,
490 Belgium.
491
492 LINDBERG, A., BROWNLIE, J., GUNN, G.J., HOUE, H., MOENNIG, V.,
493 SAATKAMP, H.W., SANDVIK, T. & VALLE, P.S. (2006) The control of bovine viral
494 diarrhoea virus in Europe: today and in the future *Revue scientifique et technique*
495 International Office of Epizootics **25**, 961-979.
496
497 MOENNIG, V. & BECHER, P. (2015) Pestivirus control programs: how far have we
498 come and where are we going? *Animal Health Research Reviews* **16**, 83 – 87.
499
500 MOHER, D., LIBERATI, A., TETZLAFF, J. & ALTMAN, D.G., The PRISMA Group
501 (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The
502 PRISMA Statement. *Journal of Clinical Epidemiology* **62**, 1006-1012.
503
504 MUVAVARIRWA, P., MUDENGE, D., MOYO, D. & JAVANGWE, S. (1995) Detection
505 of bovine-virus-diarrhoea-virus antibodies in cattle with an enzyme-linked
506 immunosorbent assay. *Onderstepoort Journal of Veterinary Research* **62**, 241-244.
507
508 NEWCOMBE, R.G. (1998) Interval Estimation for the Difference Between
509 Independent Proportions: Comparison of Eleven Methods. *Statistics in Medicine* **17**,
510 873–890.
511
512 NISKANEN, R. (1993) Relationship between the levels of antibodies to bovine viral
513 diarrhoea virus in bulk tank milk and the prevalence of cows exposed to the virus.
514 *Veterinary Record* **133**, 341-344.
515
516 NISKANEN, R., ALENIUS, S., LARSSON, B. & JACOBSSON, S-O. (1991)
517 Determination of level of antibodies to bovine virus diarrhoea virus (BVDV) in bulk
518 milk tank as a tool in the diagnosis and prophylaxis of BVDV infections in dairy
519 herds. *Archives of Virology* **3**, 245-251.
520
521 OHLSON, A., ALENIUS, S., TRÅVÉN, M. & EMANUELSON, U. (2013) A longitudinal
522 study of the dynamics of bovine corona virus and respiratory syncytial virus
523 infections in dairy herds. *Veterinary Journal* **197**, 395-400.
524

525 PRESI, P., STRUCHEN, R., KNIGHT-JONES, T., SCHOLL, S., & HEIM, D. (2011)
526 Bovine viral diarrhoea (BVD) eradication in Switzerland – Experiences of the first two
527 years. *Preventive Veterinary Medicine* **99**, 112-121.
528

529 R CORE TEAM (2015). R: A language and environment for statistical computing. R
530 Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>.
531

532 RADOSTITS, O.M., GAY, C.C., HINCHCLIFF, K. W. & CONSTABLE, P.D., (2007)
533 *Veterinary Medicine – A textbook of the diseases of cattle, horses, sheep, pigs and*
534 *goats*, 10th Edition, Elsevier.
535

536 RÜFENACHT, J., SCHALLER, P., AUDIGE, L., STRASSER, M. & PETERHANS, E.
537 (2000) Prevalence of cattle infected with bovine viral diarrhoea virus in Switzerland.
538 *Veterinary Record* **147**, 413-417.
539

540 SANDVIK, T., (2004) Progress of control and prevention programs for bovine viral
541 diarrhoea virus in Europe. *Veterinary Clinics Food Animal Practice* **20**, 151-169.
542

543 SANDVIK, T. & KROGSRUD, J. (1995) Evaluation of an antigen-capture ELISA for
544 detection of bovine viral diarrhoea virus in cattle blood samples. *Journal of Veterinary*
545 *Diagnostic Investigation* **7**, 65-71.
546

547 SCHREIBER, P., DUBOIS, F., DRÈZE, F., LACROIX, N., LIMBOURG, B. & COPPE,
548 Ph. (1999) Prevalence of bovine viral diarrhoea virus infection in Belgian white blue
549 cattle in Southern Belgium. *Veterinary Quarterly* **21**, 28-32.
550

551 SCOTTISH GOVERNMENT (2014a) BVD Eradication Programme in
552 Scotland. [http://www.gov.scot/Topics/farmingrural/Agriculture/animal-](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/)
553 [welfare/Diseases/disease/bvd/](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/) . Last accessed March 17, 2015.
554

