

Scotland's Rural College

The importance of the gestation period for welfare of lambs: maternal stressors and lamb vigour and wellbeing

Rooke, JA; Arnott, G; Dwyer, CM; Rutherford, KMD

Published in:
Journal of Agricultural Science

DOI:
[10.1017/S002185961400077X](https://doi.org/10.1017/S002185961400077X)

First published: 01/01/2015

Document Version
Peer reviewed version

[Link to publication](#)

Citation for published version (APA):

Rooke, JA., Arnott, G., Dwyer, CM., & Rutherford, KMD. (2015). The importance of the gestation period for welfare of lambs: maternal stressors and lamb vigour and wellbeing. *Journal of Agricultural Science*, 153(3), 497 - 519. Advance online publication. <https://doi.org/10.1017/S002185961400077X>

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.

The importance of the gestation period for welfare of lambs : maternal stressors and lamb vigour and well-being.

J. A ROOKE^{1*}, G. ARNOTT^{2,3}, C. M. DWYER², AND K. M. D. RUTHERFORD²

¹ *Beef and Sheep Research Centre, Future Farming Systems, SRUC, West Mains Road, Edinburgh EH9 3JG, UK*

² *Animal Behaviour and Welfare, Animal and Veterinary Sciences Research Group, SRUC, West Mains Road, Edinburgh EH9 3JG, UK*

³ *School of Biological Sciences, Queen's University Belfast, Medical Biology Centre, 97 Lisburn Road, Belfast BT9 7BL, UK*

Short title: Prenatal stress in sheep and lamb well-being.

* Correspondence: john.rooke@sruc.ac.uk

The importance of the gestation period for welfare of lambs : maternal stressors and lamb vigour and well-being.

Short title: Prenatal stress in sheep and lamb well-being.

1 SUMMARY

2

3 The prenatal period is of critical importance in defining how individuals respond to their
4 environment throughout life. Stress experienced by pregnant females has been shown to
5 have detrimental effects on offspring behaviour, health and productivity. The sheep has been
6 extensively used as a model species to inform human studies but the consequences of
7 prenatal stresses imposed on the ewe for the lamb in the farmed environment have received
8 much less attention. The stressors that pregnant ewes are most frequently exposed to
9 include sub-optimal nutrition and stressors related to housing, husbandry and environment
10 which may be acute or chronic. A systematic review of the literature was adopted to identify
11 material which had production relevant maternal stressors and lamb outcomes. This review
12 focussed upon the lamb up to weaning around the age of 100 days. Results of this review
13 clearly demonstrate that stressors imposed upon the ewe have implications for offspring
14 welfare and performance. Maternal under-nutrition imposed in the last third of pregnancy
15 consistently impaired lamb birth-weight and subsequent vigour and performance; earlier
16 under-nutrition had a more variable effect on performance. Feeding the ewe above
17 requirements did not have positive effects on lamb performance and welfare. Social and
18 husbandry stressors such as transport, shearing, mixing and physiological treatments
19 designed to mimic acute stress which would be considered disadvantageous for the ewe had
20 positive or neutral effects for the lamb, highlighting a potential conflict between the welfare of
21 the ewe and her lamb. This review also identified considerable gaps in knowledge
22 particularly in respect of the impact of disease upon the ewe during pregnancy and
23 interactions between different stressors and the response of ewe and lamb.

24

25 INTRODUCTION

26

27 The long term consequences of changes in the foetal environment have been well-
28 recognised since the first reports (Barker *et al.* 1989) describing epidemiological data linking
29 birth weight and later health in humans. In other epidemiological studies, the children born to
30 mothers who were pregnant during the Dutch famine in 1944-1945 experience increased
31 incidence of inter alia, type II diabetes and cardio-vascular disease (Lumey *et al.* 2011).
32 Other negative human health outcomes have also been seen following maternal stress
33 during pregnancy (e.g. King *et al.* 2012). These adverse effects are generally classified
34 under the developmental origins of health and disease hypothesis (Gluckman & Hanson
35 2004) and are likely mediated by epigenetic, non-Mendelian inheritance (Ford & Long 2012).
36 Amongst the variety of animal models used to investigate underlying mechanisms, the sheep
37 has proved popular since it is similar to the human in respect of maternal and foetal sizes,
38 organ development and maturity at birth (Luther *et al.* 2005). To date, however, less
39 emphasis has been placed upon the consequences of disturbances to the foetal
40 environment for the health and welfare of the lamb within the bounds of the animal
41 production environment.

42 In a parallel review on cattle, Arnott *et al.* (2012) identified a wide variety of stressors
43 the dam could be exposed to during gestation and which may perturb the uterine
44 environment with adverse consequences for the subsequent welfare and health of the
45 offspring. The stressors identified included under-nutrition (UN), social stress imposed by
46 management practices such as stocking density, acute stress from handling and transport
47 and thermal stress by being maintained outside the thermo-neutral zone. Arnott *et al.* (2012)
48 employed the systematic review process advocated by Sargeant *et al.* (2006) to minimize
49 systematic and random errors in study selection. The object of the current review was to
50 apply the approach of Arnott *et al.* (2012) to identify stressors applied to the ewe during
51 gestation which were practically relevant and to identify the consequences for the welfare of
52 the lamb. Because of the large number of studies identified and the variety of stressors
53 imposed and lamb outcomes reported, the review process was divided into two parts dealing
54 with the lamb up to weaning (current review) and from weaning into adulthood.

55

56 MATERIALS AND METHODS

57

58 Comprehensive details of the methodologies employed are given in Arnott *et al.* (2012).

59

60 Searches

61 The online database 'ISI Web of Knowledge' was used to search the literature. Within Web
62 of Knowledge the following databases were searched simultaneously: ISI Web of Science
63 (1970-present), MEDLINE (1950-present) and BIOSIS Previews (1969-present). The search
64 terms used were designed to combine words relating to sheep and to prenatal stress. The
65 final search string was as follows: (prenatal or perinatal or maternal or fetal or foetal or
66 gestation*) and (stress or programm* or nutrition*) and (sheep or ovine or ewe*). The initial
67 search was carried out in November 2009 and regularly updated until the end of December
68 2011. Recovery of other relevant articles was as described by Arnott *et al.* (2012) and
69 included an online search of relevant journals, and additions recommended by experts in the
70 field of ovine early life research.

71

72 Search results and classification

73

74 Following removal of duplicates, the initial search yielded 3069 publications. The papers,
75 and abstracts if available, were imported into a bibliographic database (Reference Manager,
76 version 11) for manipulation. Within the database, publications were initially screened for
77 relevance. This involved reading the title and removing any obviously irrelevant references
78 (2388 in total). The remaining publications were examined in more detail, using a
79 combination of the title and abstract. Those where maternal nutrition was manipulated or
80 where a stressor was applied to the dam and where offspring outcomes were measured
81 were retained for further examination.

82

83 Quality assessment

84

85 As recommended by Sargeant *et al.* (2006), a quality assessment of studies was made.
86 References were selected using the following criteria (Arnott *et al.* 2012): treatment
87 intervention adequately described; inclusion of a suitable control; use of a large enough
88 sample size; appropriate statistical methods; avoidance of data repetition (e.g. where
89 components of a single study are reported in several papers); exclusion of conference
90 abstracts / proceedings. Studies remaining at this point formed the raw material for detailed
91 review.

92

93 Organisation of review process

94

95 The remaining studies were first classified into the following categories according to
96 outcomes measured in offspring: welfare; birth-weight / growth; reproduction; others not
97 encompassed by the above groups. Based on the welfare-related aims of this review, and

98 the relatively large number of references, a decision was taken that the first two categories
99 (welfare outcomes and birth-weight / growth) would form the raw material for the review.
100 Within these two categories, a more detailed inspection of the offspring outcomes yielded
101 the following categories: behavioural changes; adverse effects on body weight (LW) and
102 live-weight gain (LWG) at key stages of life; survival and changes in physiological state such
103 as the ability to thermo-regulate, immunoglobulin G (IgG) status of the neonate and changes
104 in the hypothalamic-pituitary-adrenal (HPA) axis. The most commonly reported outcomes,
105 not surprisingly, were birth-weight, weaning-weight and LWG. Respectively there were 108,
106 60 and 43 such reports. Detailed analysis also revealed a different pattern of outcomes
107 depending on the age of the lamb. Pre-weaning (< 3 months old) studies focussed largely
108 upon outcomes relevant to neonatal survival including the ability to thermo-regulate;
109 behavioural indicators of both lamb vigour and ewe-lamb bonding. In contrast, post-weaning
110 studies (>3 months of age) tended to focus on behavioural responses in more detail,
111 assessing aspects of emotional reactivity and response to stress and including quantifying
112 physiological changes. For convenience, studies where behavioural responses such as
113 emotional reactivity were reported for lambs of less than 3 months of age, were grouped with
114 other behavioural studies.

115 The next step in the review process was to classify studies according to the prenatal
116 treatment applied. Initially, the nine hazard categories identified by Arnott *et al.* (2012) were
117 applied: social environment, housing system, nutrition and feeding method, husbandry
118 practices, environmental parameters, infectious environment and maternal health, artificial
119 challenges (involving exogenous manipulation of HPA axis function). However, a more
120 detailed inspection of the studies revealed that a nutritional treatment (70% of studies) was
121 the most frequent hazard imposed while either a behavioural (social environment; husbandry
122 practice, e.g. shearing) or physiological (artificial challenge) stress hazard made up the
123 majority (26%) of the remaining studies.

124 Therefore, given the large number of studies to be considered, it was decided to
125 address the outcomes in two sections depending upon the age (pre- or post-weaning) of the
126 lamb. Within each life-stage section, the effects of prenatal treatments on welfare relevant
127 outcomes are discussed using the two main hazard types stated above (nutrition and stress)
128 whilst noting the inevitable overlaps that occur. This review will examine pre-weaning
129 outcomes while post-weaning outcomes will be the subject of a companion review.

130 RESULTS

131 Nutrition

132 In the context of the review, UN is defined as a supply of energy and global nutrients to the
133 ewe below that required for the sum of maintenance of the ewe and for pregnancy.
134 Conversely, over-nutrition (ON) is where energy is supplied in excess of requirements. In
135 addition, there are studies where energy requirements are met but a specific nutrient is
136 supplied either in excess of, or below requirement.

137 Sheep production systems are frequently seasonal in terms of both breeding cycle
138 and herbage availability and often this results in mobilisation of maternal adipose tissue
139 when herbage availability is low. Therefore there may be a period of UN particularly in the
140 first 100 days of the 147 day gestation when supplementary feeding is not normally
141 practiced. Depending on the individual production system, ewes may be housed in late
142 gestation and fed to meet requirements for lamb growth or breeding timed so that sufficient
143 herbage is available to meet requirements. Therefore, in practice, the effects of UN are likely
144 to be of greater importance during the first 100 days of gestation. UN during late gestation is
145 most likely to occur when grass growth is inadequate or access to herbage prevented, for
146 example, by snowfall. Deficiency or excess of a specific nutrient may occur at anytime where
147 specific feeds are used or where soil micro-nutrient status induces herbage nutrient
148 imbalance.

149 Under-nutrition: birth-weight

150 Table 1 summarizes UN studies with more details of individual studies given in
151 Appendix Table S1. There were differences in the effect of UN on birth-weight depending
152 when the ewe was under-nourished. Studies can be split into two categories; first where UN
153 was applied only in the first and second thirds of pregnancy (gestation day (GD)1 to GD100
154 of the 147 day ovine pregnancy; early / mid gestation); and secondly where UN continued or
155 began after GD100 (late gestation). In late gestation (Banchemo *et al.* 2009; Corner *et al.*
156 2008, 2010a; Dwyer *et al.* 2003; Hammer *et al.* 2011; Holst *et al.* 1986; Husted *et al.* 2007;
157 Khalaf *et al.* 1979; Tygesen *et al.* 2008), regardless of the extent of UN, birth-weight was
158 reduced.

159 Where UN ended before GD100 (early/mid gestation), more variable responses were
160 observed. Studies were categorised according to the extent of UN (relative to maintenance
161 requirement): severe, <0.4; moderate, between 0.4 and 0.8; mild, between 0.8 and 1.0.
162 Where authors stated a level of UN this was adopted, otherwise the extent of UN was
163 estimated from either food intake and / or ewe LW change. The most severe UN challenge
164 before GD100 was imposed by Vincent *et al.* (1985), who restricted ewes to 0.15 of
165 requirement between GD0 and GD60. Birth-weight was reduced from 4.3 to 3.6 kg and there
166 was an accompanying increase in mortality (from 6 to 42 %), with the lambs most prejudiced

167 by low birth-weight not surviving. Holst *et al.* (1986) imposed moderate UN from mating to
168 GD103 and replicated the experiment over three years. There were no decreases in birth-
169 weight or increases in mortality; in two of three years, birth-weight was actually increased in
170 lambs born to UN ewes. A series of studies, (UN from 60 days before mating until GD30
171 (Hernandez *et al.* 2009); UN between GD30 and GD50 of pregnancy (Kenyon *et al.* 2011);
172 UN between GD50 and GD100 (Kenyon *et al.* 2002b; Kleemann *et al.* 1993) imposed
173 moderate UN without effect on birth-weight.

174 In other studies, reduced birth-weight was observed but in specific circumstances.
175 (Munoz *et al.* 2008b, 2009) applied mild UN between GD40 and GD90 of pregnancy to 1-
176 year-old, 2-year-old and adult ewes. There were ewe-age dependant effects on birth-weight;
177 in both 1- and 2-year-old ewes, birth-weight was reduced by UN whereas in adult ewes (as
178 also noted by Holst *et al.* (1986) above) birth-weight was increased by UN. Oldham *et al.*
179 (2011) in a large-scale experiment across two sites and years imposed moderate UN
180 between GD0 and GD100 and recorded a modest decrease in birth-weight on one of the two
181 sites. Rooke *et al.* (2010) imposed moderate UN between GD1 and GD90 and found that
182 whereas in Scottish Blackface ewes, lamb birth-weight was not changed by UN, lambs born
183 to UN Suffolk ewes had reduced birth-weight. In a similar study, employing moderate UN
184 between GD28 and GD100, Burt *et al.* (2007) found that whereas lambs borne to UN ewes
185 from a harsh range-land environment had similar birth-weights to control ewes, birth-weight
186 was reduced in UN ewes adapted to a “sedentary well-nourished” environment. Therefore
187 genotype may influence partition of nutrients between dam and foetus

188 In summary and in contrast to UN in late gestation, UN before GD100 reduced birth-
189 weight in only four of ten studies. Where reductions in birth-weight were observed due to UN
190 before GD100 these may have resulted from differences in ewe breed (Rooke *et al.* 2010);
191 age (Munoz *et al.* 2008b, 2009) or environment (Holst *et al.* 1986; Oldham *et al.* 2011). A
192 possible explanation for the variation in birth-weight response to early/mid UN is that foetal
193 weight may be reduced by UN but compensatory growth during late pregnancy when
194 nutrient supply was normalised allowed birth-weight to return to values not different from
195 control-fed animals (Luther *et al.* 2007) in some but not all studies.

196 Under nutrition: mortality

197 In situations where gestational UN reduces birth-weight, then associated increases in
198 mortality are likely given the well-established link between birth-weight and mortality (Wu *et al.*
199 *et al.* 2006). Indeed lamb mortality was increased in most studies (Banchero *et al.* 2009; Khalaf
200 *et al.* 1979; Munoz *et al.* 2009; Vincent *et al.* 1985) where birth-weight was reduced.
201 However, there are contradictory reports (Holst *et al.* 1986; Munoz *et al.* 2008b). In these

202 studies, where UN during early pregnancy increased birth-weight, lamb survival was
203 reduced.

204 Under-nutrition: maternal and lamb behaviours

205 An important mechanism for lamb survival is successful establishment of the ewe-lamb
206 bond. Impairment of bonding can arise both from poorer expression of the appropriate
207 maternal behaviours and/or reduced lamb vigour (often assessed by the ability to progress
208 through the necessary behaviours, e.g. standing, udder seeking, successful sucking) and
209 their interactive effects. Dwyer *et al.* (2003) in a detailed behavioural study found that while
210 UN throughout gestation did not affect lamb behavioural progress, the ewe-lamb bond was
211 less well-established as a result of UN: at 3 days after birth, scores for maternal attachment
212 and lamb behaviour were inferior in UN lambs compared to controls.

