JOHNE'S DISEASE
RESEARCH CONSORTIUM

ANNUAL REPORT 2013

JOHNE'S DISEASE
RESEARCH CONSORTIUM

CONTENTS

DEFINITIONS

AgR	AgResearch Limited
B+LNZ	Beef + Lamb New Zealand Limited
DCANZ	Dairy Companies Association of New Zealand
DNZ	DairyNZ Limited
ELISA	Enzyme Linked Immunosorbent Assay
JDRC	Johne's Disease Research Consortium
JML	Johne's Management Limited
LIC	Livestock Improvement Corporation
MAP	Mycobacterium avium paratuberculosis – the bacterium that causes Johne's disease
MIA	Meat Industry Association
MBIE	Ministry of Business, Innovation and Employment (formerly Ministry of Science and Innovation, MSI)
Paratuberculosis	Another name for Johne's disease
PTB	Paratuberculosis
UJV	Unincorporated Joint Venture

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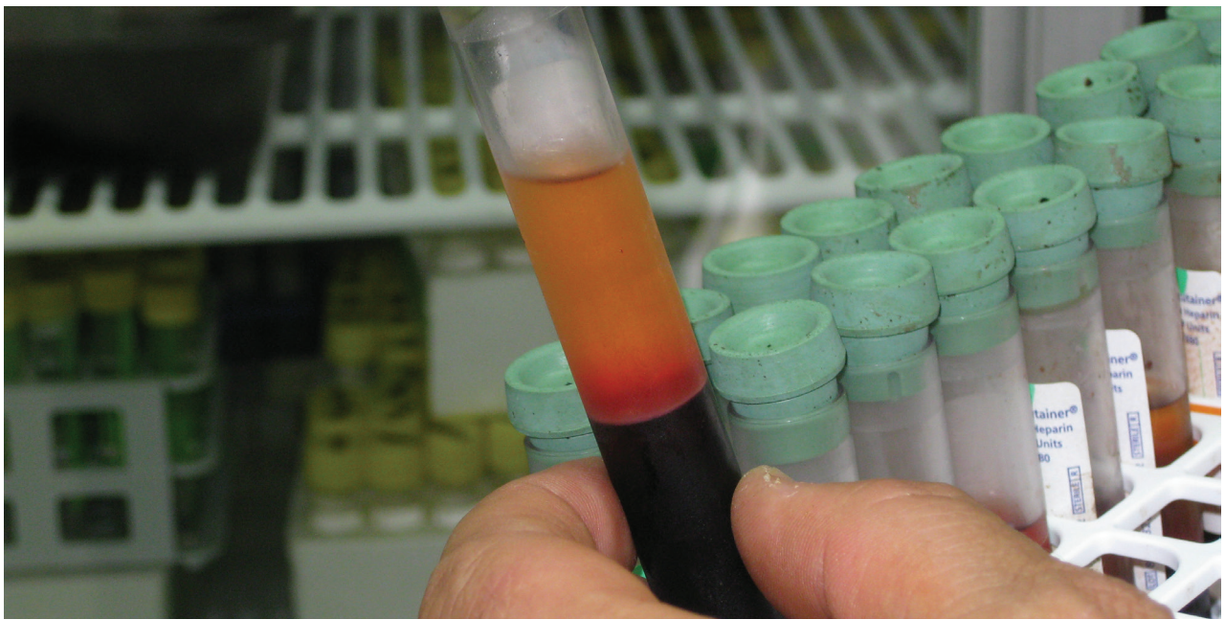
THE CONSORTIUM



The Johne's Disease Research Consortium (JDRC) was established in 2008 as a joint venture between Industry and the Science community to coordinate Johne's disease research in New Zealand. The participants in the Unincorporated Joint Venture are Beef + Lamb New Zealand Limited (B+LNZ), DairyNZ Limited (DNZ), DEEResearch Limited, AgResearch Limited (AgR), Livestock Improvement Corporation (LIC), Massey University and the University of Otago. The Meat Industry Association (MIA) and Dairy Companies Association of New Zealand (DCANZ) are associate participants in the Consortium and the Ministry of Business, Innovation and Employment (MBIE) provides funding to the Consortium via the Research Consortia funding scheme. Landcorp Farming Limited, Johne's Management Limited (JML) and The New Zealand Merino Company Limited (NZM) are also collaborators. JDRC has a total budget of $10.4M over its lifetime.

