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Strengthening Animal Production and Health through the Immune Response

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Production losses caused by SAPHIR diseases and pathogens

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EXECUTIVE SUMMARY

Background	The measure of specific production losses associated with the infection of animals by specific pathogens is a fundamental prerequisite to an estimation of the expected economic benefits derived from the introduction of new vaccines on the market. Indeed, the scope of action of a vaccine is limited to very specific biological agents, defined by their genus, specie and serotype.
Objectives	The present literature review aims at providing the project with a list quantitative estimates available in the scientific literature. It aims at identifying the data gaps and limits of the current knowledge in order to target further data collections attempted in the course of SAPHIR project.
Methods	The literature review was performed through google scholar, using appropriate research terms, and was completed and validated by a panel of scientific experts.
Results & implications	Constraints to the measure of the effect of SAPHIR pathogens on farm economic performances include the complexity of their clinical expression and the diversity of pathogens involved in the clinical syndromes associated with production losses and their synergic effects. Quantitative estimates of the impact of BRSV, *Mycoplasma bovis* and *Clostridium perfringens* are missing. More data are available on the effect of clinical syndromes (e.g. pneumonia of cattle or swine) than on the effect of single pathogens. Due mainly to publication language bias, found publications are mainly from United States. In Europe studies published in English mainly come from United Kingdom, the Netherlands and Scandinavia.

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Introduction

There have been estimates of the economic impact of endemic disease in the Great Britain (Bennett 2003, Bennett and Ijpelaar 2005) and Australia (Lane, Jubb et al. 2015). Yet to our knowledge, there has been no attempt, so far, to synthesize the data produced on the effect of endemic animal diseases, such as the ones targeted by SAPHIR project, on farm productivity and efficiency. These data are, however, a fundamental input in models aiming at estimating, in a standard and replicable way, the national economic burden represented by these diseases in each European country.

The measure of specific production losses associated with the infection of animals by specific pathogens is a fundamental prerequisite to an estimation of the expected economic benefits derived from the introduction of new vaccines on the market. Indeed, the scope of action of a vaccine is limited to very specific biological agents, defined by their genus, specie and serotype.

The present literature review aims at providing the SAPHIR project with a list quantitative estimates of production losses due to SAPHIR pathogens which are available in the scientific literature. It also aims at identifying the data gaps and limits to our current knowledge of these production losses in order to better target further data collections attempted in the course of SAPHIR project.

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1. Methodology

A literature review was performed on the production losses caused by each of the six pathogens targeted by SAHIR project. As a reminder, these pathogens are:

- The bacteria *Mycoplasma bovis* (M bovis) and the virus Bovine Respiratory Syncytial Virus (BRSV), two infectious agents of Cattle. Because of the strong role played by these two pathogens in the clinical syndrome named Bovine Respiratory Disease complex (BRD) (Griffin 2014), the same literature review was performed using the term “Bovine Respiratory Disease”.
- The Porcine Respiratory and Reproductive Syndrome Virus (PRRSV) and the bacteria *Mycoplasma hyopneumoniae* (*M hyo*), two infectious agents of swine. The disease caused by *M hyo* being often referred as Enzootic Pneumonia (EP), the same literature review was performed using the term “Enzootic Pneumonia”.
- The parasite species of genus *Eimeria* causing Coccidiosis and the bacteria *Clostridium perfringens*, causing Necrotic Enteritis (NE) in poultry.

The literature review was done using google scholar with research terms

- <Name of the pathogen or name of the syndrome> AND “Production performance”
- <Name of the pathogen or name of the syndrome> AND “performance”
- <Name of the pathogen or name of the syndrome> AND “Production losses”

Only studies providing quantitative estimates of the production losses associated with the considered clinical affection were included. The final list of articles was validated by a panel of scientists holding an expertise on each of the considered pathogens. Those experts are:

- BRSV: Jean-François Valarcher (Swedish University of Agricultural Sciences, Sweden)
- *Mycoplasma bovis*: Renaud Maillard (National Veterinary School of Toulouse, France)
- PRRSV: Chritina Nathues (Veterinary Public Health Institute, University of Bern, Switwerland)
- *Mycoplasma hyopneumoniae*: Christopher Browne (Royal Veterinary College, United Kingdom)
- Coccidiosis: Damer Blake (Royal Veterinary college, United Kingdom)
- Necrotic Enteritis: Filip Van Immerseel (Ghent University, Belgium)

2. Results

2.1. The challenge of measuring and attributing production losses to specific pathogens

The measure of specific production losses associated to infection of animals by specific pathogens is a fundamental prerequisite to an estimation of the expected economic benefits obtained by introducing new vaccines on the market. Indeed, the scope of action of a vaccine is limited to very specific biological agents, defined by their genus, specie and serotype.

Accurate measures of the specific production losses caused by pathogens are difficult to obtain from field experiments or field surveys. The following sections detail the reasons for the limited availability of data on production losses directly due to specific animal pathogens and the technical constraints of their measurement.

2.1.1. The diversity of clinical expressions and effects on production

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Infectious agents cause diverse clinical expressions and lesions in their host and the resulting production losses cannot be summarized by one parameter. One extreme example is *M bovis*, which, in Europe, is mainly known as one agent of the Bovine Respiratory Disease Complex and induce chronic pneumonia. But it is actually just one of its potential clinical expressions, which also include Mastitis, Otitis Media, Arthritis and reproductive disorders, all of these clinical features having specific effects on the production performances of the farm (Maunsell, Woolums et al. 2011) **(Table 1)**.