213 Other studies have examined effects of UN on specific aspects of ewe and lamb
214 behaviour. Munoz *et al.* (2008b, 2009) reported differential effects depending upon the age
215 of the ewe and whether UN was imposed during early (GD1 to GD40) or mid (GD40 to
216 GD90) pregnancy. There were no effects of early pregnancy UN in adult ewes but
217 primiparous, 1-year-old and therefore inexperienced UN ewes showed an increased
218 incidence of rejective behaviours. Lambs born after mid pregnancy UN of both adult and 1-
219 year-old ewes progressed more slowly through the repertoire of lamb behaviours than
220 controls. Corner *et al.* (2010a) undernourished ewes between GD70 and term by restricting
221 pasture allowance (2 v 4 cm height). UN ewes produced fewer low-pitched bleats than
222 controls whilst their lambs vocalised more. This was interpreted as a reduced expression of
223 maternal care and increased expression of lamb need. Finally, ewes of divergent breeds
224 (Blackface and Suffolk) were undernourished between GD1 and GD90 (Rooke *et al.* 2010).
225 Differences in expression of behaviour were observed (Dwyer *et al.* 2010a,b). Lambs from
226 UN Suffolk but not UN Blackface ewes tended to take longer to progress through
227 behavioural milestones. Lambs from UN dams of both breeds took longer to suck from their
228 mothers. UN ewes of both breeds displayed poorer maternal care as they were more likely
229 to prevent their lambs from sucking and less likely to approach their lambs and interact with
230 them.

231 Thus there is evidence that UN adversely affects establishment of the ewe-lamb
232 bond. The parity and thus experience of the ewe may be an important factor as poorer
233 establishment effects were found most frequently in primiparous ewes (Dwyer *et al.* 2003;
234 Munoz *et al.* 2009; Rooke *et al.* 2010).

235 Under nutrition: passive immune transfer and thermoregulation

236 Absorption of nutrients from colostrum during the first 24 h of life has a major influence on
237 lamb survival. The amounts of nutrients absorbed are dependant on the amount and
238 composition of colostrum produced by the ewe, co-operation between the ewe and lamb in
239 facilitating colostrum intake, ability of the lamb to seek the udder and consume colostrum,
240 and appropriate development of the absorptive capacity of the intestines of the lamb. The
241 amount of immunoglobulin G (IgG) present in the lamb's circulation, typically at 24 h of age,
242 and the ability of the lamb to thermo-regulate have been used as indices of adequate
243 colostrum intake. The effects of UN on these variables are inconsistent. Khalaf *et al.* (1979)
244 reported no difference in lamb plasma IgG concentration at 24 h of age as a result of late UN
245 in a study where lamb birth-weight and survival to 1 month of age were reduced. Munoz *et al.*
246 *al.* (2008b, 2009) reported increased zinc sulphate turbidity (an index of IgG absorption) as a
247 result of UN during early pregnancy in multiparous ewes but no differences in 1- and 2-year-
248 old ewes; the increase in IgG was associated with increased birth-weight compared to
249 controls. Finally, Hammer *et al.* (2011) reported two experiments (Meyer *et al.* 2010;
250 Swanson *et al.* 2008) with ewe UN imposed from GD50 to term; increased IgG
251 concentrations at 24 h of age in lambs from UN ewes were associated with decreases in
252 birth-weight. The only report of UN on the ability of the lamb to thermoregulate (Rooke *et al.*
253 2010) found no differences in lamb rectal temperatures. The increases in lamb plasma IgG
254 reported by Munoz *et al.* (2008b) and particularly (Hammer *et al.* 2011) are somewhat
255 counter-intuitive but since neither colostrum composition, intake or lamb plasma volume
256 were measured in these studies it is not possible to comment on mechanisms. However, the
257 above studies overall do suggest that the ability of the lamb to acquire IgG can be influenced
258 by maternal UN in the absence of reduced birth-weight.

259 Under nutrition: weaning weights and weight gain to weaning

260 Consistent with birth-weight, differences in the rate of growth to weaning as a result of
261 pregnancy UN depended upon when during pregnancy UN was imposed. When UN
262 occurred before GD100 (Munoz *et al.* 2008b, 2009; Oldham *et al.* 2011; Rooke *et al.* 2010;
263 Thompson *et al.* 2011) there were no effects on weaning LW or LWG. However, others
264 (Husted *et al.* 2007; Neville *et al.* 2010; Tygesen *et al.* 2008) found that weaning LW was
265 reduced when UN occurred after GD100.

266 Over-nutrition

267 Although the seasonality of sheep production means that UN is more likely to be
268 encountered than ON, it is necessary to consider whether benefits in welfare outcomes are
269 possible if requirements for maternal body maintenance and the normal growth of the
270 products of conception are exceeded. An ovine model (Wallace *et al.* 2005a) for the

271 consequences of teenage pregnancy in the human is relevant. Pregnancies were
272 established in adolescent (8 month old Dorset Horn x Greyface) ewes by embryo transfer.
273 When these ewes were offered a high quality diet ad libitum, they consumed approximately
274 2-times energy requirements (Wallace *et al.* 2005a). These ON adolescent ewes partitioned
275 nutrients to maternal growth at the expense of foetal growth such that lamb birth-weight was
276 reduced by 30%. This reduction in birth-weight is more severe than that observed with UN
277 (Wallace *et al.* 2010). Further this effect was not observed with adult ewes (Wallace *et al.*
278 2005b). A number of research groups have examined the consequences of ON in a more
279 practical setting (see Table 2 and Appendix Table S1 for details).

280 Munoz *et al.* (2008b, 2009) applied the same ON intervention to 1-year-old, 2-year-
281 old and adult ewes. ON was applied at 2-times requirements between GD1 to GD39 (similar
282 to Wallace *et al.* (2010) and then at 1.4-times requirements between GD40 and GD90. The
283 ON imposed was therefore less substantial and for a shorter time than the Wallace model. In
284 1-year-old ewes (Munoz *et al.* 2009), ON between GD1 and GD39 tended to increase lamb
285 birth-weight, whilst later ON had no effect. Lamb mortality, weaning LW and IgG status were
286 not influenced by ON. However, ON between GD40 and GD90 resulted in poorer
287 behavioural progression of lambs from birth to sucking; these lambs required more
288 assistance at lambing than their UN or control counterparts. ON during early pregnancy in 2-
289 year-old ewes (Munoz *et al.* 2009) increased birth-weight whilst ON during mid-pregnancy
290 had no effect. In common with 1-year-old ewes, this increased birth-weight was associated
291 with an increase in dystocia. In adult ewes (Munoz *et al.* 2008b), ON between GD1 and
292 GD39 resulted in increased birth-weight with no penalty of increased dystocia. Similar to 1-
293 year-old ewes, ON between GD40 and GD90 impaired behavioural progression from birth to
294 sucking. Therefore any benefits in birth-weight from ON tended to be accompanied by
295 adverse effects on dystocia and lamb vigour.

296 In studies from North Dakota State University, adolescent ewes were fed 1.4 times
297 requirement from GD40 to term. In one experiment, birth-weight was reduced in response to
298 ewe ON but there was no difference in LWG to weaning (Neville *et al.* 2010) and ewe ON
299 increased lamb morbidity and mortality and reduced lamb IgG concentrations (Hammer *et al.*
300 2011). In a subsequent experiment of similar design, ewe ON had no effect on lamb birth-
301 weight or LWG (Meyer *et al.* 2010), lamb morbidity or mortality but again lamb plasma IgG
302 decreased (Hammer *et al.* 2011).

303 In a multi-year, two site study, Merino ewes were allocated to a range of herbage
304 allowances (800 to >3000 kg herbage DM / ha) from GD100 to term and maintained on
305 these pastures until weaning (Ferguson *et al.* 2011). Thus prenatal effects may be

306 confounded by differing ewe intakes post-lambing. It was difficult to ascertain the impact of
307 herbage allowance on ewe nutritional status as ewe condition scores were not reported.
308 However, the allowances offered cover the range from UN to meeting requirement at the
309 lower allowances to ON at the highest allowance. Responses in birth-weight and survival to
310 48 h were only found at the two lowest herbage allowances (representing either UN or
311 maintenance; 800 and 1100 kg DM/ ha; Oldham *et al.* 2011) above which there were no
312 differences. Therefore there was no evidence for any responses to ON.

313 The effects of differing pasture allowances on ewe and lamb performance have been
314 studied in New Zealand. Again it is difficult to make judgments on absolute nutritional status
315 where herbage allowance was deemed at a 'normal' (Everett-Hincks *et al.* 2005) or low /
316 maintenance level (Kenyon *et al.* 2009, 2011; Morris *et al.* 2005). Overall, consistent positive
317 responses were not found in studies classified as ON. Everett-Hincks *et al.* (2005) found no
318 differences in behavioural progress of lambs to allowances of 1600 and 2000 kg DM/ha
319 between GD64 and term. MMorris *et al.* (2005) found no responses in birth-weight to
320 treatments designed to increase adolescent ewe conceptus-free LWG and fed from GD13 to
321 term, although weaning LW were increased. On the same group of animals (Corner *et al.*
322 2006a), lambs from ON treatments bleated more frequently than controls with a
323 corresponding increase in ewe low-pitched bleating frequency, possibly indicating improved
324 ewe-lamb bonding. Kenyon *et al.* (2009) offered maintenance or ad libitum herbage from
325 GD21 to term and found an increase in birth-weight of lambs from ad libitum fed ewes; this
326 difference was maintained until weaning but there was no effect on lamb survival. However,
327 when these ewe lambs produced by Kenyon *et al.* (2009) became mothers themselves (van
328 der Linden *et al.* 2010), lambs borne to ewes whose dams had been fed ad libitum were of
329 lower birth-weight than those born to lambs derived from maintenance-fed ewes: that is, any
330 benefits in increased birth-weight in one generation were antagonistic to the subsequent
331 generation. Finally, Kenyon *et al.* (2011) compared maintenance and ad libitum allowances
332 of pasture in either early (GD30 to GD50) or mid/late gestation (GD50 to term) and found no
333 advantage to the ad libitum herbage allowance.

334 Overall, it can be seen that there is no clear evidence indicative of improved lamb
335 welfare to feeding ewes during pregnancy more than that required for ewe maintenance and
336 growth of the products of conception and in some cases, there may disadvantages such as
337 increased dystocia, reduced lamb vigour and lamb survival.

338

339 Specific nutrients

340 There are three areas where the provision of specific nutrients in the maternal diet may
341 influence lamb welfare: (a) deficiency / depletion; (b) toxicity; and (c) where supply of the
342 nutrient is above requirement but below toxicity and may give a positive outcome. The
343 likelihood of an effect will depend on the extent of maternal reserves; the severity and length
344 of nutrient under/over supply and additional factors including the form in which the nutrient is
345 supplied and the potential for antagonistic effects with other nutrients (present both in deficit
346 or excess). Rooke *et al.* (2008a) reviewed this area and found relevant information mainly for
347 micro-nutrients because clinical or sub-clinical deficiencies arise in practice. The micro-
348 nutrients identified by Rooke *et al.* (2008a) which passed the stricter criteria for inclusion in
349 the systematic review process were the trace elements cobalt (Co), iodine (I) and selenium
350 (Se) and the fat soluble vitamin, α -tocopherol (vitamin E). Rooke *et al.* (2008a) also identified
351 a cohort of studies in which the fatty acid (FA) composition of the maternal diet was
352 manipulated and implications for post-natal lamb end-points investigated. It is the intention of
353 this section to summarise the relevant information from Rooke *et al.* (2008a) and to add new
354 information (see Table 3 and Appendix Table S2).

355 Cobalt

356 Cobalt is required for synthesis of vitamin B12 within the rumen; the Co status of sheep is
357 therefore assessed from plasma vitamin B12 concentrations. Quirk & Norton (1987)
358 supplemented ewes (3 to 4 years old) grazing pasture low in Co (0.046 to 0.1 mg/kg DM)
359 throughout gestation with 0.03 or 0.06 mg Co per head per day. The ewes without
360 supplementary Co were at least sub-clinically deficient. Supplementation increased lamb
361 birth-weight and LWG to levels comparable with a positive control group. Fisher &
362 MacPherson (1991) reported two experiments. In each experiment ewes were fed either a
363 Co deficient or supplemented diet throughout gestation: blood vitamin B12 concentrations
364 indicated that the un-supplemented ewes were sub-clinically deficient. In experiment 1, a
365 third group of ewes were supplemented until GD74 whereas in experiment 2,
366 supplementation began on GD74. In neither experiment was lamb birth-weight influenced by
367 Co status but mortality was reduced by Co supplementation in experiment 1 but not in
368 experiment 2. In experiment 2, lamb behavioural progression to sucking was improved by Co
369 supplementation. Finally, Mitchell *et al.* (2007) supplemented Blackface ewes of marginal Co
370 status with Co during gestation. There was no positive effect of Co status on lamb birth-
371 weight or behavioural progression to sucking. Thus, although responses varied from
372 experiment to experiment, less than adequate maternal Co status can prejudice lamb birth-
373 weight and behavioural progression. Clearly in areas of known low Co status, adequate
374 supplementation should be supplied to avoid potential problems with lamb vigour and
375 welfare.

376 Iodine

377 Iodine deficiency is marked by goitre and reduced fertility and increased neonatal mortality
378 (Suttle 2010). Recent research has focussed on the consequences of I over-supply but
379 below accepted toxicity levels. The initial finding was that excess mineral intakes, when
380 ewes were allowed free access to mineralised salt blocks in late pregnancy reduced lamb
381 plasma IgG concentrations (Crosby *et al.* 2004). In further studies, twin-bearing ewes were
382 given mineral supplements from GD90 onwards. There were no differences in ewe
383 colostrum IgG concentration nor in lamb birth-weight (Boland *et al.* 2005a,b). Cross-fostering
384 established that the depression in lamb plasma IgG occurred because of a reduced ability of
385 the lamb to absorb IgG and was a specifically dose-dependent effect of ewe I intake. The
386 depression in IgG absorption was part of a more general disruption of absorption (Boland *et*
387 *al.* 2006) and the critical period was the last two weeks before parturition (Boland *et al.* 2008;
388 Guinan *et al.* 2005). The mechanism for the disruption in IgG absorption in the lamb is
389 unclear but links with thyroid hormone metabolism are likely (Boland *et al.* 2008; Rose *et al.*
390 2007). The key practical finding from these studies was that the depression of absorption
391 was observed at I intakes less than 40% of that considered toxic and therefore intakes of
392 mineral supplements should be controlled in late pregnancy.

393

394 Selenium

395 The consequences of Se depletion and deficiency include reduced lamb vigour and survival
396 and are dealt with in detail by Suttle (2010). Rooke *et al.* (2008a) summarised all available
397 literature and found variable responses to Se supplementation during pregnancy. For
398 example, there were decreases in lamb mortality in three of seven reports and
399 improvements in lamb vigour in two of five reports from Se supplementation. The variability
400 was likely to have been due not only to differences in ewe Se status prior to supplementation
401 but also to the amount, timing, route (injection or in-feed) and form of Se supplement
402 (inorganic or organic).

403 More recently, two dietary models have been used to assess the effects of Se
404 supplementation. Munoz *et al.* (2008a) supplemented or did not supplement adult ewes with
405 0.5 mg/day of organic Se from 14 days before mating to GD90. The Se status of the ewes
406 prior to the experiment was marginal as was the control diet. Se supplementation did not
407 influence birth-weight. However lambs born to Se-supplemented ewes were quicker to
408 progress through the neonatal behaviour repertoire than control lambs, LWG to weaning was
409 improved and mortality reduced. In two studies (Meyer *et al.* 2010; Neville *et al.* 2010), ewes
410 were fed a Se-adequate (approximately 0.3 mg/d) or Se-supplemented diet (organic-Se;
411 approximately 5 mg/day) throughout pregnancy. There was no difference in lamb birth-

412 weight, LWG, mortality or plasma IgG concentration with Se supplementation in either study
413 (Hammer *et al.* 2011).

414 In conclusion, improving maternal Se status during pregnancy can improve lamb
415 outcomes but the effects are variable and likely dependant on ewe Se status prior to
416 supplementation as shown by the positive responses (Munoz *et al.* 2008a) in ewes of
417 marginal status compared to the lack of response in ewes of adequate status (Meyer *et al.*
418 2010; Neville *et al.* 2010).

