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Published in:
Journal of Agricultural Science

DOI:
10.1017/S002185961400077X

First published: 01/01/2015

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

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SUMMARY

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

INTRODUCTION

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

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

MATERIALS AND METHODS

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

Searches

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

Search results and classification

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

Quality assessment

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

Organisation of review process

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

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

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

RESULTS

Nutrition

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

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

Under-nutrition: birth-weight

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

Where UN ended before GD100 (early/mid gestation), more variable responses were observed. Studies were categorised according to the extent of UN (relative to maintenance requirement): severe, <0.4; moderate, between 0.4 and 0.8; mild, between 0.8 and 1.0. Where authors stated a level of UN this was adopted, otherwise the extent of UN was estimated from either food intake and / or ewe LW change. The most severe UN challenge before GD100 was imposed by Vincent *et al.* (1985), who restricted ewes to 0.15 of requirement between GD0 and GD60. Birth-weight was reduced from 4.3 to 3.6 kg and there was an accompanying increase in mortality (from 6 to 42 %), with the lambs most prejudiced by low birth-weight not surviving. Holst *et al.* (1986) imposed moderate UN from mating to GD103 and replicated the experiment over three years. There were no decreases in birth-weight or increases in mortality; in two of three years, birth-weight was actually increased in lambs born to UN ewes. A series of studies, (UN from 60 days before mating until GD30 (Hernandez *et al.* 2009); UN between GD30 and GD50 of pregnancy (Kenyon *et al.* 2011); UN between GD50 and GD100 (Kenyon *et al.* 2002b; Kleemann *et al.* 1993) imposed moderate UN without effect on birth-weight.

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

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

Under nutrition: mortality

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

Under-nutrition: maternal and lamb behaviours

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

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

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

Under nutrition: passive immune transfer and thermoregulation

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

Under nutrition: weaning weights and weight gain to weaning

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

Over-nutrition

Although the seasonality of sheep production means that UN is more likely to be encountered than ON, it is necessary to consider whether benefits in welfare outcomes are possible if requirements for maternal body maintenance and the normal growth of the products of conception are exceeded. An ovine model (Wallace *et al.* 2005a) for the consequences of teenage pregnancy in the human is relevant. Pregnancies were established in adolescent (8 month old Dorset Horn x Greyface) ewes by embryo transfer. When these ewes were offered a high quality diet ad libitum, they consumed approximately 2-times energy requirements (Wallace *et al.* 2005a). These ON adolescent ewes partitioned nutrients to maternal growth at the expense of foetal growth such that lamb birth-weight was reduced by 30%. This reduction in birth-weight is more severe than that observed with UN (Wallace *et al.* 2010). Further this effect was not observed with adult ewes (Wallace *et al.* 2005b). A number of research groups have examined the consequences of ON in a more practical setting (see Table 2 and Appendix Table S1 for details).

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

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

In a multi-year, two site study, Merino ewes were allocated to a range of herbage allowances (800 to >3000 kg herbage DM / ha) from GD100 to term and maintained on these pastures until weaning (Ferguson *et al.* 2011). Thus prenatal effects may be confounded by differing ewe intakes post-lambing. It was difficult to ascertain the impact of herbage allowance on ewe nutritional status as ewe condition scores were not reported. However, the allowances offered cover the range from UN to meeting requirement at the lower allowances to ON at the highest allowance. Responses in birth-weight and survival to 48 h were only found at the two lowest herbage allowances (representing either UN or maintenance; 800 and 1100 kg DM/ ha; Oldham *et al.* 2011) above which there were no differences. Therefore there was no evidence for any responses to ON.

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

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

Specific nutrients

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

Cobalt

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

Iodine

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

Selenium

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

More recently, two dietary models have been used to assess the effects of Se supplementation. Munoz *et al.* (2008a) supplemented or did not supplement adult ewes with 0.5 mg/day of organic Se from 14 days before mating to GD90. The Se status of the ewes prior to the experiment was marginal as was the control diet. Se supplementation did not influence birth-weight. However lambs born to Se-supplemented ewes were quicker to progress through the neonatal behaviour repertoire than control lambs, LWG to weaning was improved and mortality reduced. In two studies (Meyer *et al.* 2010; Neville *et al.* 2010), ewes were fed a Se-adequate (approximately 0.3 mg/d) or Se-supplemented diet (organic-Se; approximately 5 mg/day) throughout pregnancy. There was no difference in lamb birth-weight, LWG, mortality or plasma IgG concentration with Se supplementation in either study (Hammer *et al.* 2011).