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Table 1. The clinical expression of infections by Mycoplasma bovis and their associated effect on farm performances

	Clinical pneumonia	Subclinical pneumonia	Otitis media	Arthritis, Synovitis, and Periarticular Infections	Mastitis	Urogenital tract infection
Clinical condition/growth of unweaned calves	(Stipkovits, Ripley et al. 2000, Maunsell and Donovan 2009, Wilson, Goodell et al. 2009)		(Francoz, Fecteau et al. 2004, Foster, Naylor et al. 2009, Maunsell and Donovan 2009)	(Stipkovits, Rady et al. 1993, Maunsell and Donovan 2009)		
Mortality in unweaned calves	(Stipkovits, Ripley et al. 2000, Maunsell and Donovan 2009, Nicholas 2011)			(Stipkovits, Rady et al. 1993)		
Daily weight gain in feedlot cattle	(Haines, Martin et al. 2001, Shahriar, Clark et al. 2002, Arcangioli, Duet et al. 2008, Radaelli, Luini et al. 2008, Caswell, Bateman et al. 2010)	(Tschopp, Bonnemain et al. 2001, Hanzlicek, White et al. 2011)		(Hjerpe and Knight 1972, Haines, Martin et al. 2001, Shahriar, Clark et al. 2002, Gagea, Bateman et al. 2006)		
Mortality in feedlot cattle	(Haines, Martin et al. 2001, Shahriar, Clark et al. 2002, Caswell, Bateman et al. 2010)			(Haines, Martin et al. 2001, Shahriar, Clark et al. 2002)		
Fertility of female cattle						(Uhaa, Riemann et al. 1990)
Somatic Cell Count in Milk					(Wilson, Goodell et al. 2009, Sachse, Salam et al. 2010, Radaelli, Castiglioni et al. 2011, Pothmann, Spergser et al. 2015)	
Milk Yield of dairy cows					(Uhaa, Riemann et al. 1990, Gonzalez and Wilson 2003, Wilson, Goodell et al. 2009, Sachse, Salam et al. 2010, Radaelli, Castiglioni et al. 2011, Pothmann, Spergser et al. 2015)	
Mortality in dairy cows	(Pothmann, Spergser et al. 2015)				(Pothmann, Spergser et al. 2015)	
Culling of animals resistant to treatment	(Haines, Martin et al. 2001, Shahriar, Clark et al. 2002, Maunsell and Donovan 2009, Pothmann, Spergser et al. 2015)			(Haines, Martin et al. 2001, Shahriar, Clark et al. 2002)	(Pothmann, Spergser et al. 2015)	

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In pigs, PRRSV has two main clinical features (Holck and Polson 2003):

- A reproductive syndrome affecting breeding sows associated with a decreased fertility, decreased proportion of live born piglet per litter, increased pre-weaning mortality of piglets and increased rate of sow replacement.
- A respiratory syndrome affecting growing pigs resulting in reduced growth rate of pigs, increased feed-conversion ratio and increased mortality.

The other SAPHIR pathogens have a simpler clinical picture. BRSV and *M hyo* are only known to affect the respiratory systems of, respectively, cattle and pigs. Nevertheless, respiratory syndromes trigger a change in a large variety of production parameters. For example, the affection of the respiratory tract of cattle by respiratory pathogens during calfhood was shown, on the long run, to impact adult cattle performances (e.g. dairy cow's milk production and fertility and feedlot cattle growing performances) (**see Figure 1**).

2.1.2. Plurality of pathogens causing the same disease and synergic effect of pathogens

SAPHIR respiratory pathogens of swine and cattle do not cause pathognomonic clinical signs and the observed clinical expression cannot be related to a specific infectious agent without the help of a laboratory test (isolation of the pathogen itself or detection of signs of a previous infection with serological tests). Moreover, in most cases, farm production losses observed in the presence of SAPHIR pathogens infections do not result from the effect of a unique infectious agent but from the combined effect of different ones acting in synergy.

One example is the BRD syndrome, one of the greatest sanitary burdens of cattle production in Europe and USA, especially harmful to the meat industry (Griffin 2014). The expression of BRD was found to be linked with the infection of cattle by BRSV and *M bovis* but incriminated viruses also include Bovine Herpes Virus type 1 (BHV-1) and Bovine Viral Diarrhea Virus (BVDV). Furthermore, bacterial agents such as *Mannheimia Haemolytica*, *Pasteurella multocida* and *Histophilus somni* are isolated in most cases, in association with a primary infection by the abovementioned pathogens (Fulton 2009). Similarly, pneumonia in Swine herds very often results from the combined infection of fattening pigs by different agents, including PRRSV, *M hyo* and/or *Actinobacillus pleuropneumoniae* (Straw, Tuovinen et al. 1989, Holck and Polson 2003). In poultry, high infection level by *Eimeria* parasites predispose poultry flocks to subsequent infections by *Clostridum perfrigens* (Collier, Hofacre et al. 2008).

The multiplicity of infectious agents originating in the same syndrome and the synergic action of SAPHIR pathogens complicate the measure of the production losses avoided by the introduction of vaccines. Indeed, vaccines' actions are oriented against specific pathogens and not combinations of pathogens. Few studies were found to report quantitative estimates of losses due to specific respiratory agents like BRSV or *M bovis* in cattle (**See Tables 3 and 4**). Instead, numerous measures of production losses due to syndromes, like BRD, are available in the literature (**see Table 2**).

2.1.3. Finding the appropriate indicator of production performance

Average Daily Gain (ADG) is a useful and widely used indicator of the productivity of meat producing operations and is widely used as indicator of the effect of SAPHIR pathogens. The reduction of ADG can have two consequences on the farm performances, depending on the farming system and country:

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- Reduction of the weight of the animal at the time of sale or slaughter, and, therefore, decrease in production value of the farm.
- Increase of the duration of farming before the animal reaches the appropriate weight to be sold or slaughtered (in the case of beef calves or steers, growing pigs or broiler chickens) or can be inseminated (in the case of dairy cows). Obviously, it increases the cost of rearing animals as each additional day spent by the animal in a given stage requires additional labour and feed investments.