419

420 Vitamin E (α -tocopherol)

421

422 Rooke *et al.* (2008a) also reviewed all available literature on supplementing the ewe diet with
423 the anti-oxidant, vitamin E, on offspring outcomes and again reported variable responses.
424 For example, a reduction in mortality was noted in two of eight studies and improved lamb
425 vigour in two of three studies. It was concluded that there was evidence for positive
426 outcomes where ewe vitamin E status was adequate, primarily where vitamin E
427 supplementation was during the final 4 weeks of pregnancy. Kott *et al.* (1998) reported
428 reductions in lamb mortality and improved LWG in one of two experiments and Capper *et al.*
429 (2005, 2006) increased birth-weight and improved vigour with vitamin E supplementation
430 (depending on background diet composition). In both these cases, the supplementary
431 vitamin E was approximately 10-fold requirement. Rooke *et al.* (2009) offered twin-bearing
432 ewes of adequate vitamin E status, four levels of supplementary vitamin E ranging from 1 to
433 5 times requirement from GD100. No responses to supplementation were observed in lamb
434 birth-weight, mortality, LWG or vigour. It is possible that potential for a response to
435 supplementary vitamin E may depend upon whether the ewe or lamb were exposed to
436 oxidative stress. In this context, Capper *et al.* (2005, 2006) only observed improved vigour in
437 lambs to ewe vitamin E supplementation when the ewe diet contained unsaturated FA (a
438 source of nutritional oxidative stress). Similarly Dafoe *et al.* (2008) using a 2 x 2 factorial
439 design fed ewes diets with increased amounts of FA for 35 days in late pregnancy with or
440 without supplementary vitamin E. There were no differences in birth-weight but lambs borne
441 to ewes fed the diet including FA without vitamin E were less able to maintain body
442 temperature and this impairment was absent in the presence of Vitamin E.

443

444 In summary, for the three trace elements Co, I and Se and vitamin E, an inadequate
445 supply during pregnancy can have adverse consequences for lamb outcomes. The potential
446 for response will depend on several factors but sub-optimal maternal status is likely to be
447 important. However, evidence for responses to supplementation above requirement are
448 either non-existent (Co) or equivocal, with adverse effects being observed for I and no or

449 positive effects for Se and vitamin E. For positive welfare outcomes, it is therefore important
450 that adequate mineral and vitamin supplementation of the maternal diet is provided
451 particularly during the last trimester of pregnancy.

452

453 Fatty acids

454 Two hypotheses for including unsaturated FA in ewe diets have been evaluated. First,
455 inclusion of the n-6 polyunsaturated FA, linoleic acid (LA), may modify brown adipose tissue
456 in the lamb and thereby increase non-shivering thermogenesis and tolerance to chilling
457 leading to increased lamb survival. Secondly, diets fed during late pregnancy to housed
458 sheep contain no or low concentrations of the long chain n-3 polyunsaturated FA,
459 eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids. These are important for brain
460 development which is rapid during late pregnancy. It has been proposed that FA
461 supplementation may improve neural development and neonatal vigour.

462 Encinias *et al.* (2004) fed isoenergetic diets during late pregnancy (from GD100
463 onwards) which contained or did not contain safflower seeds as a source of LA. There were
464 no differences in birth-weight in either of two experiments; in one experiment a reduction in
465 mortality was found when safflower seeds were fed. When the thermogenic response was
466 examined, there was no response to the safflower seed-containing diet. Chen *et al.* (2007)
467 compared three different dietary FA inclusions containing two different proportions of
468 unsaturated FA from GD115 to term. They observed no differences between diets in birth-
469 weight or thermogenesis. In fact, inclusion of the highest FA level adversely affected
470 thermogenesis in lambs though this effect may have been confounded by reduced feed
471 intake. Finally as noted for vitamin E above, Dafoe *et al.* (2008) fed ewes supplements
472 containing safflower seed in the presence or absence of vitamin E from GD110 to term. In
473 the absence of vitamin E, the safflower seed (FA) supplement adversely affected lamb
474 thermoregulation and reduced subsequent LWG and survival. Overall these studies do not
475 support a positive effect of dietary LA or other FA in improving thermogenesis and survival of
476 the lamb.

477 Two dietary models have been used to supply n-3 FA, inclusion of fish oil, or to
478 specifically increase DHA content, by inclusion of an algal DHA source. Capper *et al.* (2005,
479 2006) included FA in the diet from GD103 as either saturated or n-3 FA in the presence or
480 absence of supplementary vitamin E. Although inclusion of n-3 FA had no birth-weight effect,
481 lambs borne to n-3 FA-fed ewes tended to stand and suck quicker than their saturated FA-
482 fed controls, indicative of improved lamb vigour. Pickard *et al.* (2008) fed DHA from algal
483 biomass for varying periods between GD84 and term. Feeding DHA for longer than 6 weeks
484 reduced the time lambs took to stand after birth with no differences in birth-weight or LWG.
485 Annett *et al.* (2008) increased the n-3 FA content of diets from GD100. The diets were fed

486 with low or high digestible undegradable protein (DUP) contents in a 2 x 2 factorial design.
487 Feeding n-3 FA in the presence of high DUP had no effect on lamb birth-weight, plasma IgG
488 concentration or LWG. However, in the presence of low DUP, survival of lambs was poorer
489 and plasma IgG lower when n-3 FA were fed. This effect is likely to have been mediated by
490 reduced ewe colostrum output for this diet combination possibly as a result of lower ewe
491 feed intakes and so the poorer survival of these lambs may not have been a prenatal effect.
492 In a subsequent experiment, Annett *et al.* (2009) fed two levels of fish oil (the greater of the
493 two levels, 40 g/kg being equivalent to Annett *et al.*, 2008) and ceased feeding the fish oils
494 24 h after birth. Although colostrum IgG output and lamb plasma IgG concentration at 24 h of
495 age was reduced by feeding fish oil, lamb survival was improved particularly at the lower
496 level of fish oil inclusion. Keithly *et al.* (2011) fed ewes algal biomass (similar to Pickard *et al.*
497 (2008)) from GD100. Lambs born to ewes fed DHA did not differ in birth-weight from controls
498 but tended to maintain higher body temperature when exposed to a cold challenge (0°C for
499 30 min at 1h after birth). Lambs born to DHA-fed ewes grew slower to 38 days of age; this
500 again may be attributed to poor colostrum and milk quality as milk fat was lower in both
501 colostrum and milk from DHA-fed ewes. Keithly *et al.* (2011) fed the experimental diets until
502 day 38 of lactation and therefore effects on milk composition and lamb LWG again may not
503 be prenatal effects. In summary, where responses can be attributed solely to effects during
504 gestation (birth-weight or lamb vigour; Annett *et al.* 2009; Capper *et al.* 2006; Pickard *et al.*
505 2008), positive effects of feeding n-3 acids have been reported; the adverse effects noted by
506 Annett *et al.* (2008) and Keithly *et al.* (2011) need consideration in a practical situation.

507

508 Stress

509

510 Ewes have been subject to a variety of stressful situations during pregnancy and the post-
511 natal consequences investigated.

512

513 Shearing

514

515 That shearing of the pregnant ewe increased lamb birth-weight was first reported by Rutter
516 *et al.* (1971) and since then many studies have investigated different aspects of the
517 response. Since Kenyon *et al.* (2003) critically reviewed the literature, their conclusions will
518 be discussed here in relation to more recent studies. Shearing induced a significant birth-
519 weight response in most studies (see Table 4 for summary). Indeed, even where the birth-
520 weight response to shearing was not significant (Banchero *et al.* 2010; Corner *et al.* 2007;
521 Jenkinson *et al.* 2009), there were numerical increases in birth-weight, confirming the
522 conclusion of Kenyon *et al.* (2003) that shearing did not decrease birth-weight.

523 Kenyon *et al.* (2003) identified timing of shearing, increases in ewe feed intake,
524 longer gestation lengths and the depth of wool stubble remaining after shearing as factors
525 that could influence any response in birth-weight and concluded that these factors did not
526 explain variation in the birth-weight response. Subsequent studies confirm this conclusion.
527 Banchemo *et al.* (2010) reported a larger increase in birth-weight in response to shearing at
528 GD70 than GD120, but only in one of two experiments. Corner *et al.* (2006b, 2007) found
529 that shearing increased gestation length but again only in one of two experiments. Keady &
530 Hanrahan (2009) reported increases in ewe feed intake in response to shearing. As an
531 overall hypothesis to explain variation in the occurrence of a birth weight response, Kenyon
532 and co-workers suggested that fulfilment of two criteria was necessary. The ewe must first
533 have the potential to respond (lambs born to unshorn ewes destined to have low birth-
534 weight) and second, the ability to respond to shearing (adequate maternal body reserves or
535 nutrition). The absence of an increase in birth-weight in response to maternal shearing
536 observed in singleton lambs (Corner *et al.* 2007, 2010b; Jenkinson *et al.* 2009) could be
537 ascribed to the first of the above criteria. However, Kenyon *et al.* (2004) failed to find any
538 interaction between ewe body condition score (over a wide range) and response to shearing.

539 Kenyon *et al.* (2003) considered three lamb responses in addition to birth-weight:
540 survival, thermoregulatory capacity and growth to weaning and found responses were
541 inconsistent. In more recent studies, thermoregulatory responses were not examined while
542 in only three studies was lamb survival reported (Corner *et al.* 2006b; Keady *et al.* 2007;
543 Keady & Hanrahan 2009) with no advantage to shearing. In ten of twelve studies weaning
544 weights were reported and there were significant increases in weaning LW in only three
545 studies (Keady *et al.* 2007; Kenyon *et al.* 2004; Sphor *et al.* 2011) and only in the latter two
546 studies was LWG to weaning increased. Other lamb responses e.g. lamb vigour and
547 behaviour not considered by Kenyon *et al.* (2003) are discussed below.

548

549 Other responses

550

551 Corner *et al.* (2006b, 2007, 2010b) focussed on the effects of shearing ewes in mid-
552 pregnancy in conjunction with other treatments. In the first experiment (Corner *et al.* 2006b),
553 ewes were gathered on GD80, fasted for 24h and then shorn or not shorn. Fewer lambs
554 borne to shorn ewes failed to suck than control ewes or ewes housed and fasted for 24 h but
555 not shorn. Corner *et al.* (2010b) compared control ewes with ewes that (a) were isolated for
556 1 h on two or ten occasions; (b) ewes that were shorn and importantly (c) ewes that were
557 sham-shorn (not shorn but otherwise treated identically to shorn ewes). Only in the shorn
558 treatment was birth-weight increased, suggesting that the birth-weight response was not
559 related to acute stress associated with shearing but a physiological response of the ewe to

560 removal of the fleece. Banchemo *et al.* (2010) in each of two experiments sheared ewes on
561 either GD70 or GD120. In both experiments, there were improvements in behavioural
562 progress of the lamb to sucking consequent upon shearing, suggesting there are responses
563 to shearing which could not be attributed directly to increased birth-weight.

564 Stressors not related to shearing also have effects on pre-weaning outcomes.
565 Roussel *et al.* (2004) isolated ewes twice weekly for the last 5 weeks of pregnancy and
566 reported increased birth-weight in response to isolation although the weight difference had
567 disappeared by weaning. In a subsequent experiment (Roussel-Huchette *et al.* 2008), ewes
568 were exposed to a similar isolation stress but an additional group of ewes were isolated and
569 transported; there were no differences in birth-weight but lambs in the transport treatment
570 were heavier at weaning. Hild *et al.* (2011) compared gentle with aversive handling of ewes
571 from GD100. Lambs borne to aversively handled ewes were heavier at birth with no
572 differences in maternal behaviour towards the lamb between treatments.

573 Finally Stott & Slee (1985) compared the effects of heat (26 °C) or cold (shorn and
574 exposed to 6 °C) exposure of ewes from GD133 on neonatal lamb outcomes. There were no
575 differences in lamb birth-weight from the treatments imposed. However lambs born to cold-
576 stressed dams were more capable of mounting a response to cold stress than control or
577 heat-stressed ewes. Thus lambs from the cold-stress treatment had the smallest reduction in
578 rectal temperature when they were subject to cold stress themselves and the greatest
579 increase in metabolic rate when stimulated by adrenaline.

580 Glucocorticoid treatment of ewes has been used to perturb the HPA axis. Lamb
581 responses were dependant upon the timing of treatment. Administration of dexamethasone
582 once in early pregnancy (GD27) had no effect on birth-weight (De Blasio *et al.* 2007; Roghair
583 *et al.* 2005). However, administration later in pregnancy reduced birth-weight. Moss *et al.*
584 (2001) injected betamethasone either once (150 mg betamethasone on GD104) or 4 times
585 (GD104, GD111, GD118 and GD125). Administration of betamethasone four times reduced
586 birth-weight compared to controls, with a single injection of betamethasone being
587 intermediate. These differences in birth-weight were still apparent at 3 months of age. Using
588 a different protocol (1.5 or 3 mg of dexamethasone on either GD130 or GD141; 2 x 2
589 factorial design), Miller *et al.* (2009) reported a litter size dependant effect of treatment; there
590 was no birth-weight reduction in single lambs but a dose dependant birth-weight reduction in
591 twins.

592 Thus there appears to be a marked difference in outcomes between behavioural and
593 chemical stress-treatments applied to ewes (see Table 4 for summary). Whereas
594 behavioural stress had no adverse consequences for lamb birth-weight or behavioural
595 progression, chemical stress in late pregnancy had adverse consequences for birth-weight.
596 Consistent with this, when Corner *et al.* (2010b; see above) applied a variety of behavioural

597 stressors with no adverse outcomes, a ewe treatment designed to mimic these events by
598 injection with cortisol reduced birth-weight.

599

600 DISCUSSION

601

602 The information presented to date has summarised evidence that prenatal treatments
603 imposed upon the ewe had effects upon the offspring that potentially impacted its well-being
604 and covered the period until approximately weaning age. There was consistent evidence that
605 the prenatal treatments did influence the offspring but there was also considerable variability
606 in response and it is therefore relevant to consider sources of variation and their impact.
607 Variability can arise from three sources: the nature of the challenge itself; the characteristics
608 of the dam and those of the lamb.

609

610 Characteristics of challenge: severity

611

612 The severity of the prenatal treatment is a product of the nature (type and intensity) of the
613 specific challenge and how long the challenge was imposed. The most relevant information
614 is that obtained where treatments were imposed within the same experiment and interactive
615 effects of treatments reported. In late gestation (from GD100 on) increasing severity of UN
616 resulted in greater reductions in birth-weight whether achieved by imposing a greater degree
617 of UN (Khalaf *et al.* 1979) or by increasing the length of UN (Bloomfield *et al.* 2003). Where
618 UN included both early / mid and late pregnancy UN (Corner *et al.* 2008; Ferguson *et al.*
619 2011; Holst *et al.* 1986; Kenyon *et al.* 2011), results were more equivocal. In only one study
620 was birth-weight significantly decreased by early / mid UN (Ferguson *et al.* 2011) and thus
621 any interactions between periods of UN could not be assessed. As noted when discussing
622 stress challenges the number (Moss *et al.* 2001) and the amount (in twin lambs only) of
623 glucocorticoid administered (Miller *et al.* 2009) reduced birth-weight. Thus the severity of
624 prenatal challenge does impact upon lamb outcome but the extent is dependent on
625 challenge type and gestational timing.

626

627 Characteristics of challenge: additivity

628

629 Ewes will likely encounter more than one type of stressor during pregnancy (e.g. UN and
630 handling). However, few experiments designed to investigate interactions between different
631 maternal treatments have been found.

632

633 Characteristics of challenge: shearing

634

635 Kenyon *et al.* (2003) in their critical review found no good evidence for interactions between
636 level of nutrition and the effect of shearing. However, two studies cited in the review did
637 address this issue specifically where either maintenance and ON (Kenyon *et al.* 2002b) or
638 maintenance and UN (Kenyon *et al.* 2002a) were compared. No interactions between
639 shearing and ON were observed but when ewes were subjected to UN, no increase in birth-
640 weight was observed in response to shearing. However, this effect could not be attributed
641 solely to the level of feeding as ewes which were allocated to UN were also the lightest ewes
642 in the experimental group and thus would have had lower body energy reserves. Although
643 shearing will increase the potential for cold stress to be imposed upon the ewe, Kenyon *et al.*
644 (2003) found little evidence for this largely because environmental conditions were not
645 reported in most studies and this is true for studies subsequent to the review. However, it
646 should be noted that even in housed conditions, environmental conditions may be important
647 (type of housing and bedding system). For example, Boe *et al.* (1991) reported an increase
648 in lamb birth-weight when ewes were shorn and housed in an un-insulated shed compare
649 with ewes housed in an insulated shed.