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

Vitamin E (α-tocopherol)

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

In summary, for the three trace elements Co, I and Se and vitamin E, an inadequate supply during pregnancy can have adverse consequences for lamb outcomes. The potential for response will depend on several factors but sub-optimal maternal status is likely to be important. However, evidence for responses to supplementation above requirement are either non-existent (Co) or equivocal, with adverse effects being observed for I and no or positive effects for Se and vitamin E. For positive welfare outcomes, it is therefore important that adequate mineral and vitamin supplementation of the maternal diet is provided particularly during the last trimester of pregnancy.

Fatty acids

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

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

Two dietary models have been used to supply n-3 FA, inclusion of fish oil, or to specifically increase DHA content, by inclusion of an algal DHA source. Capper *et al.* (2005, 2006) included FA in the diet from GD103 as either saturated or n-3 FA in the presence or absence of supplementary vitamin E. Although inclusion of n-3 FA had no birth-weight effect, lambs borne to n-3 FA-fed ewes tended to stand and suck quicker than their saturated FA-fed controls, indicative of improved lamb vigour. Pickard *et al.* (2008) fed DHA from algal biomass for varying periods between GD84 and term. Feeding DHA for longer than 6 weeks reduced the time lambs took to stand after birth with no differences in birth-weight or LWG. Annett *et al.* (2008) increased the n-3 FA content of diets from GD100. The diets were fed with low or high digestible undegradable protein (DUP) contents in a 2 x 2 factorial design. Feeding n-3 FA in the presence of high DUP had no effect on lamb birth-weight, plasma IgG concentration or LWG. However, in the presence of low DUP, survival of lambs was poorer and plasma IgG lower when n-3 FA were fed. This effect is likely to have been mediated by reduced ewe colostrum output for this diet combination possibly as a result of lower ewe feed intakes and so the poorer survival of these lambs may not have been a prenatal effect. In a subsequent experiment, Annett *et al.* (2009) fed two levels of fish oil (the greater of the two levels, 40 g/kg being equivalent to Annett *et al.*, 2008) and ceased feeding the fish oils 24 h after birth. Although colostrum IgG output and lamb plasma IgG concentration at 24 h of age was reduced by feeding fish oil, lamb survival was improved particularly at the lower level of fish oil inclusion. Keithly *et al.* (2011) fed ewes algal biomass (similar to Pickard *et al.* (2008)) from GD100. Lambs born to ewes fed DHA did not differ in birth-weight from controls but tended to maintain higher body temperature when exposed to a cold challenge (0ºC for 30 min at 1h after birth). Lambs born to DHA-fed ewes grew slower to 38 days of age; this again may be attributed to poor colostrum and milk quality as milk fat was lower in both colostrum and milk from DHA-fed ewes. Keithly *et al.* (2011) fed the experimental diets until day 38 of lactation and therefore effects on milk composition and lamb LWG again may not be prenatal effects. In summary, where responses can be attributed solely to effects during gestation (birth-weight or lamb vigour; Annett *et al.* 2009; Capper e*t al.* 2006; Pickard *et al.* 2008), positive effects of feeding n-3 acids have been reported; the adverse effects noted by Annett *et al.* (2008) and Keithly *et al.* (2011) need consideration in a practical situation.