Besides, a useful indicator of the efficiency of animal production is the Feed Conversion Ratio (FCR) (or feed efficiency), which is the ratio of the quantity of feed consumed by animals and their weight gain during the same period. In Pig and poultry, feed intake is easy to monitor. Cattle, however, are mostly fed on pasture and forage and, therefore, their feed intake estimate is mostly not measurable, which probably explains why very few studies provide estimates of FCR in cattle.

2.2. Types of studies

2.2.1. Retrospective studies

Retrospective studies are the most common way of estimating the impact of Cattle diseases (BRD, BRSV or *M bovis*) and PRRSV on farm production performances. These studies are based on available animal health and production records provided either by farms, slaughterhouses, veterinary authorities or national statistics. The epidemiological units are either individual animals, groups of animals raised together in the same condition or farms.

Retrospective studies are always faced with the problem of properly defining cases (diseased units) and controls (healthy units) and this issue is addressed in different ways. As laboratory diagnosis are rarely performed and recorded by farmers, retrospective studies are more appropriate to investigate the effect of syndromes (e.g. BRD in cattle and EP in pigs).

As historical records or clinical observations or treatment are rarely accessible, cases can be defined on the basis of the observation of lesions on slaughtered or autopsied animals (e.g. lung lesions as indicators of infections by respiratory pathogens in swine and cattle, gut lesions as indicators of infections by *Eimeria* in poultry). In some studies, lung lesions were used as categorical variables, a certain level of lesions extent defining a case. In others, lesions scores, number of lung lobes affected or the proportion of the consolidated surface of lungs were used as ordinal or continuous metrics of the severity of pneumonia (Pagot, Pommier et al. 2007, William and Green 2007). In the case of NE, caused by Clostridium perfringens, cases were defined by the condemnation of the liver at slaughter (Lovland and Kaldhusdal 1999). This approach based on lesions observation and scoring has the great advantage of accounting for subclinical cases. However the variability of techniques used to score lung lesions in both cattle (Griffin 1997) and pigs (Pagot, Pommier et al. 2007) limits the possibility of comparisons between studies.

The interpretation of the results of retrospective studies is vulnerable to confounding factors: diseased animals might be more likely to have had other pathologies or having been reared in less optimal conditions, which can have affected their production performances. This is particularly true of farm level surveys (Lovland and Kaldhusdal 2001, Haug, Gjevre et al. 2008): farms with higher level of the considered disease might also have, in average, a poorer biosecurity, building, less adapted feeding or hus-

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bandry management practices. Therefore, one important quality criteria of such studies is the appropriate matching of cases with controls or the inclusion of confounding factors in the statistical model used for analysing data.

The observation of epidemics of the considered pathogens provide the best conditions for performing case control studies, farms or animals during and before (or after) epidemics being, respectively, appropriately matched cases and controls. Such conditions are never found in the case of ubiquitous pathogens, like *Eimeria,* which are observed in nearly all farms and at all times but with varying infectious levels. However this approach is possible and was used for pathogens with epidemic patterns like PRRS (Neumann, Kliebenstein et al. 2005, Nieuwenhuis, Duinhof et al. 2012) and BRSV (Norstrom, Edge et al. 2001, Klem, Kjæstad et al. 2016).

2.2.2. Prospective cohort studies

Prospective cohort studies provide a comprehensive follow up of animals reared in the same farm or in different farms with similar environments and husbandry management. Such studies are therefore less vulnerable to confounding factors than retrospective studies.

Cohort studies are mostly implemented to measure the efficacy of a treatment or a vaccine in real farm conditions. In that, they differ from clinical trials, which are implemented in controlled laboratory conditions with artificial infections. Some of these cohort studies provide simultaneous accurate measures of the infectious pressure of the considered pathogens (e.g oocyst counts in litter or bird carcasses for coccidiosis) and of performance indicators (Braunius 1983). However most of these studies only enable a comparison of the performance parameters of animals submitted to different treatments (e,g vaccinated vs non-vaccinated) which does not necessarily represent the true effect of the pathogen. For example, vaccinated animals are not necessarily free from the pathogen and non-vaccinated animals are also not all infected. There are several examples of such studies for coccidiosis (Williams, Carlyle et al. 1999, Suo, Zhang et al. 2006) and *M hyo* (Maes, Verbeke et al. 2003).

On the other hand, some cohort studies were specifically designed for estimating the Impact of some farming conditions, including diseases, on the farm production performances (Morris, Gardner et al. 1995, Donovan, Dohoo et al. 1998, Hanzlicek, White et al. 2011). Such studies provide very accurate data.

In order to measure the effect of specific pathogens, cases are best defined either by an historic of isolation of the defined pathogen (Haug, Gjevre et al. 2008, Hanzlicek, White et al. 2011) positive PCR tests or seroconversion, i.e the production of antibodies against the considered infectious agent (Beaudeau, Ohlson et al. 2010, Nieuwenhuis, Duinhof et al. 2012). This implies that routine tests are performed on animals.

For measuring the effect of syndromes, possibly caused by different pathogens, cases and control are defined based the observation of clinical signs in the animal corresponding to the considered affection. The reliability of this definition is dubious in the field, as many clinical cases might go undetected, for example with BRD (Griffin 2014). Some authors base their definition on the record of treatments administered to animals (Schneider, Tait et al. 2009), and the number of days on treatment can be used as a continuous variable indicating the severity and duration of the disease (Donovan, Dohoo et al. 1998). It relies on the assumption that all animals with the defined syndrome receive a specific treatment. The disadvantage of this definition is the impossibility to account for the effect of the treatment itself on the

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production performance, independently on the disease occurrence. Definitions of cases based on clinical signs and records obviously exclude subclinical infections, whose impact on production performance cannot be neglected (Griffin 2014). This why many cohort study also base their distinction between healthy and diseases animals on the observation of lesions on slaughtered or autopsied animals (Morris, Gardner et al. 1995, Wittum, Woollen et al. 1996).