555 SCOTTISH GOVERNMENT (2014b) Bovine Viral Diarrhoea – Clinical
556 Signs. [http://www.gov.scot/Topics/farmingrural/Agriculture/animal-](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/guidance)
557 [welfare/Diseases/disease/bvd/guidance](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/guidance). Last accessed March 17, 2015.
558

559 SCOTTISH GOVERNMENT (2014c) BVD Eradication Scheme – Mandatory Annual
560 Screening, [http://www.gov.scot/Topics/farmingrural/Agriculture/animal-](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/eradication/Manannualscreening)
561 [welfare/Diseases/disease/bvd/eradication/Manannualscreening](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/eradication/Manannualscreening). Last accessed
562 March 17, 2015.
563

564 SCOTTISH GOVERNMENT (2015a) BVD Eradication Scheme – Approved
565 Laboratories [http://www.gov.scot/Topics/farmingrural/Agriculture/animal-](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/eradication/Manannualscreening/Approvals)
566 [welfare/Diseases/disease/bvd/eradication/Manannualscreening/Approvals](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/eradication/Manannualscreening/Approvals). Last
567 accessed November 4, 2015.
568

569 SCOTTISH GOVERNMENT (2015b) BVD Eradication Scheme – Minimum Testing
570 Methods [http://www.gov.scot/Topics/farmingrural/Agriculture/animal-](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/eradication/Manannualscreening/Minetestmethods)
571 [welfare/Diseases/disease/bvd/eradication/Manannualscreening/Minetestmethods](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/eradication/Manannualscreening/Minetestmethods).
572 Last accessed November 4, 2015.
573

574 SCOTTISH GOVERNMENT (2015c) BVD Eradication Scheme – What’s New
575 <http://www.gov.scot/Topics/farmingrural/Agriculture/animal->
576 [welfare/Diseases/disease/bvd/whatsnew](http://www.gov.scot/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/whatsnew). Last accessed July 25, 2015.
577

578 STÅHL, K., LINDBERG, A., RIVERA, H., ORTIZ, C. & MORENO-LÓPEZ, J. (2008)
579 Self-clearance from BVDV infections – A frequent finding in dairy herds in an
580 endemically infected region in Peru. *Preventive Veterinary Medicine* **83**, 285-296.
581

582 STEVENS, E.T., BROWN, M.S., BURDETT, W.M., BOLTON, M.W., NORDSTROM,
583 S.T. & CHASE, C.C.L. (2011) Efficacy of a Non-adjuvanted, Modified-live Virus
584 Vaccine in Calves with Maternal Antibodies against a Virulent Bovine Viral Diarrhea
585 Virus Type 2a Challenge Seven Months following Vaccination. *The Bovine*
586 *Practitioner* **45**, 23-31.
587

588 TAYLOR, L.F., VAN DONKERSGOOD, J., DUBOVI, E.J., HARLAND, R.J., VAN
589 DEN HURK, J.V., RIBBLE, C.S. & JANZEN, E.D. (1995) The Prevalence of Bovine
590 Viral Diarrhea Virus Infection in a Population of Feedlot Calves in Western Canada.
591 *Canadian Journal of Veterinary Research* **59**, 87-93.
592

593 THERNEAU, T. (2015). A Package for Survival Analysis in S. version 2.38,
594 <http://CRAN.R-project.org/package=survival>.
595

596 THERNEAU, T.M. & GRAMBSCH, P.M. (2000). *Modeling Survival Data: Extending*
597 *the Cox Model*. Springer, New York. ISBN 0-387-98784-3.
598

599 VANDERHEIJDEN, N., DE MOERLOOZE, L., VANDENBERGH, D., CHAPPUIS, G.,
600 RENARD, A. & LECOMTE, C. (1993) Expression of the bovine viral diarrhoea virus
601 Osloss p80 protein: its use as ELISA antigen for cattle serum antibody detection.
602 *Journal of General Virology* **74**, 1427-1431.