Stress

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

Shearing

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

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

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

Other responses

Corner *et al.* (2006b, 2007, 2010b) focussed on the effects of shearing ewes in mid-pregnancy in conjunction with other treatments. In the first experiment (Corner *et al.* 2006b), ewes were gathered on GD80, fasted for 24h and then shorn or not shorn. Fewer lambs borne to shorn ewes failed to suck than control ewes or ewes housed and fasted for 24 h but not shorn. Corner *et al.* (2010b) compared control ewes with ewes that (a) were isolated for 1 h on two or ten occasions; (b) ewes that were shorn and importantly (c) ewes that were sham-shorn (not shorn but otherwise treated identically to shorn ewes). Only in the shorn treatment was birth-weight increased, suggesting that the birth-weight response was not related to acute stress associated with shearing but a physiological response of the ewe to removal of the fleece. Banchero *et al.* (2010) in each of two experiments sheared ewes on either GD70 or GD120. In both experiments, there were improvements in behavioural progress of the lamb to sucking consequent upon shearing, suggesting there are responses to shearing which could not be attributed directly to increased birth-weight.

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

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

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

Thus there appears to be a marked difference in outcomes between behavioural and chemical stress-treatments applied to ewes (see Table 4 for summary). Whereas behavioural stress had no adverse consequences for lamb birth-weight or behavioural progression, chemical stress in late pregnancy had adverse consequences for birth-weight. Consistent with this, when Corner *et al.* (2010b; see above) applied a variety of behavioural stressors with no adverse outcomes, a ewe treatment designed to mimic these events by injection with cortisol reduced birth-weight.

DISCUSSION

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

Characteristics of challenge: severity

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

Characteristics of challenge: additivity

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

Characteristics of challenge: shearing

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

Characteristics of challenge: other studies

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

Characteristics of ewe: body reserves

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

Characteristics of ewe: breed

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

Characteristics of ewe: age

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

Characteristics of offspring: sex

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

Characteristics of offspring: litter size

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

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

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

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

Negative maternal stressors with negative lamb impacts

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

Positive maternal treatments with positive lamb impacts

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

Negative maternal stressors with positive neonatal lamb impacts

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

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

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

Positive maternal stressors with negative lamb impacts

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

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

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

A second consequence of the foetal origins hypothesis is the idea of the “predictive adaptive response” (Nettle *et al.* 2013). Thus the environment the foetus experiences during development primes it to alter its phenotype for the environment it is likely to experience during post-natal life through changes in gene expression and epigenetic mechanisms (Ford & Long 2012). Adverse consequences for adult health occur when the post-natal environment is not as expected (‘environmental mismatch’), e.g. when foetal UN is followed by plentiful nutrient supply during adult life. In most of the material reviewed here, a negative impact on the dam (e.g. UN) had a negative consequence for the offspring (e.g. lower birth-weight) probably directly through a reduction in nutrient supply to the foetus rather than by other mechanisms. Perhaps the one clear example of the effect of the foetal environment is demonstrated in the study (Kenyon *et al.* 2009; van der Linden *et al.* 2009,. 2010) where ewes were offered maintenance or ad libitum pasture and birth-weights of lambs were greater (5.7 v 5.2 kg) when ad libitum pasture was offered. When these ewe lambs were mated and fed to requirement throughout pregnancy (i.e. not ad libitum), lambs whose grand-dams had been fed maintenance were heavier (4.7 v 4.3 kg) at birth than lambs whose grand-dams had been fed ad libitum. Thus, ewe-lambs who dams had experienced maintenance conditions in utero were more able to cope with similar conditions when they became pregnant themselves than ewe-lambs which had been fed ad libitum.

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

ACKNOWLEDGEMENTS

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

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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 *et al.* 1985	EM	0.15	↓	↓		
Holst *et al.* 1986	EM	(0.6)	↑O	↓		↑ O: in 2 of 3 years of study
Kleeman *et al.* 1993	EM	(0.6-0.8)	O	O		
Erhard *et al.* 2004	EM	0.5	O			
Burt *et al.* 2007	EM	0.5	↓O			↓ O : in sedentary but not rangeland ewes
Corner *et al.* 2008	EM	(0.6-0.8)	O			
Munoz *et al.* 2008b	EM	0.6/0.8	O		O	
Hernandez *et al.* 2009	EM	(0.5)	O		O	
Munoz *et al.* 2009	EM	0.6/0.8	↓O		↓	↓O different responses for 1- and 2-year-old ewes
Rooke *et al.* 2010	EM	0.75	↓O	↓O	↓	↓O different responses between ewe breeds
Ferguson *et al.* 2011	EM	(0.7)	↓O	↓O		↓O different responses between sites; no effect on LWG
Kenyon *et al.* 2011	EM	(0.6)	O	O		
Khalaf *et al.* 1979	L	0.65	↓	↓		No effect on lamb plasma IgG