The focus of the Consortium's research programme is "behind the farm gate" and it's goal to develop practical and cost effective tools which can be used to reduce the prevalence of Johne's disease in herds or flocks in New Zealand.

JDRC contracts research services from some of New Zealand's leading science providers and maintains an industry focused research programme through interaction with its industry participants. Johne's is a complex disease and combining the resources of major industry associations with research partners has been a significant step for ensuring that research investment has been coordinated and focussed on achieving the greatest benefit for the New Zealand livestock industry. We also recognise the value of the research being carried out internationally and contribute to and draw from this global effort to combat Johne's disease in order to secure the latest developments for practical application in New Zealand.

THE DISEASE

Johne's disease (or Paratuberculosis) is a chronic, progressive, contagious and generally fatal infection of cattle, sheep, deer, goats and wildlife caused by the bacterium Mycobacterium avium subspecies paratuberculosis (or MAP). Infected animals contaminate the environment by shedding large numbers of MAP in their faeces, resulting in an increased risk of infection amongst herds and flocks. Once infected, an animal can remain unaffected and show no signs of the disease throughout their lifetime, however a small number of animals progress to clinical disease. The bacteria cause an autoimmune reaction in the gut, thickening the intestinal wall and reducing the ability of an animal to absorb nutrients from the diet. Clinically affected animals suffer from wasting and eventually die from malnutrition. There is no recognised treatment for the disease. In New Zealand there are vaccines registered for sheep and deer which while not preventing infection will, in most cases, reduce the signs of clinical disease.

JDRC IN 2012-13

In 2012-13 the focus of the JDRC research programme has been on projects designed to provide information or solutions generated on-farm to improve control and management of Johne's disease, particularly for those properties most affected by the disease.

The on-farm programme is composed of three major projects and was developed in conjunction with industry experts to address top priority research targets identified by the Dairy, Beef and Sheep and Deer sectors:

- The development of a toolbox of interventions to minimise the impact of Johne's disease in dairy cattle
- Estimating the true cause of ewe-death on sheep properties thought to be most affected by Johne's disease
- Understanding the application and impact of diagnostic tests for the management of Johne's disease in farmed deer
- All three projects are integrated with strain-typing studies.

THE IMPACT OF THE DISEASE

While results from research studies vary, evidence suggests that clinical Johne's disease has the potential to affect animal production by reducing life expectancy, meat and milk yields and the value of cull animals.

Sub-clinical disease may also affect production, but this impact is more difficult to measure.
While the financial costs of Johne's disease are minimal on farms without clinical disease, the cost on the worst affected properties can be substantial and not limited to economic impact alone.