603 WEIR, A., HEUER, C., MCDUGALL, S. & VOGES, H. (2013) Use of an enzyme-
604 linked immunosorbent assay for detecting bovine viral diarrhoea virus antibodies in
605 individual cow milk samples. *New Zealand Veterinary Journal* **61**, 305-309.
606

607 ZIMMER, G., SCHOUSTRA, W. & GRAAT, E.A.M. (2002) Predictive values of serum
608 and bulk milk sampling for the presence of persistently infected BVDV carrier in dairy
609 herds. *Research in Veterinary Science* **72**, 75-82.
610

611 ZIMMER, G.M., VAN MAANEN, C., DE GOEY, I., BRINKHOF, J., & WENTINK, G.H.
612 (2004) The effect of maternal antibodies on the detection of bovine virus diarrhoea
613 virus in peripheral blood samples. *Veterinary Microbiology* **100**, 145-149.
614

615 Table 1: Details of the papers from the PRISMA systematic review. The table shows the bulk milk and
 616 blood tests used, the results format, whether or not the PI status of individual animals was reported,
 617 whether the herds/animals tested were vaccinated or not and if the authors think it possible to link the
 618 results to another test or paper. (Abbreviations other than company names, not used previously: Ab –
 619 antibody, Ag – antigen, IPMA – immunoperoxidase monolayer assay, OD – optical density, PP –
 620 percentage positive, VNT – virus neutralisation test, VI – virus isolation)
 621

Paper	Bulk Milk (Test)	Bloods (Test)	Results reported as:	PI status reported	Vaccinated / Unvaccinated	Is link to another paper possible?
Ahmad and others 2014	No	Yes – (Herdcheck IDEXX Antigen Capture Elisa tested against immunochemisrity and RT-PCR)	Comparison of positive results across tests	No	No mention of vaccination.	Difficult to link as no sample values given for the sample to positive ratio
Beaudeau and others 2001a	Yes – (LSI BVD/BD p80 blocking ELISA)	No	Equation relating herd prevalence to percentage inhibition	No	82 of 112 used in equation no history vaccinated	No control values reported and percentage inhibition defined by OD control
Beaudeau and others 2001b	Yes – (Pourquier BVD/MD p80 milk ELISA)	Yes – (VNT on matched sera)	Comparison of OD (%) from ELISA and the VNT titre. Plot of OD (%) vs within-herd prevalence of positive animals.	No	Nothing reported.	As with previous paper, cannot read the percentages off the graphs and no equation given for relationship between OD and within-herd prevalence (unlike first Beadeau paper).
Beaudeau and others 2001c	Yes – (LSI BVD/DB p80 blocking ELISA)	Yes – (VNT and LSI BVD/BD p80 blocking ELISA)	Comparison of percentage inhibition from ELISA of serum vs VNT titre of same sample. Comparison of percentage inhibition from ELISA of bulk milk and VNT of matched serum.	No	No specific reporting of number of vaccinated herds. Makes point that “cut-off values provided by the ROC analysis were insensitive” to vaccination.	So many results that can't read the percentage inhibition from graphs for the fixed titres. Provides cut off of 50% inhibition as +/-.
Booth and others 2013 (using Booth and Brownlie 2011 for additional information)	Yes – (AHVLA indirect ELISA – claimed to be “broadly comparable” to SVANOVA indirect ELISA)	Yes – (Antigen ELISA if >6months, pooled PCR if <6months)	OD ratio, PIs, percentage BM contributors' positive, negative.	Yes	Two farms that didn't vaccinate.	No control values given, no precise calculation. Sensitivity and Specificity given in Booth and others 2011 approximate.
Bosco Cowley and others 2012	Yes – (Svanova ELISA-Ab)	Yes – (Svanova ELISA-Ab on pooled samples)	Only contingency table for relationship between blood and milk results. PP from pooled serum vs % of positive samples plotted. Polynomial relationship.	No	All analysis applied to unvaccinated herds	Polynomial relationship between PP and % positive samples not published. Need full results rather than contingency table.
Cornish and others 2005	No	Yes – (Syracuse Bioanalytical Inc. Ag ELISA with VI and RT-PCR to confirm)	Table of PI animals with results from VI, RT-PCR and ELISA with VN titre.	Yes	All dams of calves tested were vaccinated.	Could compare with similar tests on calves.
Diéguez and others 2008	Yes – (Pourquier BVD/MD p80 blocking ELISA)	Yes – (Pourquier BVD/MD p80 blocking ELISA & IDEXX ELISA antigen serum plus BVD test kit)	Plot of herd seroprevalence vs % inhibition in BTM.	Tested for but results not tabulated or plotted.	Yes	No explicit results given, just cut-offs. Could compare with other papers using the same tests if we could get the complete results.
Eiras and others 2012	Yes – (Pourquier BVD/MD/BD p80, Civtest bovis BVC p80, IDEXX HerdChek)	Yes – (Pourquier BVD/MD/BD p80 & IDEXX antigen serum kit)	Threshold of transformed optical density values of all four bulk milk tests compared against thresholds	No	24% of herds have been vaccinated 78/325.	No control values given and some herds vaccinated. If all sample results provided then a relationship between the tests might be established.