2.2.3. Clinical trials

Similar to cohort study, clinical trials are a complete follow up of animals submitted to different treatments (curative medical intervention or vaccination). The disadvantage of clinical trials is that they are performed in closely controlled conditions which are quite different from real fam environments, and animals are most often artificially infected (Graat, Ploeger et al. 1996, Jenkins, Allen et al. 2008). These biases raise the question of the reproducibility of the results in real farm conditions.

2.2.4. Expert opinion

Expert opinion is a fast and inexpensive way of estimating impacts of diseases on economic parameters when raw scientific data are missing. For example it was used to estimate the impact of pneumonia on the growing and lactating performances of dairy heifers, by elicitation of the opinion of 21 clinicians (Van der Fels-Klerx, Saatkamp et al. 2002). Unless no other sources of information are available, expert opinions should not be used, as they are based on subjective opinions, and therefore vulnerable to judgement biases.

2.2.5. Meta-analysis

Finally, a few authors estimated the correlation between the infection level by the defined pathogen and the performance reduction of animals by combining data of different studies, performing meta-analysis. In the case of Coccidiosis in broiler chickens, a synthetic estimation of the change in ADG and FCR due to infections by *Eimeria tenella, Eimeria maxima* and *Eimeria acervulina* was estimated from a meta-analysis of 67 published studies (Kipper, Andretta et al. 2013). A similar meta-analysis was performed on infection by *M hyo* in pigs, based on 13 publications (Straw, Tuovinen et al. 1989).

Such studies are extremely valuable in the perspective of an economic analysis as they provide synthetic values over a range of studies performed in different countries, with different breeds of animals and in different farming conditions, which substantially increases the representativity of their results.

2.2.6. Conclusion

- Cohort and Case control studies provide the best estimates on the effect of pathogens farm performances, provided the effect of confounder variables is appropriately controlled.
- Results of clinical trials and expert opinions should not be used as such, unless no alternative data are available.
- When a large number of relevant studies are available, the combination of their results in meta-analysis may provide the most representative measures.

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2.3. Comparison of the current knowledge of production losses due to each pathogen

Referred studies are summarized in **tables 2, 3, and 4**.

2.3.1. Qualitative identification of impacts of SAPHIR pathogens on production performances

The effect of cattle respiratory pathogens (BRSV and *M bovis*) on farm productivity and efficiency is the most difficult to synthesize, due to the diversity of short and long term impact of infections on the production and reproduction performances of cattle and the complexity of the European dairy and beef value chains. These impacts are summarized in **figure 1.**

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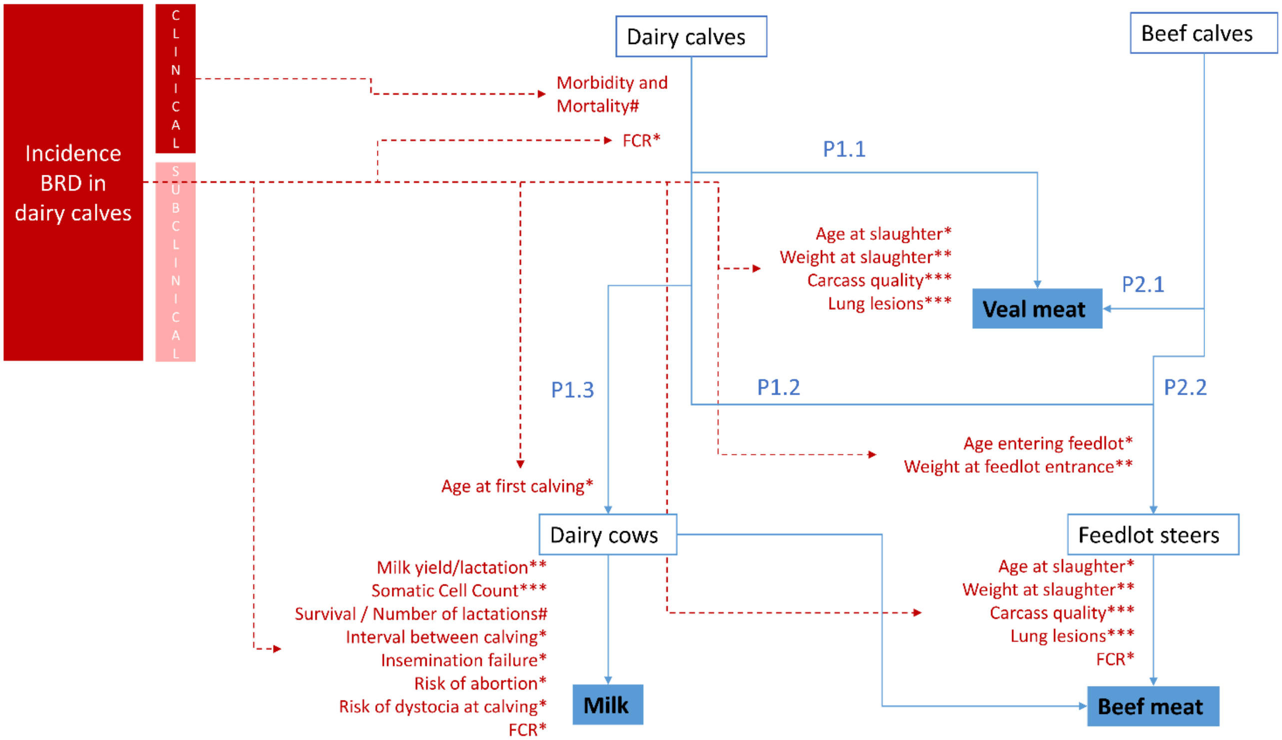