650

651 Characteristics of challenge: other studies

652

653 Kott *et al.* (1998) have noted that supplementary vitamin E improved lamb survival in the
654 early but not late part of the lambing season, suggesting a response to supplementation
655 when the environment was more challenging. There are experiments where different
656 nutritional perturbations have been combined. Supplementation with Se and variation in
657 nutrition has been examined (Meyer *et al.* 2010; Munoz *et al.* 2008a; Swanson *et al.* 2008).
658 Munoz *et al.* (2008a) reported only one interaction from the many possible, indicating effects
659 of Se and nutrition were largely independent. In two experiments of similar design (Meyer *et al.*
660 *et al.* 2010; Swanson *et al.* 2008), there were interactions between treatments for birth-weight
661 in one experiment and for lamb morbidity / mortality in both experiments. Where the amounts
662 of protein and fish oil fed were varied (Annett *et al.* 2008) there were interactions such that
663 lamb survival was prejudiced when fish oil was fed against a low protein but not high protein
664 background. The limited evidence suggests that whether different nutritional treatments have
665 additive or interactive effects will be treatment dependent. More importantly, to translate the
666 experimental data into practical recommendations, an understanding of how different
667 stressors interact is a prerequisite and a need for future study.

668

669 Characteristics of ewe: body reserves

670 The extent of maternal body energy reserves (recorded as body condition score (BCS)
671 where higher scores, normally on a 5 point scale, indicate increasing adiposity) and their
672 mobilisation may reduce the impact of nutrition. There are few studies where the interactive
673 effects of BCS and nutrition have been specifically addressed. The interactive effects of
674 heavy and light ewes (differing in BCS between 2 and 3) and maintenance and ad libitum
675 pregnancy feeding have been investigated in New Zealand (Kenyon *et al.* 2009; van der
676 Linden *et al.* 2009, 2010). Birth-weight was only reduced where ewes of low BCS were fed a
677 maintenance rather than ad libitum diet, suggesting that ewes of greater adiposity (BCS 3)
678 were able to buffer the effects of maintenance feeding from maternal reserves. Many of the
679 studies reviewed reported ewe BCS when treatments were imposed. However when the
680 effects of UN, whether in early/ mid or late pregnancy, were examined in relation to ewe
681 BCS, no clear pattern emerged between ewe BCS and the effect of nutritional treatment
682 probably because of the many other potentially confounding factors.

683 Characteristics of ewe: breed

684 Although many studies report the breed of sheep used, only two have directly compared
685 breeds with similar outcomes (Burt *et al.* 2007; Rooke *et al.* 2010). Burt *et al.* (2007)
686 compared ewes of the same original genotype but maintained either in a harsh rangeland or
687 more favourable conditions for 30 years whereas Rooke *et al.* (2010) compared ewes of a
688 hill (Scottish Blackface) with a lowland breed (Suffolk). In both cases, lamb birth-weight was
689 reduced in response to maternal UN only in the ewes adapted to favourable conditions,
690 suggesting an adaptive response of ewes accustomed to harsh conditions which partitioned
691 nutrients in favour of the foetus rather than maternal tissues. Therefore, breed may be an
692 important and largely unquantified determinant of response. The sire breed may also be
693 relevant. Tygesen *et al.* (2008) bred Shropshire ewes to Shropshire rams selected either for
694 high or low *Longissimus dorsi* cross-sectional area. Late pregnancy UN reduced birth-weight
695 more severely in lambs sired by the high *L. dorsi* ram and this effect was still present at 110
696 days after birth.

697 Characteristics of ewe: age

698 The best described effect of ewe age is the model of Wallace *et al.* (2005a) where 8 month
699 old ewes were allowed ad libitum access to good quality feed. Lambs borne to the ON ewes
700 had severely reduced birth-weight. However, this is a specific model where pregnancies
701 were generated by embryo transfer and recipient ewes had limited energy reserves (BCS
702 2.4) and the energy intakes achieved were 2-fold maintenance. Munoz *et al.* (2008b, 2009)
703 examined the effects of ON in 1 and 2 year old and adult ewes in a more practical context
704 where intakes were lower at 1.4 times maintenance and BCS was higher (3.4) and found no

705 adverse effects. Thus the practical impacts of the Wallace model appear of limited value in
706 an agricultural context.

707 Characteristics of offspring: sex

708 Offspring sex was included in the statistical model used in many studies either directly or as
709 a covariate for birth-weight, and the vast majority of studies reported no significant sex
710 effects. There were, however, a few exceptions: Erhard *et al.* (2004) reported that female but
711 not male lamb birth-weight was reduced by UN. There were also sex-related outcomes in
712 response to dose of dexamethasone (Miller *et al.* 2009): male but not female lamb birth-
713 weight was reduced at a higher dose of steroid. However, female lambs exposed to the
714 higher dose of steroids had increased rectal temperatures than other females and grew
715 faster to weaning; there were no such effects on male lambs. In general therefore, for the
716 prenatal challenges studied so far, there are few interactions between maternal treatment
717 and lamb sex in offspring responses.

718 Characteristics of offspring: litter size

719 It may be expected that the increased nutrient demand required to produce the greater
720 weight of products of conception (foetus plus placenta) would render twin and triplet lambs
721 more susceptible to effects particularly of maternal nutrition. When triplet lambs were
722 compared with other litter sizes there was evidence for a greater adverse effect of UN on
723 triplets. Everett-Hincks *et al.* (2005) reported that lamb survival and ewe-lamb behaviours
724 improved with increasing pasture allowance in triplets but not in twins. Similarly lamb survival
725 in triplets but not other litter sizes was adversely affected when nutrition was reduced in late
726 pregnancy (Kleemann *et al.* 1993). Birth-weight of both twins and triplets was reduced as a
727 result of UN (Khalaf *et al.* 1979). In contrast to the above, Corner *et al.* (2008) found no
728 differences between twins and triplets.

729 When comparing singles and twins, reports were less consistent. No differences
730 were reported between singles and twins (Corner *et al.* 2007, 2008; Holst *et al.* 1986;
731 Oldham *et al.* 2011). However, reduced twin but not single lamb birth-weight due to UN was
732 noted by Kenyon *et al.* (2009) and Khalaf *et al.* (1979). The variable responses in single and
733 twin lambs to shearing has already been noted.

734 In summary, the impact of maternal treatments on offspring outcomes was influenced
735 by other variables. The most important are ewe body reserves, breed and litter size. In
736 relation to the treatments imposed themselves there is a need for more evidence most
737 particularly on how the effects of different maternal stressors interact.

738 The material reviewed here can be viewed in terms of the balance between the welfare
739 of the ewe and lamb resulting from the relative impacts of stressors on the ewe and the
740 outcomes on the lamb. Where impacts are negative or positive for both ewe and lamb then
741 assessment of welfare impact is straightforward. More problematic is where a negative
742 impact on the ewe has a positive outcome for the lamb and vice versa.

743 Negative maternal stressors with negative lamb impacts

744 UN and corticosteroid treatment of the ewe were the stressors that had negative impacts
745 upon the lamb. With one exception (Holst *et al.* 1986), negative impacts upon lamb survival,
746 expression of maternal or lamb behaviours etc were not observed in the absence of a
747 reduction in birth-weight. Therefore avoidance of reduced birth-weight is key to avoiding
748 adverse effects on lamb welfare. Consistent decreases in lamb birth-weight are only
749 observed when the ewe is under-nourished in the last third of gestation. Therefore, adequate
750 feeding during this period is important for lamb welfare. In the first two thirds of gestation, the
751 effect of UN on birth-weight is less consistent. This difference is consistent with a change in
752 the major demand for nutrients from that required for placental development to foetal
753 development in late pregnancy. The variability in response also probably reflects plasticity in
754 response of the foetus to early UN allowing catch-up growth when adequate nutrition is
755 restored. In terms of welfare, the length and severity of UN necessary for a negative effect
756 on lamb birth-weight has been largely unexplored. In late pregnancy, Bloomfield *et al.* (2003)
757 who restricted ewes to 2% of control energy intakes for 10 or 20 days from GD105 reported
758 a progressive reduction in lamb birth-weight as the time of restriction increased but this was
759 a severe restriction of intake close to starvation.

760 Positive maternal treatments with positive lamb impacts

761

762 The positive maternal treatments which have been reported are over-nutrition of the ewe
763 and feeding specific dietary components to ewes of adequate status. In this context,
764 supplementary FA are the most relevant example as for the other minerals (Co, I and Se)
765 and vitamin E, it is not clear in most cases whether control ewes were in adequate rather
766 than deficient status (Co, Se and vitamin E) or receiving toxic amounts (I) of the trace
767 elements. There was no clear evidence indicative of improved lamb welfare to over-feeding
768 ewes during pregnancy and in some cases, there may be disadvantages. Similarly dietary
769 LA or other FA did not improve lamb thermogenesis or survival. Only where the ewe was fed
770 n-3 FA have positive responses in birth-weight and survival been noted but there may be
771 accompanying adverse effects on ewe milk yield. Overall, there is no clear evidence for
772 positive lamb outcomes to feeding the ewe nutrients in excess of requirements and in fact

773 there are potentially adverse effects (see below), and so nutrition to meet the requirements
774 of ewe and developing foetus is optimal for both ewe and lamb welfare.

775

776 Negative maternal stressors with positive neonatal lamb impacts

777 The most striking example of a conflict in welfare terms is shearing of the pregnant ewe. This
778 imposes stress because of the handling of the ewe associated with shearing and possible
779 thermal stress associated with removal of the fleece. This has to be weighed against the
780 consistently observed increase in lamb birth-weight. The mechanism is unclear but
781 increased nutrient supply to the foetus is a strong candidate. Maternal feed intake (e.g.
782 Keady & Hanrahan 2009); gestation length (Banchero *et al.* 2010; Corner *et al.* 2006b) and
783 plasma glucose concentrations (independent of feed intake; Morris *et al.* 2000; Symonds *et al.*
784 1988) have been noted to increase after shearing. All the above would increase nutrient
785 supply to placental and foetal tissues. The response in lamb birth-weight appears to be
786 related to removal of the fleece specifically as sham-shearing (Corner *et al.* 2010b) did not
787 provoke an increase in lamb birth-weight. The welfare balance between ewe and lamb will
788 depend upon conditions experienced by the ewe after shearing. A negative impact on the
789 ewe is more likely if the ewe remains outside on pasture after shearing but will be minimised
790 if the ewe is housed, and shearing may in fact be positive for the ewe if the housed
791 environment and the stocking density of ewes is such that the unshorn ewe may be exposed
792 to heat stress.

793 Other maternal treatments which can be classified as stress-related have also been
794 associated with positive lamb outcomes. Isolation and transport of the ewe (Roussel *et al.*
795 2004; Roussel-Huchette *et al.* 2008) was associated with increases in lamb birth-weight and
796 weight gain. Aversive handling of the ewe (Hild *et al.* 2011) tended to increase lamb weight
797 at 24 h of age. Lambs borne to ewes cold-stressed for the last 14 d before parturition were
798 better able to respond to a cold challenge (Stott & Slee 1985). Finally in one experiment
799 where ewes were treated with corticosteroids (Roghair *et al.* 2005) lamb birth-weight was
800 increased, although this was not a consistent response.

801 From the above and in contrast to UN, stress-related treatments imposed on the ewe
802 (shearing, handling, isolation) do not appear to have adverse effects on the lamb and in fact
803 may have beneficial effects. Clearly the welfare balance needs to be judged on a case by
804 case basis.

805 Positive maternal stressors with negative lamb impacts

806 Examples relate primarily to ON of the ewe. The model developed by Wallace *et al.* (2005b)
807 for teenage pregnancy where ON adolescent ewes partition nutrients to maternal growth at
808 the expense of foetal growth is the clearest example and although when ON was evaluated
809 in conditions more applicable to sheep husbandry, the adverse effects upon lamb birth-
810 weight were less apparent they have still been reported (e.g. Kenyon *et al.* 2011; Munoz *et*
811 *al.* 2008b, 2009; Swanson *et al.* 2008).

812 The present review should be considered in light of the foetal origins of adult disease
813 hypothesis, where the uterine environment the foetus is exposed to influences development,
814 with postnatal consequences particularly for adult health as exemplified by the development
815 of hypertension, cardiovascular disease and type II diabetes in the human (Barker *et al.*
816 2002). Although the current review addresses effects upon offspring up to weaning, effects
817 into adulthood being dealt with in a future review, specific features of the hypothesis are
818 worthy of note.

819 First the offspring responses to any perturbation of the uterine environment depends
820 upon when during pregnancy the perturbation is imposed, in other words, there are specific
821 windows in development during which the foetus is sensitive. These have been summarised
822 for the sheep by Symonds *et al.* (2010). Although most challenges imposed upon the ewe,
823 such as UN, were chronic in nature, the importance of specific windows can be
824 demonstrated. The timing of UN has already been discussed. A more specific example is the
825 response to administration of steroids on GD27 which although it did not perturb birth-weight
826 (De Blasio *et al.* 2007; Roghair *et al.* 2005), increased resting blood pressure of the offspring
827 at 2 years of age (Dodic *et al.* 2002).

828 A second consequence of the foetal origins hypothesis is the idea of the “predictive
829 adaptive response” (Nettle *et al.* 2013). Thus the environment the foetus experiences during
830 development primes it to alter its phenotype for the environment it is likely to experience
831 during post-natal life through changes in gene expression and epigenetic mechanisms (Ford
832 & Long 2012). Adverse consequences for adult health occur when the post-natal
833 environment is not as expected (‘environmental mismatch’), e.g. when foetal UN is followed
834 by plentiful nutrient supply during adult life. In most of the material reviewed here, a negative
835 impact on the dam (e.g. UN) had a negative consequence for the offspring (e.g. lower birth-
836 weight) probably directly through a reduction in nutrient supply to the foetus rather than by
837 other mechanisms. Perhaps the one clear example of the effect of the foetal environment is
838 demonstrated in the study (Kenyon *et al.* 2009; van der Linden *et al.* 2009,. 2010) where
839 ewes were offered maintenance or ad libitum pasture and birth-weights of lambs were
840 greater (5.7 v 5.2 kg) when ad libitum pasture was offered. When these ewe lambs were

841 mated and fed to requirement throughout pregnancy (i.e. not ad libitum), lambs whose
842 grand-dams had been fed maintenance were heavier (4.7 v 4.3 kg) at birth than lambs
843 whose grand-dams had been fed ad libitum. Thus, ewe-lambs who dams had experienced
844 maintenance conditions in utero were more able to cope with similar conditions when they
845 became pregnant themselves than ewe-lambs which had been fed ad libitum.

846 In conclusion, this review has identified maternal UN as the chief maternal challenge
847 that has consistent adverse outcomes for the lamb, mainly manifest through reductions in
848 birth-weight. Lamb birth-weight is reduced consistently when UN is imposed after day 100 of
849 pregnancy. Although UN imposed earlier in pregnancy has a more variable effect on birth-
850 weight, absence of a depression in birth-weight does not imply that foetal development is not
851 perturbed by UN. Perturbed foetal development may have longer-term consequences for the
852 lamb than those examined during the pre-weaning period upon which this review has
853 focussed; these consequences will be discussed in a companion review. The current review
854 has also focussed primarily on consequences for the welfare of the lamb. The immediate
855 and longer-term consequences of the maternal treatments for the ewe must also be
856 considered when animal welfare is assessed. This is particularly important for maternal
857 treatments, such as shearing, which may have a positive outcome for the lamb. The overall
858 balance of welfare for both ewe and lamb should be considered. Finally the review has
859 highlighted areas requiring future study. The most important of these is the consideration of
860 interactions between different maternal stressors which have not been investigated and
861 which is important in practice since the ewe is likely to encounter more than one stressor
862 during normal animal husbandry. In this context, the scarcity of studies considering the
863 impact of disease in the ewe on lamb outcomes is noteworthy although the ethical
864 considerations of carrying out such studies are recognised.