Holst *et al.* 1986	L	(0.85)	↓			
Bloomfield *et al.* 2003	L	0.02/0.04	↓			
Dwyer *et al.* 2003	L	0.65	↓		↓	
Everett-Hincks *et al.* 2005	L	(?)	↓	O		
Husted *et al.* 2007	L	0.5	↓			Decreased LWG to weaning
Corner *et al.* 2008	L	(0.6-0.8)	↓		↓	
Banchero *et al.* 2009	L	(?)	↓	↓		No difference in LWG to weaning
Swanson *et al.* 2008	L	0.6	↓	O		Increased lamb plasma IgG in UN treatment
Tygessen *et al.* 2008	L	0.50	↓			Decreased weaning weight; interaction with sire genotype
Meyer *et al.* 2010	L	0.6	↓	O		Increased lamb plasma IgG in UN treatment
Ferguson *et al.* 2011;	L	(0.7)	↓	↓		Decreased LWG to weaning
Kenyon *et al.* 2011	L	(0.6)	↓			
Wallace *et al.* 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 *et al.* 2005	L	↑	O		O	
Wallace *et al.* 2005b	L	O				Adult ewes
Corner *et al.* 2006a	L	O	O	↑		
Munoz *et al.* 2008b	EM	O	O		↓	
Kenyon *et al.* 2009	L	↑	O			ON increased birth-weight of F_1 generation but reduced birth-weight of F_2 generation
Munoz *et al.* 2009	EM	↑ O	O	O	↓	Different responses in 1- and 2-year-old ewes
Swanson *et al.* 2008	L	↓	↓			No difference in LWG to weaning; lower plasma IgG in ON lambs
Meyer *et al.* 2010	L	O	O			Lower plasma IgG in over-nutrition lambs
Ferguson *et al.* 2011	L	O	O			No difference in LWG to weaning
Wallace *et al.* 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 *et al.* 2007	Co	Early	O			↓			Marginal
Boland *et al.* 2005b	I	Late	O		↓				Adequate
Rose *et al.* 2007	I	Late	↑		↓			O	Adequate
Boland *et al.* 2008	I	Late	↓O		↓				Adequate
Munoz *et al.* 2008a	Se	Early/mid	O	↑	↑	↑		↑	Marginal
Swanson *et al.* 2008	Se	Throughout	O	O	↓			o	Adequate
Meyer *et al.* 2010	Se	Throughout	O	O					Adequate
Kott *et al.* 1998	Vit E	Late	O	↑O				↑o	Marginal; response season dependant
Capper *et al.* 2005	Vit E	Late	↑		o	O			Adequate
Dafoe *et al.* 2008	Vit E	Late	O	O			↑		Adequate; response FA dependant
Rooke *et al.* 2009	Vit E	Late	O			O			Adequate
Encinias *et al.* 2004	FA	Late	O	↑			O	O	

Capper *et al.* 2005	FA	Late	O			↑			
Chen *et al.* 2007	FA	Late	O				↓		Level dependant
Dafoe *et al.* 2008	FA	Late	O	O			↓	O	Vit E dependant
Pickard *et al.* 2008	FA	Late	O			↑		O	
Annett *et al.* 2008	FA	Late	O		↓			O	
Annett *et al.* 2009	FA	Late	O	↑	↓			O	Survival: level of fish oil dependant
Keithly *et al.* 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 *et al.* 2004	Social	↑	O		O - cortisol		
Roussel-Hachette *et al.* 2008	Social	O	↑O				Ewe stressor dependant.
Stott & Slee 1985	Husbandry				↑O - cold		Ewe stressor dependant.
Kenyon *et al.* 2004	Husbandry/ shearing	↑	O				
Kenyon *et al.* 2005	Husbandry/ shearing	↑	O				
Corner *et al.* 2006b	Husbandry/ shearing	↑O		↑		O - MB	Ewe stressor dependant.
Corner *et al.* 2007	Husbandry/ shearing	↑O			O - cortisol		Twin lambs only
Jenkinson *et al.* 2007	Husbandry/ shearing	↑	O				Twin lambs only
Keady *et al.* 2007	Husbandry/ shearing	↑	↑			O-survival	
Keady & Hanrahan 2009	Husbandry/ shearing	↑	O			O-survival	