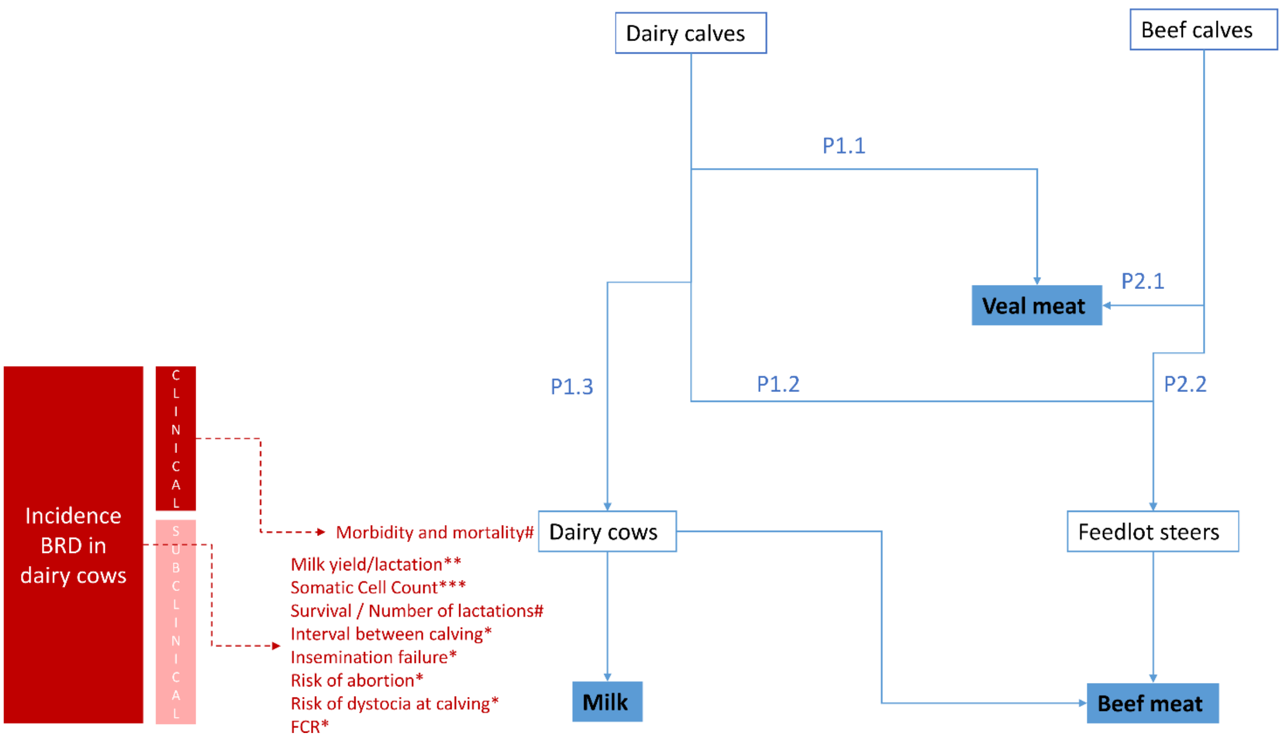

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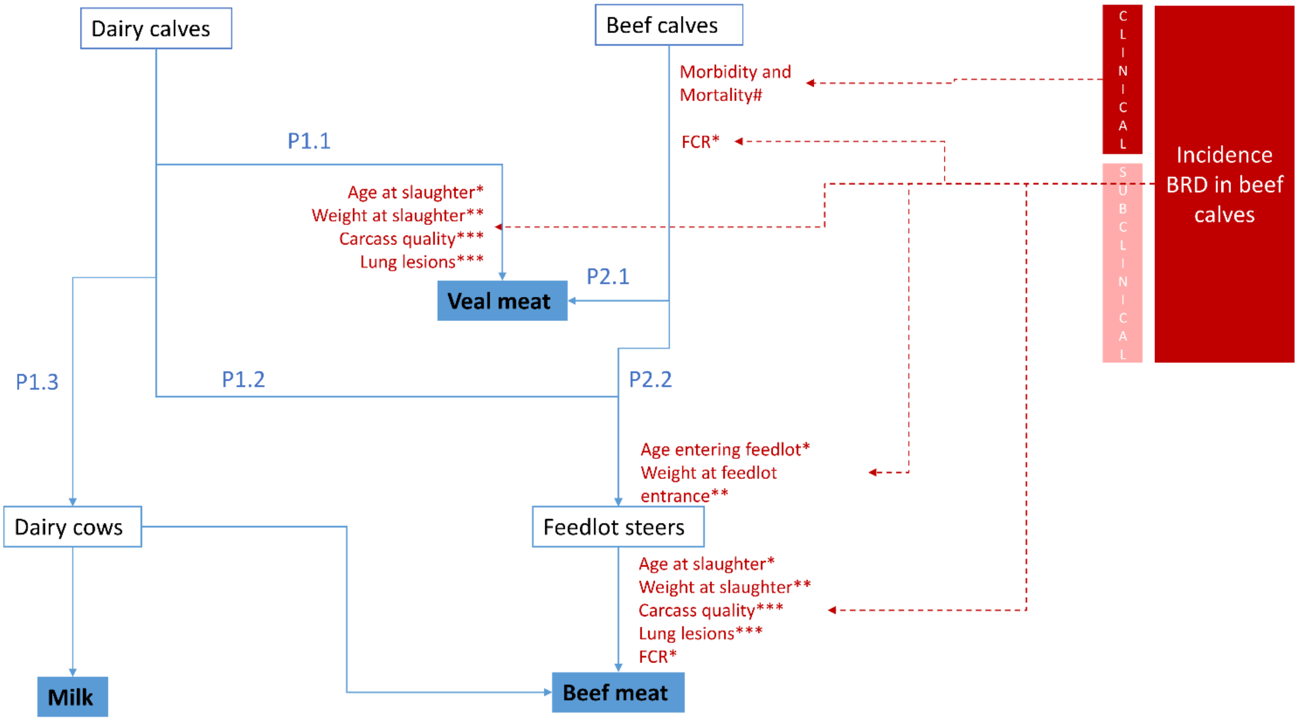