865 ACKNOWLEDGEMENTS

866 We gratefully acknowledge funding from the UK Department for Environment, Food and
867 Rural Affairs (Defra, Project AW0509: Early environment effects on animal welfare, health
868 and productivity) and the Scottish Government (SPASE Module 2: Effects of early
869 environment on behaviour, reproduction, welfare and product quality of livestock

870 REFERENCES

871 ANNETT, R. W., CARSON, A. F., & DAWSON, L. E. R. (2008). Effects of digestible
872 undegradable protein (DUP) supply and fish oil supplementation of ewes during late
873 pregnancy on colostrum production and lamb output. *Animal Feed Science and*
874 *Technology* **146**, 270-288.

875 ANNETT, R. W., DAWSON, L. E. R., EDGAR, H., & CARSON, A. F. (2009). Effects of
876 source and level of fish oil supplementation in late pregnancy on feed intake, colostrum
877 production and lamb output of ewes. *Animal Feed Science and Technology* **154**, 169-182.

878 ARNOTT, G., ROBERTS, D., ROOKE, J. A., TURNER, S. P., LAWRENCE, A. B., &
879 RUTHERFORD, K. M. D. (2012). BOARD INVITED REVIEW: The importance of the
880 gestation period for welfare of calves: maternal stressors and difficult births. *Journal of*
881 *Animal Science* **90**, 5021-5034.

882 BANCHERO, G., VAZQUEZ, A., MONTOSI, F., DE BARBIERI, I., & QUINTANS, G.
883 (2010). Pre-partum shearing of ewes under pastoral conditions improves the early vigour
884 of both single and twin lambs. *Animal Production Science* **50**, 309-314.

885 BANCHERO, G. E., QUINTANS, G., LINDSAY, D. R., & MILTON, J. T. B. (2009). A pre-
886 partum lift in ewe nutrition from a high-energy lick or maize or by grazing *Lotus uliginosus*
887 pasture, increases colostrum production and lamb survival. *Animal* **3**, 1183-1188.

888 BARKER, D. J. P., ERIKSSON, J. G., FORSEN, T., & OSMOND, C. (2002). Fetal origins of
889 adult disease: strength of effects and biological basis. *International Journal of*
890 *Epidemiology* **31**, 1235-1239.

891 BARKER, D. J. P., OSMOND, C., GOLDING, J., KUH, D. & WADSWORTH, M. E. J. (1989).
892 Growth in utero, blood pressure in childhood and adult life, and mortality from
893 cardiovascular disease. *British Medical Journal* **298**, 564-567.

894 BLOOMFIELD, F. H., OLIVER, M. H., GIANNOULIAS, C. D., GLUCKMAN, P. D., HARDING,
895 J. E., & CHALLIS, J. R. G. (2003). Brief undernutrition in late-gestation sheep programs
896 the hypothalamic-pituitary-adrenal axis in adult offspring. *Endocrinology* **144**, 2933-2940.

897 BOE, K., NEDKVITNE, J. J., & AUSTBO, D. (1991). the effect of different housing systems
898 and feeding regimes on the performance and rectal temperature of sheep. *Animal*
899 *Production* **53**, 331-337.

900 BOLAND, T. M., BROPHY, P. O., CALLAN, J. J., QUINN, P. J., NOWAKOWSKI, P., &
901 CROSBY, T. F. (2005a). The effects of mineral supplementation to ewes in late
902 pregnancy on colostrum yield and immunoglobulin G absorption in their lambs. *Livestock*
903 *Production Science* **97**, 141-150.

904 BOLAND, T. M., CALLAN, J. J., BROPHY, P. O., QUINN, P. J., & CROSBY, T. F. (2006).
905 Lamb serum vitamin E and immunoglobulin G concentrations in response to various
906 maternal mineral and iodine supplementation regimens. *Animal Science* **82**, 319-325.

907 BOLAND, T. M., GUINAN, M., BROPHY, P. O., CALLAN, J. J., QUINN, P. J.,
908 NOWAKOWSKI, P., & CROSBY, T. F. (2005b). The effect of varying levels of mineral and
909 iodine supplementation to ewes during late pregnancy on serum immunoglobulin G
910 concentrations in their progeny. *Animal Science* **80**, 209-218.

911 BOLAND, T. M., HAYES, L., SWEENEY, T., CALLAN, J. J., BAIRD, A. W., KEELY, S., &
912 CROSBY, T. F. (2008). The effects of cobalt and iodine supplementation of the pregnant
913 ewe diet on immunoglobulin G, vitamin E, T-3 and T-4 levels in the progeny. *Animal* **2**,
914 197-206.

915 BURT, B. E., HESS, B. W., NATHANIELSZ, P. W., & FORD, S. P. (2007). Flock differences
916 in the impact of maternal dietary restriction on offspring growth and glucose tolerance in
917 female offspring. *Society for Reproduction and Fertility Supplement* **64**, 411-424.

918 CAL-PEREYRA, L., BENECH, A., DA SILVA, S., MARTIN, A., & GONZALEZ-MONTANA, J.
919 (2011). Energy metabolism in shorn and unshorn pregnant ewes under two different
920 nutritional planes. Effects on the energetic storage of their lambs. *Archivos de Medicina*
921 *Veterinaria* **43**, 277-285.

922 CAPPER JL, WILKINSON RG, MACKENZIE AM, & SINCLAIR LA (2006). Polyunsaturated
923 fatty acid supplementation during pregnancy alters neonatal behavior in sheep. *Journal of*
924 *Nutrition* **136**, 397-403.

925 CAPPER, J. L., WILKINSON, R. G., KASAPIDOU, E., PATTINSON, S. E., MACKENZIE, A.
926 M., & SINCLAIR, L. A. (2005). The effect of dietary vitamin E and fatty acid
927 supplementation of pregnant and lactating ewes on placental and mammary transfer of
928 vitamin E to the lamb. *British Journal of Nutrition* **93**, 549-557.

929 CHEN, C. Y., CARSTENS, G. E., GILBERT, C. D., THEIS, C. M., ARCHIBEQUE, S. L.,
930 KURZ, M. W., SLAY, L. J., & SMITH, S. B. (2007). Dietary supplementation of high levels
931 of saturated and monounsaturated fatty acids to ewes during late gestation reduces
932 thermogenesis in newborn lambs by depressing fatty acid oxidation in perirenal brown
933 adipose tissue. *Journal of Nutrition* **137**, 43-48.

934 CORNER, R., KENYON, P., STAFFORD, K., WEST, D., LOPEZ-VILLALOBOS, N.,
935 MORRIS, S., & OLIVER, M. (2008). Effect of nutrition from mid to late pregnancy on the
936 performance of twin- and triplet-bearing ewes and their lambs. *Australian Journal of*
937 *Experimental Agriculture* **48**, 666-671.

938 CORNER, R., KENYON, P., STAFFORD, K., WEST, D., & MORRIS, S. (2006a). The effect
939 of nutrition during pregnancy on the behaviour of adolescent ewes and their lamb(s)
940 within 12 hrs of birth. *Proceedings of the New Zealand Society of Animal Production* **66**,
941 439-443.

942 CORNER, R., KENYON, P., STAFFORD, K., WEST, D., MORRIS, S., & OLIVER, M.
943 (2010a). The effects of pasture availability for twin- and triplet-bearing ewes in mid and
944 late pregnancy on ewe and lamb behaviour 12 to 24 h after birth. *Animal* **4**, 108-115.

945 CORNER, R. A., KENYON, P. R., STAFFORD, J. K., WEST, D. M., & OLIVER, M. H.
946 (2006b). The effect of mid-pregnancy shearing or yarding stress on ewe post-natal

947 behaviour and the birth weight and post-natal behaviour of their lambs. *Livestock Science*
948 **102**, 121-129.

949 CORNER, R. A., KENYON, P. R., STAFFORD, K. J., WEST, D. M., & OLIVER, M. H.
950 (2007). The effect of mid-pregnancy shearing and litter size on lamb birth weight and
951 postnatal plasma cortisol response. *Small Ruminant Research* **73**, 115-121.

952 CORNER, R. A., KENYON, P. R., STAFFORD, K. J., WEST, D. M., & OLIVER, M. H.
953 (2010b). The effect of different types of stressors during mid- and late pregnancy on lamb
954 weight and body size at birth. *Animal* **4**, 2065-2070.

955 CROSBY, T. F., BOLAND, T. M., BROPHY, P. O., QUINN, P. J., CALLAN, J. J., & JOYCE,
956 D. (2004). The effects of offering mineral blocks to ewes pre-mating and in late pregnancy
957 on block intake, pregnant ewe performance and immunoglobulin status of the progeny.
958 *Animal Science* **79**, 493-504.

959 DAFOE, J. M., KOTT, R. W., SOWELL, B. F., BERARDINELLI, J. G., DAVIS, K. C., &
960 HATFIELD, P. G. (2008). Effects of supplemental safflower and vitamin E during late
961 gestation on lamb growth, serum metabolites, and thermogenesis. *Journal of Animal*
962 *Science* **86**, 3194-3202.

963 DE BLASIO, M. J., DODIC, M., JEFFERIES, A. J., MORITZ, K. M., WINTOUR, E. M., &
964 OWENS, J. A. (2007). Maternal exposure to dexamethasone or cortisol in early
965 pregnancy differentially alters insulin secretion and glucose homeostasis in adult male
966 sheep offspring. *American Journal of Physiology-Endocrinology and Metabolism* **293**,
967 E75-E82.

968 DODIC, M., ABOUANTOUN, T., O'CONNOR, A., WINTOUR, E. M., & MORITZ, K. M.
969 (2002). Programming effects of short prenatal exposure to dexamethasone in sheep.
970 *Hypertension* **40**, 729-734.

971 DWYER, C. M., LAWRENCE, A. B., BISHOP, S. C., & LEWIS, M. (2003). Ewe-lamb bonding
972 behaviours at birth are affected by maternal undernutrition in pregnancy. *British Journal of*
973 *Nutrition* **89**, 123-136.

974 DWYER, C. M., McILVANEY, K., COOMBS, T., ASHWORTH, C. J., & ROOKE, J. A.
975 (2010a). The effect of maternal undernutrition during the first 90 days of gestation on
976 neonatal lamb behaviour and survival. *International Conference on Developmental*
977 *Origins of Health and Disease, Munich 2010*, 96.

978 DWYER, C. M., McILVANEY, K. M., COOMBS, T. M., ROOKE, J. A., & ASHWORTH, C. J.
979 (2010b). Undernutrition in early to mid pregnancy causes deficits in the expression of
980 maternal behaviour in sheep that may affect lamb survival. *Proceedings of the 44th*
981 *Congress of the International Society of Applied Ethology, Uppsala, Sweden*, 45.

982 ENCINIAS, H. B., LARDY, G. P., ENCINIAS, A. M., & HAUER, M. L. (2004). High linoleic
983 acid safflower seed supplementation for gestating ewes: Effects on ewe performance,
984 lamb survival, and brown fat stores. *Journal of Animal Science* **82**, 3654-3661.

985 ERHARD, H. W., BOISSY, A., RAE, M. T., & RHIND, S. M. (2004). Effects of prenatal
986 undernutrition on emotional reactivity and cognitive flexibility in adult sheep. *Behavioural*
987 *Brain Research* **151**, 25-35.

988 EVERETT-HINCKS, J. M., BLAIR, H. T., STAFFORD, K. J., LOPEZ-VILLALOBOS, N.,
989 KENYON, P. R., & MORRIS, S. T. (2005). The effect of pasture allowance fed to twin-
990 and triplet-bearing ewes in late pregnancy on ewe and lamb behaviour and performance
991 to weaning. *Livestock Production Science* **97**, 253-266.

992 FERGUSON, M., THOMPSON, A., GORDON, D., HYDER, M., KEARNEY, G., OLDHAM,
993 C., & PAGANONI, B. (2011). The wool production and reproduction of Merino ewes can
994 be predicted from changes in liveweight during pregnancy and lactation. *Animal*
995 *Production Science* **51**, 763-775.

996 FISHER, G. E. J. & MACPHERSON, A. (1991). Effect of Cobalt deficiency in the pregnant
997 ewe on reproductive-performance and lamb viability. *Research in Veterinary Science* **50**,
998 319-327.

999 FORD, S. & LONG, N. (2012). Evidence for similar changes in offspring phenotype following
1000 either maternal undernutrition or overnutrition: potential impact on fetal epigenetic
1001 mechanisms. *Reproduction Fertility and Development* **24**, 105-111.

1002 GLUCKMAN, P. D. & HANSON, M. A. (2004). Developmental origins of disease paradigm: A
1003 mechanistic and evolutionary perspective. *Pediatric Research* **56**, 311-317.

1004 GUINAN, M., HARRISON, G., BOLAND, T. M., & CROSBY, T. F. (2005). The effect of
1005 timing of mineral supplementation of the ewe diet in late pregnancy on immunoglobulin G
1006 absorption by the lamb. *Animal Science* **80**, 193-200.

1007 HAMMER, C. J., THORSON, J. F., MEYER, A. M., REDMER, D. A., LUTHER, J. S.,
1008 NEVILLE, T. L., REED, J. J., REYNOLDS, L. P., CATON, J. S., & VONNAHME, K. A.
1009 (2011). Effects of maternal selenium supply and plane of nutrition during gestation on
1010 passive transfer of immunity and health in neonatal lambs. *Journal of Animal Science* **89**,
1011 3690-3698.

1012 HERNANDEZ, C. E., MATTHEWS, L. R., OLIVER, M. H., BLOOMFIELD, F. H., &
1013 HARDING, J. E. (2009). Effects of sex, litter size and periconceptual ewe nutrition on
1014 the ewe-lamb bond. *Applied Animal Behaviour Science* **120**, 76-83.

1015 HILD, S., COULON, M., SCHROEER, A., ANDERSEN, I., & ZANELLA, A. (2011). Gentle vs.
1016 aversive handling of pregnant ewes: I. Maternal cortisol and behavior. *Physiology &*
1017 *Behavior* **104**, 384-391.

1018 HOLST, P. J., KILLEEN, I. D., & CULLIS, B. R. (1986). Nutrition of the pregnant ewe and its
1019 effect on gestation length, lamb birth-weight and lamb survival. *Australian Journal of*
1020 *Agricultural Research* **37**, 647-655.

1021 HUSTED, S. M., NIELSEN, M. O., TYGESEN, M. P., KIANI, A., BLACHE, D., &
1022 INGVARTSEN, K. L. (2007). Programming of intermediate metabolism in young lambs
1023 affected by late gestational maternal undernourishment. *American Journal of Physiology-*
1024 *Endocrinology and Metabolism* **293**, E548-E557.

1025 JENKINSON, C. M. C., KENYON, P. R., BLAIR, H. T., BREIER, B. H., & LUCKMAN, P. D.
1026 (2009). Birth weight effect in twin-born lambs from mid-pregnancy shearing is associated
1027 with changes in maternal IGF-I concentration. *New Zealand Journal of Agricultural*
1028 *Research* **52**, 261-268.

1029 KEADY, T. W. J., HANRAHAN, J., & FLANAGAN, S. (2007). Effects of extended grazing
1030 during mid, late or throughout pregnancy, and winter shearing of housed ewes, on ewe
1031 and lamb performance. *Irish Journal of Agricultural and Food Research* **46**, 169-180.

1032 KEADY, T. W. J. & HANRAHAN, J. P. (2009). Effects of shearing at housing, grass silage
1033 feed value and extended grazing herbage allowance on ewe and subsequent lamb
1034 performance. *Animal* **3**, 143-151.

1035 KEITHLY, J. I., KOTT, R. W., BERARDINELLI, J. G., MOREAUX, S., & HATFIELD, P. G.
1036 (2011). Thermogenesis, blood metabolites and hormones, and growth of lambs born to
1037 ewes supplemented with algae-derived docosahexaenoic acid. *Journal of Animal Science*
1038 **89**, 4305-4313.

1039 KENYON, P., PAIN, S., HUTTON, P., JENKINSON, C., MORRIS, S., PETERSON, S., &
1040 BLAIR, H. (2011). Effects of twin-bearing ewe nutritional treatments on ewe and lamb
1041 performance to weaning. *Animal Production Science* **51**, 406-415.