	BVDV, SVANOVA (Svanovir BVDV-Ab)		established from blood tests.			
Foddai and others 2015	Yes – (Danish blocking ELISA (Bitsch and others 1997) & SVANOVA BVDV-Ab ELISA)	Yes – (Danish blocking ELISA (Bitsch and others 1997) & SVANOVA BVDV-Ab ELISA)	Graphs of PP vs blocking % for both milks and bloods.	No	No mention of vaccination.	Could compare to others using the same test. Numbers little difficult to read accurately from plots.
Graham and others 2003	Yes – (SVANOVA indirect BVDV-Ab ELISA & LSI blocking ELISA NS2-3)	Yes – (SVANOVA indirect BVDV-Ab ELISA & LSI blocking ELISA NS2-3 & VNT described in Graham and others 1997)	Mean results of tests from groups before and after vaccination. Plots (with best fit lines) of Indirect ELISA COD against VN titre and % inhibition of blocking ELISA	No	All animals vaccinated during testing	If the lines of best had been published they could be used to compare the results of Indirect ELISA COD with either VN titre or blocking ELISA – if other animals have used the same vaccines.
Hanon and others 2014	No	Yes – (ADIAGENE, Adiavet BVDv RRT-PCR test & IDEXX BVDV Ag/serum plus ELISA)	Predicted probability of PI animal based on the C_i value from the RRT-PCR.	Yes	No mention of vaccination.	If the equation or similar for the model had been reported then could find the probability of PI from any other study using the same test.
Houe 1994	Yes – (Indirect ELISA)	Yes – (Meyling's own test)	Virus positive ~ ab positive ~ antibody titer in BM (related to OD)	Yes	Unvaccinated	There are no explicit details provided on the indirect ELISA used but could link with Houe and Meyling 1991 as it too uses Meyling's test.
Houe and others 1995	No	Yes – (IPMA (Meyling 1984) & VNT	Tabulated values % of antibody positive vs mean/median antibody titer results.	Yes	Mixture of vaccination history.	Could relate to other herds using those tests with the same vaccination history.
Humphry and others 2012	Yes – (SVANOVA indirect ELISA (percentage positive), the test from Drew and others 1999 and SVANOVA indirect ELISA (corrected OD))	No	percentage positive OD Corrected OD All linked to Swedish classes	No	Unvaccinated	Could possibly link this to other papers using the same tests.
Kuta and others 2013	Yes – (SVANOVA BVDV-Ab ELISA and SVANOVA BVDV-Ab ELISA confirmation format)	No	Correlation of COD values from initial ELISA and PP values from confirmatory ELISA for 28 herds that were double tested.	Yes	Unvaccinated	Could be used to compare COD with PP from SVANOVA ELISA tests – providing the confirmation test is essentially the same as original.
Lanyon and others 2013	No	Yes – (IDEXX BVDV Total Ab and VNT Titre	Regression equation linking VNT titre result and sample to positive ratio of ELISA	No	Unvaccinated	Could be used to compare other VNT Titre results and ELISA results using the same test.
Lanyon and others 2014b	Yes – (IDEXX BVDV Total Ab Test)	Yes – (IDEXX BVDV Total Ab Test and RT-PCR)	Percentage of herds testing positive / negative for both blood and milk tests. Relationship between milk and blood sample to positive ratios also presented.	No	No mention of vaccination	Relationship of bulk milk to serum results could provide link if the same test has been used.
Muvavarirwa and others 1995	No	Yes – (ELISA (as described by Howard and others 1985) & serum neutralisation test)	Comparison of results from ELISA and values of SN titre	No	No mention of vaccination	Could compare with results from the same test or with SN titre.