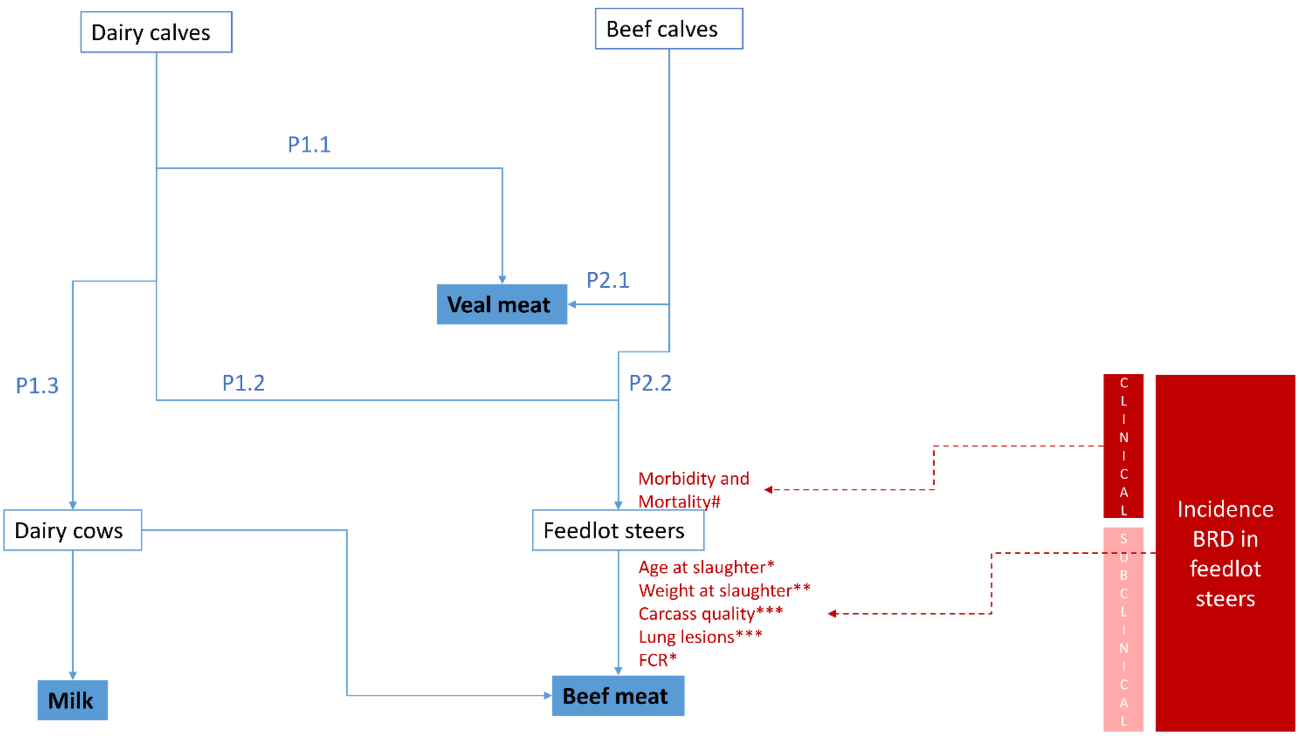

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Effect of BRD on production parameters: need to provide quantitative estimate for each effect

Effects of BRD infection (from literature data/SAPHIR data):
* Increased rearing cost
** Decreased production
*** Decreased product quality
# Decreased production, decreased rearing cost, increased treatment costs

Flow in the value chain

Flows of animals in the cattle value chain :
P1.1 Proportion dairy calves used for veal meat production
P1.2 Proportion dairy calves used for fattening
P1.3 Proportion dairy calves used for milk production
P2.2 Proportion beef calves used for fattening
P2.1 Proportion beef calves used for veal meat production

Figure 1. Synthetic graph of the cattle value chain and short-term and long-term effects of Bovine Respiratory Diseases on cattle production and reproduction performances

The effects of other SAPHIR pathogens, in swine and poultry, are less complex to apprehend. In poultry, NE and coccidiosis mainly impact the growing performances and mortality rate of broilers and the quality of their carcass (i.e. risk of carcass condemnation in the case of NE). Swine EP only impacts the ADG and FCR of fattening pigs. PRRS has a more complex effect on swine production, as it also impacts reproductive performances of sows, mortality rates and viability of piglets.

2.3.2. Missing data

Quantitative estimates of the specific effect of infections by BRSV and M bovis on farm performances are missing. The effect of BRSV on fertility, milk yield and somatic cell count (SCC) in dairy cows was well documented by surveys performed in Sweden and Norway, but we did not identify any study on the specific effect of the virus on growth performances of calves. There also is a lack of quantified estimates of the impact of *M bovis* on farm performances (**Table 2**).

The impact of BRD on FCR in feedlot cattle was investigated in two American studies (Holland, Burciaga-Robles et al. 2010, Brooks, Raper et al. 2011). We did not find any studies measuring the impact of cattle respiratory diseases on FCR in dairy cows or calves. This is probably due to the obvious technical limitations met in the ruminant sector where recording animals' feed intake is much less easy than in monogastric. However quantitative estimates of the impact of BRD on ADG are widely available. To be relevant, the reduction in ADG must be estimated on the whole cattle production period, as a reduction in daily gain registered during the infection can be later partly compensated through compensatory growth (i.e. a ADG higher than the average) (Brooks, Raper et al. 2011).

Furthermore, several studies reported the effect of BRD on the quality of the carcass, which has an incidence on the price paid to the farmer (Reinhardt, Busby et al. 2009, Schneider, Tait et al. 2009).