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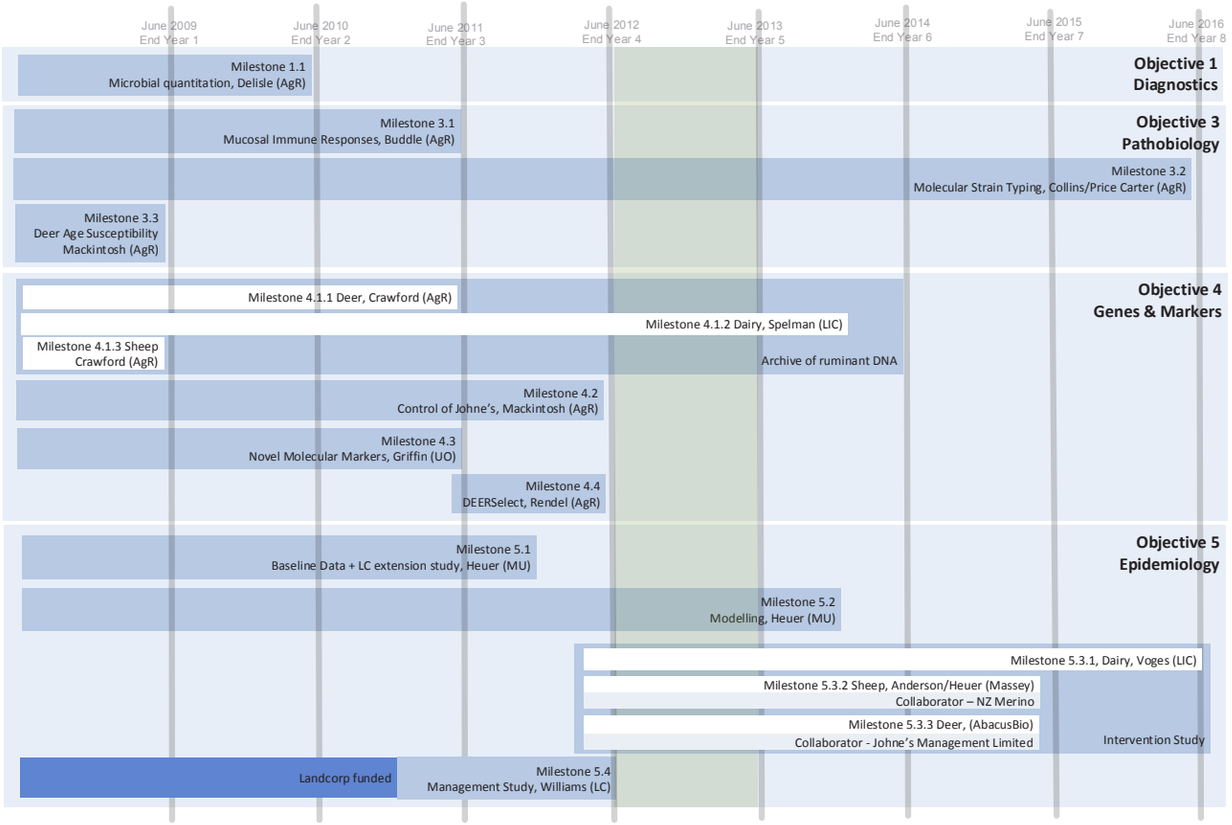
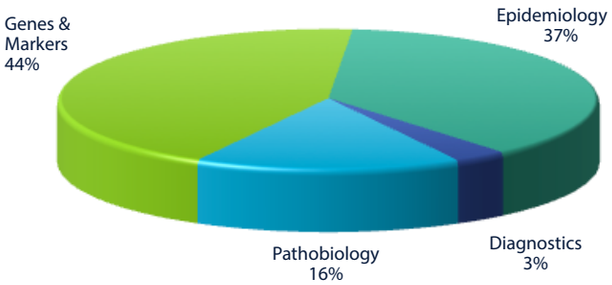
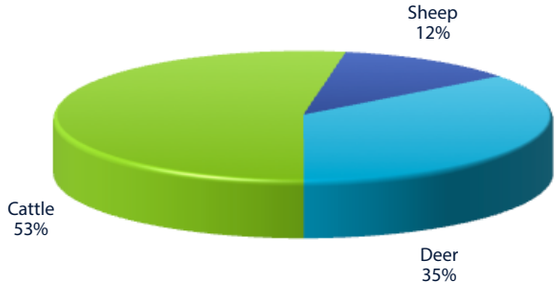
SCIENCE PROGRAMME



Science Funding by Objective



Species Funding Allocation



SECTOR WIDE DEVELOPMENTS

Reducing the impact of Johne's disease on farm is a multifaceted goal for the Consortium. The disease is complex and MAP is a difficult organism to study. The bacteria grow slowly in culture systems, are difficult to detect and their effect on ruminant animals is most often long-term. The disease also manifests itself differently in different species which leads to a need for tailored management practices across the sectors. There are, however, many common factors between the species and much to learn about how the disease behaves in New Zealand's multispecies, pastoral grazing environments, which could improve our overall ability to manage the disease long-term.

Diagnostics

The diagnosis of Johne's disease in cattle, sheep and deer remains a challenging area of research. The work of the Consortium has added support and understanding to New Zealand's ability to diagnose the disease using traditional diagnostic methods, but has not resulted in the development of new diagnostic techniques. Existing methods (including ELISAs, PCR and pathology based assays) are most robust for the diagnosis of clinical stages of disease but a test for reliably diagnosing sub-clinical or infected animals remains to be found. Understanding the limits of a diagnostic test's capability is an important outcome for practical application on-farm and JDRC research has contributed to knowledge in this area.