1042 KENYON, P. R., BLAIR, H. T., JENKINSON, C. M. C., MORRIS, S. T., MACKENZIE, D. D.
1043 S., PETERSON, S. W., FIRTH, E. C., & JOHNSTON, P. L. (2009). The effect of ewe size
1044 and nutritional regimen beginning in early pregnancy on ewe and lamb performance to
1045 weaning. *New Zealand Journal of Agricultural Research* **52**, 203-212.

1046 KENYON, P. R., MOREL, P. C. H., & MORRIS, S. T. (2004). Effect of liveweight and
1047 condition score of ewes at mating, and shearing mid-pregnancy, on birthweights and
1048 growth rates of twin lambs to weaning. *New Zealand Veterinary Journal* **52**, 145-149.

1049 KENYON, P. R., MORRIS, S. T., REVELL, D. K., & MCCUTCHEON, S. N. (2002a).
1050 Maternal constraint and the birthweight response to mid-pregnancy shearing. *Australian*
1051 *Journal of Agricultural Research* **53**, 511-517.

1052 KENYON, P. R., MORRIS, S. T., REVELL, D. K., & MCCUTCHEON, S. N. (2002b). Nutrition
1053 during mid to late pregnancy does not affect the birthweight response to mid pregnancy
1054 shearing. *Australian Journal of Agricultural Research* **53**, 13-20.

1055 KENYON, P. R., MORRIS, S. T., REVELL, D. K., & MCCUTCHEON, S. N. (2003). Shearing
1056 during pregnancy - review of a policy to increase birthweight and survival of lambs in New
1057 Zealand pastoral farming systems. *New Zealand Veterinary Journal* **51**, 200-207.

1058 KENYON, P. R., SHERLOCK, R. G., PARKINSON, T. J., & MORRIS, S. T. (2005). The
1059 effect of maternal shearing and thyroid hormone treatments in mid pregnancy on the birth
1060 weight, follicle, and wool characteristics of lambs. *New Zealand Journal of Agricultural
1061 Research* **48**, 293-300.

1062 KHALAF, A. M., DOXEY, D. L., BAXTER, J. T., BLACK, W. J. M., FITZSIMONS, J., &
1063 FERGUSON, J. A. (1979). Late pregnancy ewe feeding and lamb performance in early
1064 life .1. Pregnancy feeding levels and perinatal lamb mortality. *Animal Production* **29**, 393-
1065 399.

1066 KING, S., DANCAUSE, K., TURCOTTE-TREMBLAY, A-M., VERU, F. & LAPLANTE, D. P.
1067 (2012). Using natural disasters to study the effects of prenatal maternal stress on child
1068 health and development. *Birth Defects Research (Part C)* **96**, 273-288.

1069 KLEEMANN, D. O., WALKER, S. K., WALKLEY, J. R. W., PONZONI, R. W., SMITH, D. H.,
1070 GRIMSON, R. J., & SEAMARK, R. F. (1993). Effect of nutrition during pregnancy on birth-
1071 weight and lamb survival in FecB Booroola South Australian merino ewes. *Animal
1072 Reproduction Science* **31**, 213-224.

1073 KOTT, R. W., THOMAS, V. M., HATFIELD, P. G., EVANS, T., & DAVIS, K. C. (1998).
1074 Effects of dietary vitamin E supplementation during late pregnancy on lamb mortality and
1075 ewe productivity. *Journal of the American Veterinary Medical Association* **212**, 997-1000.

1076 LUMEY, L. H., STEIN, A. D. & SUSSER, E. (2011). Prenatal famine and adult health. *Annual
1077 Review of Public Health* **32**, 237-262.

1078 LUTHER, J., AITKEN, R., MILNE, J., MATSUZAKI, M., REYNOLDS, L., EDMER, D., &
1079 WALLACE, J. (2007). Maternal and fetal growth, body composition, endocrinology, and
1080 metabolic status in undernourished adolescent sheep. *Biology of Reproduction* **77**, 343-
1081 350.

1082 LUTHER, J. S., REDMER, D. A., REYNOLDS, L. P., & WALLACE, J. M. (2005). Nutritional
1083 paradigms of ovine fetal growth restriction: implications for human pregnancy. *Human
1084 fertility* **8**, 179-187.

1085 MEYER, A. M., REED, J. J., NEVILLE, T. L., TAYLOR, J. B., HAMMER, C. J., REYNOLDS,
1086 L. P., REDMER, D. A., VONNAHME, K. A., & CATON, J. S. (2010). Effects of plane of
1087 nutrition and selenium supply during gestation on ewe and neonatal offspring
1088 performance, body composition, and serum selenium. *Journal of Animal Science* **88**,
1089 1786-1800.

- 1090 MILLER, D. R., JACKSON, R. B., BLACHE, D., & ROCHE, J. R. (2009). Metabolic maturity
1091 at birth and neonate lamb survival and growth: The effects of maternal low-dose
1092 dexamethasone treatment. *Journal of Animal Science* **87**, 3167-3178.
- 1093 MITCHELL, L. M., ROBINSON, J. J., WATT, R. G., MCEVOY, T. G., SHWORTH, C. J.,
1094 ROOKE, J. A., & DWYER, C. M. (2007). Effects of cobalt/vitamin B₁₂ status in ewes on
1095 ovum development and lamb viability at birth. *Reproduction, Fertility and Development*
1096 **19**, 553-562.
- 1097 MORRIS, S. T., KENYON, P. R., & WEST, D. M. (2005). Effect of hogget nutrition in
1098 pregnancy on lamb birthweight and survival to weaning. *New Zealand Journal of*
1099 *Agricultural Research* **48**, 165-175.
- 1100 MORRIS, S. T., MCCUTCHEON, S. N., & REVELL, D. K. (2000). Birth weight responses to
1101 shearing ewes in early to mid gestation. *Animal Science* **70**, 363-369.
- 1102 MOSS, T. J. M., SLOBODA, D. M., GURRIN, L. C., HARDING, R., CHALLIS, J. R. G., &
1103 NEWNHAM, J. P. (2001). Programming effects in sheep of prenatal growth restriction and
1104 glucocorticoid exposure. *American Journal of Physiology-Regulatory Integrative and*
1105 *Comparative Physiology* **281**, R960-R970.
- 1106 MUNOZ, C., CARSON, A. F., MCCOY, M. A., DAWSON, L. E. R., O'CONNELL, N. E., &
1107 GORDON, A. W. (2008a). Nutritional status of adult ewes during early and mid-
1108 pregnancy. 2. Effects of supplementation with selenised yeast on ewe reproduction and
1109 offspring performance to weaning. *Animal* **2**, 64-72.
- 1110 MUNOZ, C., CARSON, A. F., MCCOY, M. A., DAWSON, L. E. R., O'CONNELL, N. E., &
1111 GORDON, A. W. (2008b). Nutritional status of adult ewes during early and mid-
1112 pregnancy. 1. Effects of plane of nutrition on ewe reproduction and offspring performance
1113 to weaning. *Animal* **2**, 52-63.
- 1114 MUNOZ, C., CARSON, A. F., MCCOY, M. A., DAWSON, L. E. R., O'CONNELL, N. E., &
1115 GORDON, A. W. (2009). Effect of plane of nutrition of 1-and 2-year-old ewes in early and
1116 mid-pregnancy on ewe reproduction and offspring performance up to weaning. *Animal* **3**,
1117 657-669.
- 1118 NETTLE, D., FRANKENHUIS, W. E. & RICKARD, I. J. (2013). The evolution of predictive
1119 adaptive responses in human life history. *Proceedings Of The Royal Society B-Biological*
1120 *Sciences* **280**, 2013134313
- 1121 NEVILLE, T. L., CATON, J. S., HAMMER, C. J., REED, J. J., LUTHER, J. S., TAYLOR, J.
1122 B., REDMER, D. A., REYNOLDS, L. P., & VONNAHME, K. A. (2010). Ovine offspring
1123 growth and diet digestibility are influenced by maternal selenium supplementation and
1124 nutritional intake during pregnancy despite a common postnatal diet. *Journal of Animal*
1125 *Science* **88**, 3645-3656.

1126 OLDHAM, C., THOMPSON, A., FERGUSON, M., GORDON, D., KEARNEY, G., &
1127 PAGANONI, B. (2011). The birthweight and survival of Merino lambs can be predicted
1128 from the profile of liveweight change of their mothers during pregnancy. *Animal*
1129 *Production Science* **51**, 776-783.

1130 PICKARD, R. M., BEARD, A. R., SEAL, C. J., & EDWARDS, S. A. (2008). Neonatal lamb
1131 vigour is improved by feeding docosahexaenoic acid in the form of algal biomass during
1132 late gestation. *Animal* **2**, 1186-1192.

1133 QUIRK, M. F. & NORTON, B. W. (1987). The relationship between the cobalt nutrition of
1134 ewes and the vitamin-B12 status of ewes and their lambs. *Australian Journal of*
1135 *Agricultural Research* **38**, 1071-1082.

1136 ROGHAI, R. D., SEGAR, J. L., SHARMA, R. V., ZIMMERMAN, M. C., JAGADEESHA, D.
1137 K., SEGAR, E. M., SCHOLZ, T. D., & LAMB, F. S. (2005). Newborn lamb coronary artery
1138 reactivity is programmed by early gestation dexamethasone before the onset of systemic
1139 hypertension. *American Journal of Physiology-Regulatory Integrative and Comparative*
1140 *Physiology* **289**, R1169-R1176.

1141 ROOKE, I. A., DWYER, C. M., & ASHWORTH, C. J. (2008a). The potential for improving
1142 physiological, behavioural and immunological responses in the neonatal lamb by trace
1143 element and vitamin supplementation of the ewe. *Animal* **2**, 514-524.

1144 ROOKE, J. A., HOUDIJK, J. G. M., MCILVANEY, K., ASHWORTH, C. J., & DWYER, C. M.
1145 (2010). Differential effects of maternal undernutrition between days 1 and 90 of
1146 pregnancy on ewe and lamb performance and lamb parasitism in hill or lowland breeds.
1147 *Journal of Animal Science* **88**, 3833-3842.

1148 ROOKE, J. A., MATHESON, S., ISON, S., JACK, M., ASHWORTH, C. J., & DWYER, C. M.
1149 (2009). The effect of late pregnancy supplementation of ewes with vitamin E on lamb
1150 vigour. *Animal* **3**, 1555-1561.

1151 ROSE, M. T., WOLF, B. T., & HARESIGN, W. (2007). Effect of the level of iodine in the diet
1152 of pregnant ewes on the concentration of immunoglobulin G in the plasma of neonatal
1153 lambs following the consumption of colostrum. *British Journal of Nutrition* **97**, 315-320.

1154 ROUSSEL, S., HEMSWORTH, P. H., BOISSY, A., & DUVAUX-PONTER, C. (2004). Effects
1155 of repeated stress during pregnancy in ewes on the behavioural and physiological
1156 responses to stressful events and birth weight of their offspring. *Applied Animal*
1157 *Behaviour Science* **85**, 259-276.

1158 ROUSSEL-HUCHETTE, S., HEMSWORTH, P. H., BOISSY, A., & DUVAUX-PONTERC, C.
1159 (2008). Repeated transport and isolation during pregnancy in ewes: Differential effects on
1160 emotional reactivity and weight of their offspring. *Applied Animal Behaviour Science* **109**,
1161 275-291.

1162 RUTTER, W., LAIRD, T. R., & BROADBEN, P. J. (1971). Effects of clipping pregnant ewes
1163 at housing and of feeding different basal roughages. *Animal Production* **13**, 329-336.

1164 SARGEANT, J. M., RAJIC, A., READ, S., & OHLSSON, A. (2006). The process of
1165 systematic review and its application in agri-food public-health. *Preventive Veterinary*
1166 *Medicine* **75**, 141-151.

1167 SPHOR, L., BANCHERO, G., CORREA, G., OSORIO, M., & QUINTANS, G. (2011). Early
1168 prepartum shearing increases milk production of wool sheep and the weight of the lambs
1169 at birth and weaning. *Small Ruminant Research* **99**, 44-47.

1170 STOTT, A. W. & SLEE, J. (1985). The effect of environmental-temperature during pregnancy
1171 on thermoregulation in the newborn lamb. *Animal Production* **41**, 341-347.

1172 SUTTLE NF (2010). *Mineral Nutrition of Livestock*. Wallingford, Oxon: Cabi.

1173 SWANSON, T. J., HAMMER, C. J., LUTHER, J. S., CARLSON, D. B., TAYLOR, J. B.,
1174 REDMER, D. A., NEVILLE, T. L., REED, J. J., REYNOLDS, L. P., CATON, J. S., &
1175 VONNAHME, K. A. (2008). Effects of gestational plane of nutrition and selenium
1176 supplementation on mammary development and colostrum quality in pregnant ewe
1177 lambs. *Journal of Animal Science* **86**, 2415-2423.

1178 SYMONDS, M. E., BRYANT, M. J., SHEPHERD, D. A. L., & LOMAX, M. A. 1988). Glucose-
1179 metabolism in shorn and unshorn pregnant sheep. *British Journal of Nutrition* **60**, 249-
1180 263.

1181 SYMONDS, M. E., SEBERT, S. P., & BUDGE, H. (2010). Nutritional regulation of etal growth
1182 and implications for productive life in ruminants. *Animal* **4**, 1075-1083.

1183 THOMPSON, A., FERGUSON, M., CAMPBELL, A., GORDON, D., KEARNEY, G.,
1184 OLDHAM, C., & PAGANONI, B. (2011). Improving the nutrition of Merino ewes during
1185 pregnancy and lactation increases weaning weight and survival of progeny but does not
1186 affect their mature size. *Animal Production Science* **51**, 784-793.

1187 TYGESEN, M. R., TAUSON, A. H., BLACHE, D., HUSTED, S. M., & NIELSEN, M. O.
1188 (2008). Late foetal life nutrient restriction and sire genotype affect postnatal performance
1189 of lambs. *Animal* **2**, 574-581.

1190 VAN DER LINDEN, D. S., KENYON, P. R., BLAIR, H. T., LOPEZ-VILLALOBOS, N.,
1191 JENKINSON, C. M. C., PETERSON, S. W., & MACKENZIE, D. D. S. (2009). Effects of
1192 ewe size and nutrition on fetal mammary gland development and lactational performance
1193 of offspring at their first lactation. *Journal of Animal Science* **87**, 3944-3954.

1194 VAN DER LINDEN, D. S., KENYON, P. R., LOPEZ-VILLALOBOS, N., JENKINSON, C. M.
1195 C., PETERSON, S. W., & BLAIR, H. T. (2010). Effects of ewe size and nutrition during
1196 pregnancy on performance of 2-year-old female offspring. *Journal of Agricultural Science*
1197 **148**, 465-475.

- 1198 VINCENT, I. C., WILLIAMS, H. L., & HILL, R. (1985). The influence of a low-utrient intake
1199 after mating on gestation and perinatal survival of lambs. *British Veterinary Journal* **141**,
1200 611-617.
- 1201 WALLACE, J. M., MILNE, J. S., GREEN, L. R., & AITKEN, R. P. (2011). Postnatal
1202 hypothalamic-pituitary-adrenal function in sheep is influenced by age and sex, but not by
1203 prenatal growth restriction. *Reproduction Fertility and Development* **23**, 275-284.
- 1204 WALLACE, J. M., REGNAULT, T. R. H., LIMESAND, S. W., HAY, W. W., & ANTHONY, R.
1205 V. (2005a). Investigating the causes of low birth weight in contrasting ovine paradigms.
1206 *Journal of Physiology-London* **565**, 19-26.
- 1207 WALLACE, J. M., MILNE, J. S., & AITKEN, R. P. (2005b). The effect of overnourishing
1208 singleton-bearing adult ewes on nutrient partitioning to the gravid uterus. *British Journal*
1209 *of Nutrition* **94**, 533-539.
- 1210 WALLACE, J. M., MILNE, J. S., & AITKEN, R. P. (2010). Effect of weight and adiposity at
1211 conception and wide variations in gestational dietary intake on pregnancy outcome and
1212 early postnatal performance in young adolescent sheep. *Biology of Reproduction* **82**, 320-
1213 330.
- 1214 WU, G., BAZER, F. W., WALLACE, J. M., & SPENCER, T. E. (2006). BOARD-INVITED
1215 REVIEW: Intrauterine growth retardation: Implications for the animal sciences. *Journal of*
1216 *Animal Science* **84**, 2316-2337.