It is important to differentiate the effects of clinical and subclinical BRD, which are evaluated by different approaches: In studies measuring the effect of clinical BRD, cases are defined by the observation of clinical signs or the application of a treatment on animals whereas in studies measuring the effect of subclinical BRD on performances, cases are defined by the observation of lung lesions at slaughter.

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Studies on the impact of BRD pathogens on production performances of dairy cows produced contradictory results. In general all authors agree BRD increases the average age at first calving of dairy heifers, which is coherent with the observed impact of the disease on dairy calves' ADG (Virtala, Mechor et al. 1996, Donovan, Dohoo et al. 1998, Rossini 2004, Stanton, Emms et al. 2010). Two studies report an increases risk of dystocia at calving in dairy cows with a record of respiratory disease during caflhood (Warnick, Erb et al. 1994, Stanton, Kelton et al. 2012). All authors failed to demonstrate a significant impact of BRD occurence in calfhood on milk yield (Britney, Martin et al. 1984, Warnick, Erb et al. 1995, Rossini 2004, Stanton, Kelton et al. 2012) and milk SCC (Rossini 2004). However, two studies conducted at herd level in Sweden demonstrated a significant correlation between seropositivity for BRSV and reduced milk production and increased SCC (Beaudeau, Ohlson et al. 2010, Ohlson, Emanuelson et al. 2010). Similarly, dairy cows seropositive for *M bovis* were found to be less productive (Uhaa, Riemann et al. 1990).

(Britney, Martin et al. 1984) did not find any significant effect of BRD on cows' reproductive performances. (Beaudeau, Ohlson et al. 2010) and (Ohlson, Emanuelson et al. 2010) suggested an effect of BRSV infection status on the number of reproductive failures but failed to demonstrate a significant association between BRSV infection and fertility, whereas (Uhaa, Riemann et al. 1990) showed M bovis infection significantly increases the interval between each calving. Although BRD is known to increase the risk of abortion, no quantitative estimate of this effect was found in the literature.

Most of the recorded studies were conducted in United States or in another non-European county (e.g. Canada or South Africa). The European studies we found were performed either in United Kingdom, Sweden, Norway or the Netherlands. Although it seems reasonable to assume that several European countries did not perform any research on the topic, it also appears that language barrier is a strong limitation to the present review. In countries like France, Portugal or Germany, relevant data were published but only in national languages. Some of these French and German studies were included in the present review but many are missing.

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Table 2. Studies providing quantitative estimates of the impact of SAPHIR pathogens of cattle and Bovine Respiratory Diseases on farm performance parameters

Cattle	Performance parameter	BRD	BRSV	Mycoplasma bovis
Feedlot cattle	ADG/Time to reach the growth target	(Bateman, Martin et al. 1990, Wittum, Woollen et al. 1996, Griffin 1997, Gardner, Dolezal et al. 1999, Roeber, Speer et al. 2001, Thompson, Stone et al. 2006, Waggoner, Mathis et al. 2007, William and Green 2007, Bareille, Seegers et al. 2008, Babcock, White et al. 2009, Montgomery, Sindt et al. 2009, Schneider, Tait et al. 2009, Holland, Burciaga-Robles et al. 2010, Brooks, Raper et al. 2011)	(Martin, Nagy et al. 1999)	(Martin, Nagy et al. 1999, Tschopp, Bonnemain et al. 2001, Hanzlicek, White et al. 2011)
	FCR	(Holland, Burciaga-Robles et al. 2010, Brooks, Raper et al. 2011)		
	Mortality	(Bateman, Martin et al. 1990, Healy, Monaghan et al. 1993, Loneragan, Dargatz et al. 2001, Bareille, Seegers et al. 2008, Holland, Burciaga-Robles et al. 2010, Brooks, Raper et al. 2011)		
	Carcass quality	(Roeber, Speer et al. 2001, Waggoner, Mathis et al. 2007, Garcia, Thallman et al. 2009, Montgomery, Sindt et al. 2009, Reinhardt, Busby et al. 2009, Schneider, Tait et al. 2009, Holland, Burciaga-Robles et al. 2010, Brooks, Raper et al. 2011)		
Beef calves	ADG/Time to reach the growth target	(Scott 1995, Assié, Bouet et al. 2001, Assié, Delobel et al. 2003, Pesneau 2008)		Study ANSES-Vetagro-Sup Lyon (France). Results are confidential.
	FCR			
	Mortality	(Scott 1995, Andrews 2000)		

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Dairy calves/heifers	ADG/Time to reach the growth target	(Van der Mei and Van den Ingh 1987, Virtala, Mechor et al. 1996, Donovan, Dohoo et al. 1998, Stanton, Kelton et al. 2012)		
	FCR			
	Mortality	(Waltner-Toews, Martin et al. 1986, Curtis, White et al. 1989, Sivula, Ames et al. 1996, Rossini 2004, Stanton, Kelton et al. 2012, Schaffer, Larson et al. 2016)	(Beaudeau, Ohlson et al. 2010)	
Dairy cows	Age at first calving	(Waltner-Toews, Martin et al. 1986, Correa, Curtis et al. 1988, Warnick, Erb et al. 1994, Rossini 2004, Stanton, Kelton et al. 2012, Schaffer, Larson et al. 2016)		(Uhaa, Riemann et al. 1990)
	Milk yield	(Britney, Martin et al. 1984, Warnick, Erb et al. 1995, Rossini 2004, Stanton, Kelton et al. 2012, Schaffer, Larson et al. 2016)	(Van der Poel, Mourits et al. 1995, Norstrom, Edge et al. 2001, Beaudeau, Ohlson et al. 2010, Ohlson, Emanuelson et al. 2010)	(Uhaa, Riemann et al. 1990)
	SCC (subclinical mastitis)	(Rossini 2004)	(Beaudeau, Ohlson et al. 2010, Ohlson, Emanuelson et al. 2010)	(Uhaa, Riemann et al. 1990)
	Calving complication	(Warnick, Erb et al. 1994, Stanton, Kelton et al. 2012)		
	Fertility	(Britney, Martin et al. 1984, Schaffer, Larson et al. 2016)	(Beaudeau, Ohlson et al. 2010, Ohlson, Emanuelson et al. 2010)	(Uhaa, Riemann et al. 1990)
	Risk of abortion			
	Survival: life duration	(Britney, Martin et al. 1984, Warnick, Erb et al. 1997, Rossini 2004, Schaffer, Larson et al. 2016)		
Bulls	Fertility		(Alm, Koskinen et al. 2009)	
	ADG/Time to reach the growth target		(Klem, Kjæstad et al. 2016)	
	FCR		(Klem, Kjæstad et al. 2016)	