Species Interaction

Data from the JDRC Prevalence study carried out by Massey University[1] in combination with strain typing at AgResearch[2] have shed some light on the impact of pastoral co-grazing on disease transmission. Researchers found strong evidence that MAP is transmitted between cattle, sheep and deer in New Zealand. While the two major strains of MAP, Type C and Type S, were thought to be found largely only in cattle and deer or sheep, respectively, our studies have shown that a significant number of cattle in New Zealand are infected with Type S strains and sheep with Type C strains. There are also clearly different Type C sub-strains circulating in dairy cattle than those Type C sub-strains circulating in deer, perhaps due to the relative lack of contact between dairy cattle and deer herds in New Zealand or a difference in pathogenicity of these strain types for different animal hosts.

Survey data have also shown evidence that there are relationships between the occurrence of disease and species co-grazing. Co-grazing with a diseased animal raises the likelihood of the disease being found in the co-grazed species by 6-10 fold, while a lack of disease can reduce the risk for the second species.

Industry Resources

Three major factors have been identified as important in reducing the impact of MAP on farm; controlling on-farm transmission, preventing entry of the disease into the herd and maximising herd/flock health. Guidelines for the management of livestock, based on these three principles, are now available for cattle, sheep and deer.

In 2013 JDRC established an Expert Working Group, whose responsibility is to maintain an overview of the science and management of Johne's disease both within New Zealand and internationally. The group will provide a cross-sector perspective and advice to the JDRC Board regarding best practice for the management of Johne's disease in New Zealand. It currently has 12 members, selected from across the dairy, beef and sheep and deer sectors, with expertise in farming, science, veterinary practice, extension activities, food safety and regulatory control; who are appointed by the JDRC Board. It is intended that this group will be the forum for pan-sector JD activities when the Consortium ends in 2016.

[1] Cord Heuer, Cristobal Verdugo, Massey University [2] Des Collins, Marion Price-Carter, AgResearch

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SHEEP AND BEEF SECTOR

Ovine Johne's

The JDRC prevalence survey completed in 2011[1], showed that approximately 79% of sheep are infected with MAP in New Zealand. However, only a small portion of animals progress to clinical stages of the disease. Most sheep do not succumb to the disease in their productive lifespan and have only intermittent periods when they are shedding bacteria. A JDRC project to sample DNA from skinny ewes at the processing works[3] was abandoned in 2009 as an insufficient number of animals were found infected with MAP in their tissues at slaughter. We have concluded that in most flocks JD is a low level threat to animal health, but that there are a small number of farms where the disease is causing loss that needs to be better understood.

Johne's disease in sheep is usually sporadic, difficult to diagnose and can be masked by the presence of other causes of ill-thrift in the flock, such as poor nutrition or parasitism. As a result the true impact of the disease on affected farms can be difficult to determine. Computer models can be used as a low cost means to look at how Johne's disease might be controlled. Researchers at Massey University[4] have developed a simulation model which mimics New Zealand's management of sheep, accounting for the impact of seasonal lambing, intermittent shedding and age-related animal management. Initial results suggest that early detection and removal of high shedders is likely to be the most effective means of controlling the disease in sheep flocks. The model also suggests that vaccination may be cost effective if annual mortality due to Johne's disease is greater than 1%.

In 2012, in collaboration with The New Zealand Merino Company, JDRC began a study to investigate the cause of ewe death on properties suspected to have high rates of Johne's disease[5] . Twenty properties have been enrolled in the study and results from the trial are anticipated in 2015. The study relies on recording accurate tallies of ewes at four points during the year, diagnostic records and post-mortem examination of fading ewes to track the cause of death on farm.

The data from this study will be used to provide evidence about loss of production due to OJD ewe mortality, then using the simulation model as a tool, losses due to mortality, reduced weight gain and weaning rates will be compared with the cost of interventions for controlling the disease over time (e.g. vaccination or test & cull).

[3] *Alan Crawford; AgResearch Limited*

Bovine Johne's disease

The incidence of Johne's disease in beef cattle in New Zealand is very low. Data from the Prevalence study[1] suggest that approximately 30% of beef herds are infected with MAP but that clinical disease is rare. The impact of the disease is, therefore, very low.