Banchero *et al.* 2010	Husbandry/ shearing	↑O		↑		Twin lambs only
Corner *et al.* 2010b	Husbandry/ shearing	↑	O			
Cal-Pereyra *et al.* 2011	Husbandry/ shearing	↑				
Sphor *et al.* 2011	Husbandry/ shearing	↑	↑			
Hild *et al.* 2011	Husbandry	↑		O	↑ - MB	
Roghair *et al.* 2005	Artificial	↑				
De Blasio *et al.* 2007	Artificial	↓O				Ewe stressor dependant
Miller *et al.* 2009	Artificial	O		↓	O -survival	
Corner *et al.* 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 *et al.* 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 *et al.* 1985	Under	Nutrition restricted to 0.15 requirement from mating until GD60	Birth-weight reduced and poorer survival for first 48h after birth
Holst *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 2004	Under	Between mating and GD95, ewes fed 0.5 or 1.0 requirement.	No difference in birth-weight
Everett-Hincks *et al.* 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 *et al.* 2005	Over	Adult ewes fed to meet requirements or ad libitum (approx. 1.8 requirements throughout gestation	No difference in birth-weight
Corner *et al.* 2006a (Morris *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 2008 (Corner *et al.* 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-weeight 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 *et al.* 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 *et al.* 2008	Under	Ewes mated with either high or low index (*L. dorsi* 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 *et al.* 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 *et al.* 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 *et al.* 2009, 2011; van der Linden *et al.* 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 *et al.* 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.	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. Survival tended to be poorer in lambs from 1 year old under-nourished ewes; no difference in 2 year old ewes. 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.
Swanson *et al.* 2008; Neville *et al.* 2010; Hammer *et al.* (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 *et al.* 2010; Hammer *et al.* 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 *et al.* 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 *et al.* 2011; Oldham *et al.* 2011; Thompson *et al.* 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.

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Kenyon *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 2005b, 2006	I	Expt 1 Ewes fed supplements from GD100 containing supplementary minerals; minerals with iodine excluded or iodine only (40 mg/day) Expt 2 Ewes fed from GD100 with 9, 18 and 27 mg I /day	Expt 1 no effect on birth-weight or colostrum intake; I only or all minerals depress lamb IgG absorption and plasma vitamin E concentration Expt 2 Progressive depression in lamb plasma IgG and vitamin E concentration as amount of I fed increased.
Capper *et al.* 2005, 2006	FA / Vit E	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	Vitamin E: increased birth-weight; no effect on maternal care or lamb behaviours. Fatty acids: no effect on birth-weight; lambs born to fish oil fed ewes suckled more quickly.
Chen *et al.* 2007	FA	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	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.
Mitchell *et al.* 2007	Co	Ewes were supplemented or not supplemented with a Co bolus 24 days before mating.	No birth-weight differences. Supplemented lambs slower to progress through behavioural milestones.

Rose *et al.* 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 o age decreased linearly with I supplementation
Boland *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 suckl;ing
Swanson *et al.* 2008; Neville *et al.* 2010; Hammer *et al.* 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 *et al.* 2010; Hammer *et al.* 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 *et al.* 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 ºC) or control environment (6ºC) 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 2005	Artificial	Ewes infused with betamethasone continuously for 48 h at GD27	Birth-weight greater in treated lambs (but litter size smaller)
Corner *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.*	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 *et al.* 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 *et al.* 2011	Husbandry / shearing	Ewes shorn or not shorn on GD110	No Birth-weight increase in response to shearing.
Hild *et al.* 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 *et al.* 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