Niskanen 1993	Yes – (SVANOVA indirect ELISA)	Yes – (SVANOVA indirect ELISA)	Absorbance value ~ percentage prev of ab positive lactating cows in herds.	No	Unvaccinated	Should link to any other SVANOVA indirect ELISA (control values given)
Niskanen and others 1991	Yes – (SVANOVA indirect ELISA)	Yes – (SVANOVA indirect ELISA)	# ab positive ~ absorbance values of bulk milk.	PIs were removed	Unvaccinated	Should link to any other SVANOVA indirect ELISA (control values given). PIs removed in between two of the yearly results.
Rüfenacht and others 2000	Yes – (Authors' own ELISA)	Yes – (Antigen capture ELISA (Strasser) and RT-PCR (Wirz))	Herd abpositive prevalence ~ Antigen ELISA positive (1 st and 2 nd tests) /ab ELISA positive /RT-PCR positive	Yes	Unvaccinated	Test is author created so very difficult to link to a more widely used test.
Sandvik and Krogsrud 1995	No	Yes – (SVANOVA ELISA ab test, Moredun antigen test)	Tabulated values of antibody OD vs antigen OD.	No	Unvaccinated	Could possibly be used to create link between SVANOVA test and antigen results.
Schreiber and others 1999	No	Yes – (Specific test unclear)	Table of number of animals in herd with number of seropositive and PI per herd	Yes	37% vaccinated but type of vaccine produces few to none antibodies	Can link between other herds with PI animals although specific test used unclear.
Ståhl and others 2008	Yes- (SVANOVA indirect ab ELISA)	Yes – (IDEXX BVDVB Ag/Serum)	Table of number of positive spot blood tests and mean OD for the bulk milk tank.	Yes	7 out of 55 herds vaccinated	Could create link between bulk milk and number of positive young stock if same tests used.
Taylor and others 1995	No	Yes – (Bespoke Ab ELISA with VNT and PCR)	Table of each pen with titre, ELISA, VN and PCR results with number of animals tested per pen.	Yes	No specific mention of vaccination for BVDV.	Difficult to compare as the ELISA created was bespoke.
Vanderheijden and others 1993	No	Yes – (Would appear to be bespoke p80 ELISA test & SN)	Table comparing SN titre vs p80 results.	Yes	2 tests specifically designated as vaccinated or unvaccinated.	Could compare with other results from same test.
Weir and others 2013	Yes – (IDEXX ELISA)	Yes – (IDEXX ELISA)	Plot of milk S/P ratio vs serum S/P ratio with regression line.	No	Unvaccinated	Could be used to compare results from previous tests if regression line had been provided.
Zimmer and others 2002	Yes – (Ceditest BVD blocking ELISA)	Yes – (Ceditest BVD blocking ELISA)	Proportion of herd ab+ vs status of herd from btm	Yes	No mention of vaccination.	Could be used to compare with btm results using the same test.
Zimmer and others 2004	No	Yes – (Antibody test via VNT, Antigen test via VI, Synbiotics ELISA and RT-PCR)	Table showing results for each calf tested – titre vs antigen test and RT-PCR and serological titre.	Yes	No mention of vaccination	Useful comparison with other studies on calves and using the same tests.

622

623

624

625 Table 2: The number of papers still available to the authors after each step of the PRISMA
 626 systematics review

Step of PRISMA	1- Web of Science	2 - Search Terms	3 - Filter Results	5 - Remove No Abstract	6 - Remove Conference Papers	7 - Collect Papers	8 - Screening Questions
Number of Papers remaining following that step	> 10 ⁹	654	508	386	352	259	28 electronic and 2 non-electronic.

627

628 Figure 1: Time taken (days) from an initial antibody test to retesting for antigen, separated by
629 initial antibody test type (milk and blood) and result (negative/not-negative). (Red, solid: initial
630 negative blood test. Green, dotted: initial not-negative blood test. Blue, dashed: initial negative
631 milk test. Purple, long-dashed: initial not-negative milk test.) Data is taken from the Scottish
632 BVDV eradication scheme 2013 – 2014.

633
634 Figure 2: Frequency distribution of percentage positivity results from 220 BVDV bulk milk tests
635 from a survey of 220 Scottish Farms. Previously published in Humphry and others 2012.

636
637 Figure 3: Number of seropositive animals from 10 young stock sampled in a survey of 274
638 Scottish herds. Previously published in Brülisauer and others 2010.

639
640 Figure 4: Plot of the blocking percentage of antibody reaction in a bulk milk tank against days
641 after the removal of the last persistently infected animal. A Linear regression line is also shown.
642 Reproduced with permission from Houe 1999.

643