Strain typing studies[2] have indicated that beef cattle in New Zealand are predominantly infected with Type S strains, likely due to intensive direct contact between sheep and beef cattle on farms. Sheep strains have been shown to be less virulent than cattle strains and it is thought that this may possibly be impacting disease prevalence.

In 2012-13 JDRC has been developing guidelines for the management of Johne's disease in beef cattle, for those farms that need help managing the disease. Experts agree that traditional hygiene-based solutions for the management of the Johne's disease are mostly impractical for New Zealand beef production systems and, therefore, practical recommendations for the management of stock are limited to the test and cull of clinical animals. The beef cattle guidelines are due for publication in early 2014.

[4] Cord Heuer, Nelly Marquetoux; Massey University *[5] Peter Anderson, Marlborough Veterinary Centre, Cord Heuer, Massey University*

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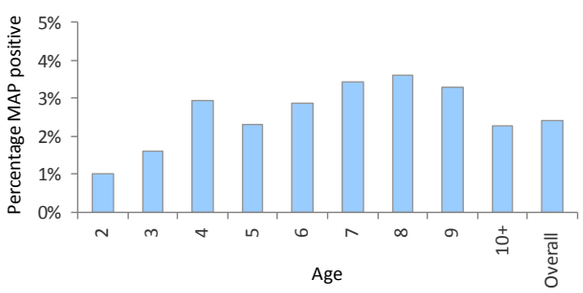
DAIRY SECTOR

In the course of the JDRC research programme, DNA has been collected from approximately 2000 dairy cattle affected with Johne's disease from across New Zealand[6]. From this resource and other studies (both within the JDRC programme and others) researchers have gained valuable insights into the impact of Johne's disease on dairy cattle in New Zealand. We believe that approximately 60% of NZ dairy cattle are infected with MAP, but similar to other species, the rates of clinical disease within herds is usually low (<1%). Analysis of phenotypic data from the DNA study has confirmed that Johne's disease reduces the productivity of dairy cattle both seasonally and across the lifetime of a cow. The study showed that milk, fat and protein yields were significantly lower in JD positive cows, with affected cattle producing an average of 14% less in the 2009-10 season compared to healthy cows. Cattle are most likely to affected between lactations 3-6. While Jersey cows were more likely to be test positive than Holstein-Friesians, the disease had a greater impact on production rates in Holstein-Friesians than in Jerseys.

While a great deal of information is available from international research regarding the management of Johne's disease in housed dairy cattle, there is a lack of information about how to manage the disease in pastoral grazing environments. In 2012 JDRC began an intervention study with Livestock Improvement Corporation[7] , to investigate practical methods for disease control in New Zealand, to provide assistance for the small percentage of high prevalence dairy herds. The programme is largely focussed on calf health, and minimising the transmission of MAP to the most vulnerable animals in a herd. Twenty herds from across New Zealand have been enrolled in the three-year study where practical interventions to lower the incidence of JD on farm will be trialled and levels of JD in herds monitored. A toolbox for the management of the disease is being developed that will be refined through the study and available to all farmers as best practice recommendations by the conclusion of the programme.



[6] *Richard Spelman, Ric Sherlock; Livestock Improvement Corporation, Penny Back; Massey University, Hinrich Voges*
[7] *Geoff Corbett, Anna Lowe; Livestock Improvement Corporation, Project Manager Jaimie Hunnam, Cognosco, Hinrich Voges*

DEER SECTOR

The JDRC Prevalence Study[1] indicated that 50-55% of deer are infected with MAP, but that the rate of clinical disease is low within herds. Unique to deer is the early onset of clinical disease, with yearlings and rising two year old stock most likely to succumb to clinical disease, which has the potential to reduce the productive lifetime of affected stock significantly.

A computer model developed by Massey University[1] to test the effectiveness of control measures for the disease in deer predicts that the most effective means of reducing the prevalence and incidence of disease on farm is the early detection and removal of high shedding and clinical animals. In trials carried out by Landcorp Farming Limited[8] the use of test and cull was effective in reducing the incidence of serum test positive animals in herds from around 20% to below 5% over a period of three years. Further improvement could be anticipated if a tailored approach incorporating other deer industry recommended management techniques was implemented.