Table 1 Summary of pre-weaning outcomes of under-nutrition (UN) studies classified by stage of gestation when UN applied

| Study | Stage | Severity (of control) | Birth-weight | Survival | Maternal care Lamb behaviour | Others /comment |
|------------------------------|-------|--------------------------|--------------|----------|------------------------------------|--|
| Vincent <i>et al.</i> 1985 | EM | 0.15 | ↓ | ↓ | | |
| Holst <i>et al.</i> 1986 | EM | (0.6) | ↑O | ↓ | | ↑ O: in 2 of 3 years of study |
| Kleeman <i>et al.</i> 1993 | EM | (0.6-0.8) | O | O | | |
| Erhard <i>et al.</i> 2004 | EM | 0.5 | O | | | |
| Burt <i>et al.</i> 2007 | EM | 0.5 | ↓O | | | ↓ O : in sedentary but not rangeland ewes |
| Corner <i>et al.</i> 2008 | EM | (0.6-0.8) | O | | | |
| Munoz <i>et al.</i> 2008b | EM | 0.6/0.8 | O | | O | |
| Hernandez <i>et al.</i> 2009 | EM | (0.5) | O | | O | |
| Munoz <i>et al.</i> 2009 | EM | 0.6/0.8 | ↓O | | ↓ | ↓O different responses for 1- and 2-year-old ewes |
| Rooke <i>et al.</i> 2010 | EM | 0.75 | ↓O | ↓O | ↓ | ↓O different responses between ewe breeds |
| Ferguson <i>et al.</i> 2011 | EM | (0.7) | ↓O | ↓O | | ↓O different responses between sites; no effect on LWG |
| Kenyon <i>et al.</i> 2011 | EM | (0.6) | O | O | | |
| Khalaf <i>et al.</i> 1979 | L | 0.65 | ↓ | ↓ | | No effect on lamb plasma IgG |

| | | | | | |
|-----------------------------------|---|-----------|---|---|--|
| Holst <i>et al.</i> 1986 | L | (0.85) | ↓ | | |
| Bloomfield <i>et al.</i> 2003 | L | 0.02/0.04 | ↓ | | |
| Dwyer <i>et al.</i> 2003 | L | 0.65 | ↓ | | ↓ |
| Everett-Hincks <i>et al.</i> 2005 | L | (?) | ↓ | O | |
| Husted <i>et al.</i> 2007 | L | 0.5 | ↓ | | Decreased LWG to weaning |
| Corner <i>et al.</i> 2008 | L | (0.6-0.8) | ↓ | | ↓ |
| Banchero <i>et al.</i> 2009 | L | (?) | ↓ | ↓ | No difference in LWG to weaning |
| Swanson <i>et al.</i> 2008 | L | 0.6 | ↓ | O | Increased lamb plasma IgG in UN treatment |
| Tygessen <i>et al.</i> 2008 | L | 0.50 | ↓ | | Decreased weaning weight; interaction with sire genotype |
| Meyer <i>et al.</i> 2010 | L | 0.6 | ↓ | O | Increased lamb plasma IgG in UN treatment |
| Ferguson <i>et al.</i> 2011; | L | (0.7) | ↓ | ↓ | Decreased LWG to weaning |
| Kenyon <i>et al.</i> 2011 | L | (0.6) | ↓ | | |
| Wallace <i>et al.</i> 2011 | L | 0.75 | ↓ | | No difference in live-weight at weaning |

EM: UN period ends before GD100; L UN continues or begins after GD100. Severity of challenge: values in brackets are where severity of challenge not given by authors but estimated from data published)

↑, ↓, O, increase, decrease or not different from control group fed to meet requirement.

For studies with multiple references, first published study is cited.

Table 2. Summary of over-nutrition (ON) studies with pre-weaning outcomes

| Study | Stage | Birth-weight | Survival | Maternal care | Lamb behaviour | Other / comment |
|-----------------------------------|-------|--------------|----------|---------------|----------------|--|
| Everett-Hincks <i>et al.</i> 2005 | L | ↑ | O | | O | |
| Wallace <i>et al.</i> 2005b | L | O | | | | Adult ewes |
| Corner <i>et al.</i> 2006a | L | O | O | ↑ | | |
| Munoz <i>et al.</i> 2008b | EM | O | O | | ↓ | |
| Kenyon <i>et al.</i> 2009 | L | ↑ | O | | | ON increased birth-weight of F ₁ generation but reduced birth-weight of F ₂ generation |
| Munoz <i>et al.</i> 2009 | EM | ↑ O | O | O | ↓ | Different responses in 1- and 2-year-old ewes |
| Swanson <i>et al.</i> 2008 | L | ↓ | ↓ | | | No difference in LWG to weaning; lower plasma IgG in ON lambs |
| Meyer <i>et al.</i> 2010 | L | O | O | | | Lower plasma IgG in over-nutrition lambs |
| Ferguson <i>et al.</i> 2011 | L | O | O | | | No difference in LWG to weaning |
| Wallace <i>et al.</i> 2011 | L | ↓ | | | | Adolescent (8 month old) ewes; no difference in weaning live-weight. |

↑, ↓, O, increase, decrease or not different from control group fed to meet requirement. EM: ON period ends before GD100; L, ON continues or begins after GD 90-100.

For studies with multiple references, first published study is cited.

Table 3. Summary of studies where specific nutrient content of the diet is varied with pre-weaning outcomes

| Study | Nutrient | Period | Birth-weight | Survival | Plasma IgG | Lamb behaviour | Thermo-regulation | Weight gain | Control diet status / comment |
|-----------------------------|----------|------------|--------------|----------|------------|----------------|-------------------|-------------|-------------------------------------|
| Quirk & Norton 1987 | Co | Throughout | ↑ | | | | | ↑ | Deficient |
| Fisher & MacPherson 1991 | Co | Throughout | O | ↑ | | ↑ | | | Deficient |
| Mitchell <i>et al.</i> 2007 | Co | Early | O | | | ↓ | | | Marginal |
| Boland <i>et al.</i> 2005b | I | Late | O | | ↓ | | | | Adequate |
| Rose <i>et al.</i> 2007 | I | Late | ↑ | | ↓ | | | O | Adequate |
| Boland <i>et al.</i> 2008 | I | Late | ↓O | | ↓ | | | | Adequate |
| Munoz <i>et al.</i> 2008a | Se | Early/mid | O | ↑ | ↑ | ↑ | | ↑ | Marginal |
| Swanson <i>et al.</i> 2008 | Se | Throughout | O | O | ↓ | | | o | Adequate |
| Meyer <i>et al.</i> 2010 | Se | Throughout | O | O | | | | | Adequate |
| Kott <i>et al.</i> 1998 | Vit E | Late | O | ↑O | | | | ↑o | Marginal; response season dependant |
| Capper <i>et al.</i> 2005 | Vit E | Late | ↑ | | o | O | | | Adequate |
| Dafoe <i>et al.</i> 2008 | Vit E | Late | O | O | | | ↑ | | Adequate; response FA dependant |
| Rooke <i>et al.</i> 2009 | Vit E | Late | O | | | O | | | Adequate |
| Encinias <i>et al.</i> 2004 | FA | Late | O | ↑ | | | O | O | |

| | | | | | | | | | |
|----------------------------|----|------|---|---|---|---|---|---|---------------------------------------|
| Capper <i>et al.</i> 2005 | FA | Late | O | | | ↑ | | | |
| Chen <i>et al.</i> 2007 | FA | Late | O | | | | ↓ | | Level dependant |
| Dafoe <i>et al.</i> 2008 | FA | Late | O | O | | | ↓ | O | Vit E dependant |
| Pickard <i>et al.</i> 2008 | FA | Late | O | | | ↑ | | O | |
| Annett <i>et al.</i> 2008 | FA | Late | O | | ↓ | | | O | |
| Annett <i>et al.</i> 2009 | FA | Late | O | ↑ | ↓ | | | O | Survival: level of fish oil dependant |
| Keithly <i>et al.</i> 2011 | FA | Late | O | | | | | O | O |

↑, ↓, O, increase, decrease or not different from control group; adequacy of control diet is given where relevant. Co, cobalt; I, iodine; Se, selenium; Vit E, vitamin E; FA, fatty acids

For studies with multiple references, first published study is cited.

Table 4 Summary of studies where ewes were shorn[†] or other behavioural or physiological stress was applied to the ewe and resulting lamb pre-weaning outcomes were measured.

| Study | Stressor type | Birth-weight | Live-weight gain | Lamb behaviour | Lamb stress response | Other outcome | Comments |
|-------------------------------------|------------------------|--------------|------------------|----------------|----------------------|---------------|-------------------------|
| Roussel <i>et al.</i> 2004 | Social | ↑ | O | | O - cortisol | | |
| Roussel-Hachette <i>et al.</i> 2008 | Social | O | ↑O | | | | Ewe stressor dependant. |
| Stott & Slee 1985 | Husbandry | | | | ↑O - cold | | Ewe stressor dependant. |
| Kenyon <i>et al.</i> 2004 | Husbandry/ shearing | ↑ | O | | | | |
| Kenyon <i>et al.</i> 2005 | Husbandry/ shearing | ↑ | O | | | | |
| Corner <i>et al.</i> 2006b | Husbandry/ shearing | ↑O | | ↑ | | O - MB | Ewe stressor dependant. |
| Corner <i>et al.</i> 2007 | Husbandry/ shearing | ↑O | | | O - cortisol | | Twin lambs only |
| Jenkinson <i>et al.</i> 2007 | Husbandry/ shearing | ↑ | O | | | | Twin lambs only |
| Keady <i>et al.</i> 2007 | Husbandry/ shearing | ↑ | ↑ | | | O-survival | |
| Keady & Hanrahan 2009 | Husbandry/ shearing | ↑ | O | | | O-survival | |

| | | | | | | |
|--------------------------------|------------------------|----|---|---|-------------|------------------------|
| Banchero <i>et al.</i> 2010 | Husbandry/ shearing | ↑O | | ↑ | | Twin lambs only |
| Corner <i>et al.</i> 2010b | Husbandry/ shearing | ↑ | O | | | |
| Cal-Pereyra <i>et al.</i> 2011 | Husbandry/ shearing | ↑ | | | | |
| Sphor <i>et al.</i> 2011 | Husbandry/ shearing | ↑ | ↑ | | | |
| Hild <i>et al.</i> 2011 | Husbandry | ↑ | | O | ↑ - MB | |
| Roghair <i>et al.</i> 2005 | Artificial | ↑ | | | | |
| De Blasio <i>et al.</i> 2007 | Artificial | ↓O | | | | Ewe stressor dependant |
| Miller <i>et al.</i> 2009 | Artificial | O | | ↓ | O -survival | |
| Corner <i>et al.</i> 2010b | Artificial | ↓ | O | | | |

↑, ↓, O, positive or negative change or not different from control group.

† Studies recorded for shearing of ewes are in addition to those cited by Kenyon *et al.* 2003.

Appendix Table S1 Summary of under-nutrition (UN) and over-nutrition (ON) with pre-weaning outcomes

| Study | Over / under nutrition | Maternal treatment | Offspring outcome |
|----------------------------|------------------------|---|--|
| Khalaf <i>et al.</i> 1979 | Under | Nutrition restricted from GD100 to term; two treatments: either 0.6 or 0.9 requirement | In twin lambs, birth-weight decreased, reduced more with more severe UN. Mortality greater in lambs from more severely undernourished ewes which also exhibited slower growth rates. No treatments effects on lamb IgG status. |
| Vincent <i>et al.</i> 1985 | Under | Nutrition restricted to 0.15 requirement from mating until GD60 | Birth-weight reduced and poorer survival for first 48h after birth |
| Holst <i>et al.</i> 1986 | Under | In three experiments, 2 x 2 factorial arrangement of UN between GD45 and GD105 and from GD105 to term. UN estimated as 0.6 and 0.9 of requirement in mid and late gestation | Effects most marked in twins. In all years late UN reduced birth-weight whilst in 2 of 3 years UN in mid gestation increased birth-weight. Mid gestation UN increased lamb mortality. |

| | | | |
|-----------------------------------|--------------|--|---|
| Kleeman <i>et al.</i> 1993 | Under | Designed as 2 x 2 factorial experiment but estimation of UN suggests that only under-nourished between GD 50 and GD100 (0.7 requirement) | No differences observed in birth-weight and survival |
| Bloomfield <i>et al.</i> 2003 | Under | Between GD105 and GD115 or GD105 and GD125, ewes were severely undernourished (0.3 MJ/day; control 14 MJ/day). | Birth-weight reduced progressively with length of UN period |
| Dwyer <i>et al.</i> 2003 | Under | Nutrition restricted to 0.65 of requirement from GD28 to term. | Birth-weight reduced. No direct effect on progression of lamb through behavioural repertoire from birth to suckling. UN had adverse effects on maternal behaviour (reduced licking of lamb; increased aggressiveness towards lamb; poorer maternal attachment scores) |
| Erhard <i>et al.</i> 2004 | Under | Between mating and GD95, ewes fed 0.5 or 1.0 requirement. | No difference in birth-weight |
| Everett-Hincks <i>et al.</i> 2005 | Under / Over | Pasture allowance varied from 800 to 2000 kg DM /ha from GD64 to term. Difficult to estimate intake as proportion of requirement but likely 800 is under and 2000 ON | Birth-weight reduced in 800 and increased in 2000 kg pasture allowances. No differences in lamb survival. Minor differences in lamb behaviour. |

| | | | |
|---|-------|--|---|
| Wallace <i>et al.</i> 2005 | Over | Adult ewes fed to meet requirements or ad libitum (approx. 1.8 requirements throughout gestation) | No difference in birth-weight |
| Corner <i>et al.</i> 2006a (Morris <i>et al.</i> 2005) | Over | Ewe pasture allowance from GD13 managed to maintain or increase ewe conceptus-free Birth-weight by 0.075 or 0.15 kg/day | No effect on birth-weight. No effect on survival. Maternal behaviour score superior on highest plane of nutrition. |
| Burt <i>et al.</i> 2007 | Under | Ewes of two contrasting long-term (30 yr) management histories (severe range-land or sedentary) fed 0.5 of requirement between GD28 and GD74 | Birth-weight reduced in sedentary but not range-land ewes. |
| Husted <i>et al.</i> 2007 | Under | Nutrition restricted to 0.5 of requirement from GD100 | Birth-weight reduced by UN. LWG to day 70 post-natal reduced by UN |
| Corner <i>et al.</i> 2008 (Corner <i>et al.</i> 2010) | Under | Using 2 x 2 factorial allowance, ewes allocated to two pasture allowances (700 or 1300 kg DM/ha) between GD70 and GD107 or GD107 and term. From maternal live-weight change only ewes maintained on 700 kg DM/ ha under-nourished (estimated 0.6 – 0.8 of requirement) | Birth-weight reduced on 700 kg DM/ha throughout allowance. Low-pitched ewe bleats less frequent on UN (poorer maternal care). Differences in lamb bleats. |

| | | | |
|------------------------------|------------|--|--|
| Munoz <i>et al.</i> 2008b | Under/Over | 3 x 2 factorial arrangement of nutrition; between mating and GD39 (early), adult ewes fed 0.6, 1.0 or 2.0 requirement and between GD40 and GD90 (mid), 0.8 and 1.4 of requirement | Birth-weight of early UN greater than feeding to meet or exceed requirement. No other birth-weight differences. No differences in mortality. No differences in lamb behaviour due to early treatments. Lambs from over (1.4 requirement) nutrition in mid pregnancy slower to progress through behaviours to suckling: difficult to interpret because comparison is with UN. |
| Tygesen <i>et al.</i> 2008 | Under | Ewes mated with either high or low index (<i>L. dorsi</i> cross-sectional area) sire and fed 0.50 of energy intake of controls. | Overall birth-weight reduced. Interaction with sire: birth-weight reduction greater with high index sire. Weaning weight of high index sired lambs also reduced |
| Banchero <i>et al.</i> 2009 | Under | From GD130 ewes maintained on native or improved pasture with or without supplementary feed; Difficult to judge degree of UN (no pasture intakes) and there may have been long-term UN prior to GD130 (maintained on poor quality native pasture). | Birth-weight lower and survival poorer on native pasture only diet. |
| Hernandez <i>et al.</i> 2009 | Under | Ewes fed approximately 0.5 of requirement from 60 days before to GD30 | No differences in birth-weight or ewe and lamb behaviours |