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The impact of SAPHIR swine diseases on pig farm production parameters is better documented, especially the effect of EP on pigs' growing performances (**Table 3**). However specific measures of the effect *M hyo* on the production performances of fattening pigs are scarce. The only estimate of its effect on FCR which was found in the literature relies on a comparison between vaccinated and non-vaccinated herds, which is dubious (Maes, Verbeke et al. 2003).

Found studies were conducted in United States, Canada, United Kingdom, Spain, Belgium, France, Finland and the Netherlands.

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Table 3. Studies providing quantitative estimates of the impact of SAPHIR pathogens of swine and Swine Enzootic Pneumonia (EP) on farm performance parameters

Pigs	Performance parameter	EP	PRRS	Mycoplasma hyopneumoniae
Fattening stage	ADG/Time to reach the growth target	(Jericho, Done et al. 1975, Straw 1991, Hill, Scheidt et al. 1994, Morris, Gardner et al. 1995, Pagot, Pommier et al. 2007) **Meta-analysis:** (Straw, Tuovinen et al. 1989)	(Dee, Joo et al. 1997, Neumann, Kliebenstein et al. 2005, Holtkamp, Kliebenstein et al. 2013, Dunkelberger, Boddicker et al. 2015)	(Rautiainen, Virtala et al. 2000) **Comparison vaccinated/non vaccinated** (Dohoo and Montgomery 1996, Maes, Verbeke et al. 2003)
	FCR	(Jericho, Done et al. 1975) **Meta-analysis** (Straw, Tuovinen et al. 1989)	(Dee, Joo et al. 1997, Neumann, Kliebenstein et al. 2005, Holtkamp, Kliebenstein et al. 2013)	**Comparison vaccinated/non vaccinated** (Maes, Verbeke et al. 2003)
	Mortality	Not applicable	(Dee, Joo et al. 1997, Neumann, Kliebenstein et al. 2005, Nieuwenhuis, Duinhof et al. 2012, Holtkamp, Kliebenstein et al. 2013, Dunkelberger, Boddicker et al. 2015)	Not applicable
Breeding stage	Farrowing rate	Not applicable	(Brouwer, Frankena et al. 1994, Neumann, Kliebenstein et al. 2005, Schaefer and Morrison 2007, Nieuwenhuis, Duinhof et al. 2012, Holtkamp, Kliebenstein et al. 2013)	Not applicable
	Live born/litter		(Brouwer, Frankena et al. 1994, Neumann, Kliebenstein et al. 2005, Schaefer and Morrison 2007, Nieuwenhuis, Duinhof et al. 2012, Holtkamp, Kliebenstein et al. 2013)	
	Pre-weaning mortality		(Brouwer, Frankena et al. 1994, Schaefer and Morrison 2007, Nieuwenhuis, Duinhof et al. 2012, Holtkamp, Kliebenstein et al. 2013)	
	Replacement rate of sows		(Brouwer, Frankena et al. 1994, Holtkamp, Kliebenstein et al. 2013)	

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The effect of subclinical coccidiosis on ADG and FCR of broilers was well documented and was synthesized in a meta-analysis. However, studies on NE are scarce. Many clinical trials were performed to demonstrate the efficiency of a specific treatment on NE incidence and production performances, but their results were not synthesized in a meta-analysis and are not exploitable as such. No study was found on the impact of both pathogens on the laying sector (**Table 4**).
Studies come from various countries, including United Kingdom, the Netherlands, Norway, Brazil and China.

Table 4. Studies providing quantitative estimates of the impact of SAPHIR pathogens of poultry on farm performance parameters

Poultry	Performance parameter	Coccidiosis	Necrotic Enteritis
Broiler	ADG/Time to reach the growth target	**Comparison vaccinated/non vaccinated** (Williams, Carlyle et al. 1999, Suo, Zhang et al. 2006) **Meta-analysis** (Kipper, Andretta et al. 2013)	(Lovland and Kaldhusdal 2001)
	FCR	**Comparison vaccinated/non vaccinated** (Williams, Carlyle et al. 1999, Suo, Zhang et al. 2006) **Meta-analysis** (Kipper, Andretta et al. 2013)	(Lovland and Kaldhusdal 2001)
	European Broiler Index	**Comparison between treatments** (Braunius 1983)	
	European Production Index	(Haug, Gjevre et al. 2008)	
	Mortality	**Comparison vaccinated/non vaccinated** (Williams, Carlyle et al. 1999, Suo, Zhang et al. 2006)	(Lovland and Kaldhusdal 2001)
	Liver condemnations	Not applicable	(Lovland and Kaldhusdal 2001)
Layer	Egg production		

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Glossary

ADG: Average Daily Gain

BRD: Bovine Respiratory Disease

BRSV: Bovine Respiratory Syncytial Virus

BVDV: Bovine Viral Diarrhea Virus

EP: Enzootic Pneumonia

FCR: Feed Conversion Ratio

NE: Necrotic Enteritis

PRRSV: Porcine Reproductive and Respiratory Syndrome Virus

SCC: Somatic Cell Count

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