| | | | |
|--|------------|--|--|
| Kenyon <i>et al.</i> 2009, 2011; van der Linden <i>et al.</i> 2009, 2010 | Over | Using a 2 x 2 factorial design, heavy and light ewes from the same flock were maintained on pasture (1330 v 2304 kg DM/ha) allowances designed to provide maintenance or ad libitum intakes between GD21 and GD140 | Lambs born to ad lib ewes were heavier at birth and weaning. However, lamb birth-weight and weight gain of female lambs from ad lib ewes were less and slower than maintenance treatment. |
| Munoz <i>et al.</i> 2009 | Under/Over | 3 x 2 factorial arrangement of nutrition between mating and GD39 (early), one or two year old ewes fed 0.6, 1.0 and 2.0 requirement and between GD40 and GD90 (mid) 0.8 and 1.4 of requirement. | <p>Birth-weight tended to be greater in 2.0 early treatment in 1 year old ewes; birth-weight was lower in 0.6 requirement, early treatment in 2 year old ewes.</p> <p>Survival tended to be poorer in lambs from 1 year old under-nourished ewes; no difference in 2 year old ewes.</p> <p>Ewes (1 year old) undernourished in early pregnancy showed reduced maternal care. In mid-pregnancy under-nourished ewes exhibited better maternal care and their lambs suckled faster than over-nourished ewes.</p> |
| Swanson <i>et al.</i> 2008; Neville <i>et al.</i> 2010; Hammer <i>et al.</i> (expt 1;2011) | Under/Over | Between GD50 and term, ewes were fed 0.6, 1.0 or 1.4 of requirement | Birth-weight was reduced in both under and ON treatments. No difference in weight gain to weaning. Mortality greater in ON treatment. Lamb plasma IgG greater in UN treatment and reduced in ON treatment. |

| | | | |
|---|------------|--|--|
| Meyer <i>et al.</i> 2010; Hammer <i>et al.</i> expt 2, 2011 | Under/Over | Between GD40 and term, ewes were fed 0.6, 1.0 or 1.4 of requirement | Birth-weight and early LWG (to day 19) tended to be reduced in UN treatment. No difference in mortality. Lamb IgG was greatest in under and lowest in ON treatment. |
| Rooke <i>et al.</i> 2010 | Under | Using a 2 x 2 factorial design, ewes of two contrasting breeds were fed 0.75 or 1.0 requirement from GD1 to GD90 | While birth-weight of a breed selected for rapid lean tissue growth was reduced by UN, there was no effect on a breed selected to withstand a harsh environment. Survival was poorer in lambs from under-nourished ewes. UN ewes expressed poorer levels of maternal care. UN lambs were slower to progress through behaviour to suckling. |
| Ferguson <i>et al.</i> 2011; Oldham <i>et al.</i> 2011; Thompson <i>et al.</i> 2011 | Under/Over | Multisite / multiyear experiment (2 year/ 2 sites). 2 x 5 factorial design. Ewes fed to lose / maintain weight/condition score between GD0 and GD100 and then offered 5 pasture allowances (800, 1100, 1400, 2000 and >3000 kg DM /ha) from GD100 until weaning. From weights, GD0-100 UN estimated 0.7 requirement. Post GD100 all treatments appear greater than requirement with possible exception of 800 kg DM/ha | Early (GD0 to GD100) UN: birth-weight reduced in 2 of 4 (site/year) combinations. No effect on lamb survival or LWG to weaning. GD100 to term: In 3/4 site/year occasions, birth-weight reduced at 800 kg DM/ha. No differences between higher allowances. Same effect for survival and weaning weight. |

| | | | |
|----------------------------|------------|---|--|
| Kenyon <i>et al.</i> 2011 | Under/Over | Using a 3 x 2 factorial design ewes were offered pasture to achieve intakes equivalent to 0.6, 1.0 and 1.5 requirement between GD30 and GD50 and to meet 1.0 or 1.5 requirement between GD50 and term | No effect of early (GD30 to GD50) nutrition on birth-weight or LWG to weaning; Lambs born to ON ewes (GD50 to term) were lighter at birth. |
| Wallace <i>et al.</i> 2011 | Under/Over | Ewes (8 month old) consumed 0.75, 1.0 or ~2.2 requirement from GD7 to term. | Both under and ON reduced birth-weight; no difference in live-weight at weaning. |

Appendix Table S2 Summary of studies where specific nutrients in ewe diet were changed and resulting lamb pre-weaning outcomes

| Study | Nutrient | Maternal treatment | Offspring outcome |
|-----------------------------|----------|---|---|
| Quirk & Norton, 1987 | Co | Ewes grazing low Co (<0.1 mg/kg DM) supplemented with 0.03 or 0.06 mg Co /day throughout gestation | Birth-weight and LWG to weaning increased by supplementation; no difference between levels of Co. |
| Fisher & MacPherson 1991 | Co | Ewes fed Co deficient (0.06 mg/kg DM) or supplemented (0.1 mg Co/day). Supplemented diets fed throughout; from GD0 to GD74; or from GD74 to term. | Mortality reduced by supplementation; no effect on birth-weight; lamb behavioural progress faster with supplementation throughout; supplementation GD0- GD74 intermediate |
| Kott <i>et al.</i> 1998 | Vit E | Supplementary vitamin E fed from GD120; increased intake from 20 to 158 mg/ kg diet DM | Season dependant response. In first half of lambing season supplementation reduced mortality and increased growth rate to weaning. |
| Encinias <i>et al.</i> 2004 | FA | Ewes fed diet in which safflower seed replaced maize from GD100 | No difference in birth or weaning weight. Survival improved with safflower. No evidence for improved thermoregulation with safflower seed. |

| | | | |
|----------------------------------|------------|---|--|
| Boland <i>et al.</i> 2005b, 2006 | I | <p>Expt 1 Ewes fed supplements from GD100 containing supplementary minerals; minerals with iodine excluded or iodine only (40 mg/day)</p> <p>Expt 2 Ewes fed from GD100 with 9, 18 and 27 mg I /day</p> | <p>Expt 1 no effect on birth-weight or colostrum intake; I only or all minerals depress lamb IgG absorption and plasma vitamin E concentration</p> <p>Expt 2 Progressive depression in lamb plasma IgG and vitamin E concentration as amount of I fed increased.</p> |
| Capper <i>et al.</i> 2005, 2006 | FA / Vit E | <p>Using a 2 x 2 factorial design ewes were fed from GD100, low (50 mg/kg) or high (500 mg/kg) vitamin E and saturated (Megalac) or unsaturated (fish oil) fatty acid (60 g/kg) containing diets</p> | <p>Vitamin E: increased birth-weight; no effect on maternal care or lamb behaviours.</p> <p>Fatty acids: no effect on birth-weight; lambs born to fish oil fed ewes suckled more quickly.</p> |
| Chen <i>et al.</i> 2007 | FA | <p>Using a 2 x 3 factorial design ewes were fed from GD107, diets containing 20, 40 or 80 g / kg, saturated or polyunsaturated fatty acid (linseed) supplements</p> | <p>No birth-weight differences. Rectal temperature after cold exposure lower on 80 g/kg diet (no fatty acid effect) and ability to oxidize fatty acids reduced.</p> |
| Mitchell <i>et al.</i> 2007 | Co | <p>Ewes were supplemented or not supplemented with a Co bolus 24 days before mating.</p> | <p>No birth-weight differences. Supplemented lambs slower to progress through behavioural milestones.</p> |

| | | | |
|----------------------------|------------|--|--|
| Rose <i>et al.</i> 2007 | I | Ewes were supplemented with increasing amounts of I from GD102; 6 levels from 0 to 20 mg/kg diet DM: | Birth-weight increased with increasing I supplementation; no difference in weaning weights. Plasma IgG at 24 h of age decreased linearly with I supplementation |
| Boland <i>et al.</i> 2008 | I | Ewes were fed no supplementary or 27 mg/day from GD126 or 27 mg /day from GD140. | I fed for 7 days reduced birth-weight; fed for 21 d - no reduction. Lamb plasma IgG at 24 h of age reduced more severely by feeding I for 21 d rather than 7 d. Lamb plasma vitamin E reduced by I supplement at 72 h of age. |
| Munoz et al 2008a | Se | Ewes fed supplement (or not) of 0.5 mg Se / day from mating to GD90. | No difference in birth-weight but mortality lower in Se-supplemented treatment. Se-supplemented lambs grew fast to weaning. Plasma IgG higher in Se-supplemented lambs and these lambs showed more rapid behavioural progress. |
| Dafoe <i>et al.</i> 2008 | FA / Vit E | Using a 2 x 2 factorial design, from GD100 to GD135 ewes were fed either barley or safflower seed (PUFA) based diets with or without 350 mg/kg vitamin E | No differences in birth-weight, weaning weight or mortality. Thermoregulation was poorer in safflower seed diet with no vitamin E supplement. |
| Pickard <i>et al.</i> 2008 | FA | From GD80 onwards, ewes were fed or not fed a supplement containing 12 g DHA / day between | No difference in birth-weight or live weight gain. All supplemented lambs were quicker to stand |

| | | | |
|---|-------|--|---|
| | | GD84 and GD105, GD84 and GD126, GD84 and term | than un-supplemented lambs. |
| Annett <i>et al.</i> 2008 | FA | Ewes were fed barley-based diet containing or not containing fish oil (74 g/kg) from GD105 | Feeding fish oil had no effect on birth or weaning weights but reduced lamb plasma IgG at 24 h of age. |
| Annett <i>et al.</i> 2009 | FA | Ewes were fed 20 or 40 g/day of either herring or salmon oil from GD105 | Feeding fish oil reduced ewe colostrum IgG output and lamb IgG concentration at 24 h of age. No effect on lamb birth or weaning weight. Lamb survival improved by fish oil; quadratic response with benefits greatest at 20 g/day |
| Rooke <i>et al.</i> 2009 | Vit E | Ewes were fed increasing amounts (from 50 to 250 mg/day from GD98). | No effect of vitamin E on birth or weaning weights, or upon behavioural progress of lambs to suckling |
| Swanson <i>et al.</i> 2008; Neville <i>et al.</i> 2010; Hammer <i>et al.</i> expt 1; 2011 | Se | From mating, ewes were offered adequate (10 µg /kg live-weight) or high Se (82 µg/kg live-weight). | No effect on birth or weaning weights; plasma IgG at 24 h of age lower in high Se; no effect on mortality. |

| | | | |
|---|----|---|--|
| Meyer <i>et al.</i> 2010; Hammer <i>et al.</i> expt 2, 2011 | Se | From mating, ewes were offered adequate (4 µg /kg live-weight) or high Se (65 µg/kg live-weight). | No effect on birth-weight; no effect on mortality of plasma IgG at 24 h of age |
| Keithly <i>et al.</i> 2011 | FA | From GD117, ewes were fed or not fed 12 g DHA / day. | No effect on birth-weight but DHA-treatment lighter at 38 days of age. No difference in thermoregulation |

Table S3 Summary of studies where a behavioural or physiological stress was applied to the ewe and resulting lamb pre-weaning outcomes were measured.

| Study | Stressor type | Maternal treatment | Offspring outcome |
|----------------------------|-------------------------|---|--|
| Stott & Slee 1985 | Environment / Husbandry | Ewes either maintained in warm (26 °C) or control environment (6°C) or cold stressed (shorn and exposed to -20 °C for 2h daily for 7 d) from GD133. | Lambs from cold-stressed ewes had smaller decrease in rectal temperature at 12 h old than control or warm treatments and greater increase in metabolic rate in response to adrenaline challenge at 36 h old. |
| Moss <i>et al.</i> 2001 | Artificial | Ewes given a single (1 x ;GD104) or four (4 x; GD104, GD111, GD118, GD125) injections with betamethasone | Survival of 4x treated lambs lesser than control or 1x lambs. Birth and 3 month of age weight lower in 4x lambs; 1x birth-weight intermediate. |
| Kenyon <i>et al.</i> 2004 | Husbandry / shearing | Twin-bearing ewes were shorn at GD70 | Lamb birth-weight increased by shearing. Weaning weights but not rate of weight gain to weaning increased. |
| Roussel <i>et al.</i> 2004 | Social | Ewes isolated for 1h in presence of absence of dog weekly for last 5 weeks of pregnancy (total of 10 occasions) | Pre-natally stressed lambs had greater birth-weights but no difference at 8 month of age. Cortisol response to isolation at 25 d old not different. |
| Kenyon <i>et al.</i> 2005 | Husbandry / shearing | Twin bearing ewes shorn or not shorn at day 70; unshorn ewes not treated or treated with thyroxine (GD55, GD70, GD115) with or without thyroidectomy (GD55) | Lamb birth-weight increased by shearing; no effect of thyroid treatments. No treatment effect on weaning weights. |

| | | | |
|-------------------------------------|----------------------|---|--|
| Roghair <i>et al.</i> 2005 | Artificial | Ewes infused with betamethasone continuously for 48 h at GD27 | Birth-weight greater in treated lambs (but litter size smaller) |
| Corner <i>et al.</i> 2006b | Husbandry / shearing | Ewes were fasted for 24 h and handled with dogs on GD79 and GD80 and then not shorn (yarded) or shorn (shorn). | Shorn treatment increased lamb birth-weight; yarded no effect. No treatment effect on maternal behaviour but fewer lambs from shorn treatment did not suckle successfully. |
| De Blasio <i>et al.</i> 2007 | Artificial | Ewes infused with betamethasone or cortisol continuously for 48 h at GD27 | Birth-weight tended to be lower in betamethasone treatment; cortisol no effect. |
| Corner <i>et al.</i> 2007 | Husbandry / shearing | Ewes shorn or not shorn on GD79 | Birth-weight greater in shorn treatment; no differences in cortisol response to stress (castration) between treatments. |
| Roussel-Hachette <i>et al.</i> 2008 | Social | Ewes were either isolated in presence or absence of dog or transported in isolation for 1 h; treatments applied on 10 occasions over last 5 weeks or pregnancy. | No effect of treatments on birth-weight but lambs from isolated treatment heavier at 3 months than control or transport treatments. |
| Keady & Hanrahan. 2009 | Husbandry / shearing | Ewes shorn or not shorn on GD63 | Birth-weight increased by shearing. Weaning weights and weight gain to weaning not increased by shearing. No difference in mortality. |
| Miller <i>et al.</i> 2009 | Artificial | Ewes injected with dexamethasone (low or high dose) on either GD130 or GD141 of pregnancy. | No effect of treatment on birth-weight or survival. Lambs born to dexamethasone treated ewes latency to bleat longer; no other differences in lamb behaviour. |
| Banchero <i>et al.</i> | Husbandry / | Treatments were shearing of the ewe at GD70 or | Birth-weight of twin lambs greater on day 70 |

| | | | |
|--------------------------------|----------------------|---|---|
| 2010 | shearing | GD120 of gestation. | treatment than day 100 than unshorn treatments; singletons not significant. More lambs from both shorn treatments suckled successfully than controls irrespective of litter size. |
| Corner <i>et al.</i> 2010b | Husbandry / shearing | Ewe treatments applied: (a) isolation for 1h on 2 occasions (GD75 ,GD78); (b) isolation for 1 h on 10 occasions (between GD75 and GD105; (c) injection of cortisol on 10 occasions between GD75 and GD105; (d) sham-shorn on 10 occasions between GD75 and GD105; (e) shorn on GD76 | Birth-weight increased by shorn and decreased by cortisol treatments. No differences from control in live-weight at 63 days old. |
| Cal-Pereyra <i>et al.</i> 2011 | Husbandry / shearing | Ewes shorn or not shorn on GD110 | No Birth-weight increase in response to shearing. |
| Hild <i>et al.</i> 2011 | Husbandry | Ewes daily subjected to gentle or aversive handling for last 32 days of pregnancy | Aversive treatment resulted in tendency for greater weight at 24h of age; no differences in lamb neonatal behaviours; ewes aversively handled groomed lambs for longer.. |
| Sphor <i>et al.</i> 2011 | Husbandry / shearing | Ewes shorn or not shorn on GD53 | Single-bearing ewes only; increase in birth-weight and weaning weight and rate of gain to weaning in response to shearing |