Through considerable investment over a number of years the Deer industry in New Zealand has developed a robust support system for the management and control of Johne's disease in farmed deer. Johne's Management Limited (JML) is a Deer Industry funded company that promotes the control of Johne's disease in farmed deer in New Zealand and maintains a national database of JD-like lesions (JDSLN) detected in deer at processing. JML provides training and resources for the industry and supports the Johne's Consultancy Network (JCN), a network of veterinary professionals with specialist training in the management of Johne's disease in deer. Industry efforts to reduce the impact of disease appear to be having a positive effect, however there are a number of refinements that can be made and the JDRC on-farm deer study, initiated in 2012-13, in collaboration with JML[9], has been developed to assist with this.

AbacusBio Limited[10] have been engaged to manage a three phase project aimed at providing a better understanding of the application of diagnostics to the management of Johne's disease in deer, understanding how JML's database of JD-suspect lesions (JDSLN) relates to on-farm experience of disease and providing case studies which demonstrate how Johne's disease has been successfully managed on farm using the tools currently available to deer farmers. Results from the study are expected in early 2015 and will be used to formulate best-practice guidelines for the use of diagnostic tests for JD in deer.

[8] Gordon Williams; Landcorp Farming Limited [9] Solis Norton; Johne's Management Limited [10] Peter Fennessy, Neville Jopson; AbacusBio Limited

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2008-2013 FINDINGS AND ACHIEVEMENTS

ALL SPECIES

Population based estimates of prevalence indicate 60% of dairy cattle, 52% of deer, 79% of sheep and 44% of beef cattle in New Zealand are infected with MAP. Levels of clinical disease are much lower, and within herd incidence of clinical disease is very low (<1%)	The incidence of Johne's disease shows regional variations in New Zealand, affecting deer and cattle most severely in the South Island and sheep in the North Island
There is strong evidence that MAP is transmitted between species when animals are co-grazed, increasing the likelihood of infection on multi-species farms	While increasing the risk of disease transmission, co-grazing appears to have potential beneficial effects on deer herds by reducing the incidence of clinical JD when jointly farmed with sheep
There are at least 20 sub strains of Type C and 8 sub strains of Type S MAP found in New Zealand dairy cattle, beef cattle, sheep and deer however four of these sub-strains are responsible for ~89% of all infections	Both dairy cattle and deer are usually infected with Type C strains of MAP, however there is a clearly different Type C sub-strain found in dairy cattle to that found in deer
On some farms animals can be infected with more than one strain type of MAP, suggesting the animals have been infected on more than one occasion	**2012 - 13** Computer models predict that early detection and removal of high shedders will be the most effective means of reducing the impact of Johne's disease in a herd of deer or flock of sheep
The performance of faecal culture, pooled faecal culture, serological tests and combinations of these tests for herd level diagnosis of MAP infection has been investigated and knowledge applied to monitoring the status of sheep flocks, beef cattle and deer herds	Surveys of deer, cattle and sheep have indicated that both infection with MAP and clinical disease affect productivity; lower pregnancy rates were seen in JD positive beef and deer herds, lower culling rates in JD positive beef herds, and higher culling rates in JD positive deer herds

SHEEP & BEEF

Computer modelling shows that co-grazing beef and sheep increases the prevalence of disease in both species. The longer the co-grazing period the higher the prevalence becomes.	2012 - 13	Computer modelling suggests JD is more difficult to control in sheep than beef cattle as interventions, such as test and cull, reduce prevalence faster and to lower levels in beef than sheep
Surveys and anecdotal evidence suggest that in most sheep flocks JD is a low level threat to animal health. Further information is needed about the true cause of ewe deaths on farm to understand the value of controlling the disease on farm		Clinical Johne's disease is rare in beef cattle in New Zealand. Most herds are infected with Type S strains of MAP, likely due to direct contact between sheep flocks
Preliminary modelling data suggests that vaccination for Johne's disease would be cost effective if annual mortality due to Johne's disease is >1%	2012 - 13	Guidelines have been published for the management of Johne's disease in sheep flocks

DAIRY CATTLE

More than 5000 dairy herds have been screened for Paratuberculosis by bulk vat milk ELISA; 1% herds tested positive and 5% herds were classified as suspect	2012 - 2013	Bulk milk vat ELISA testing can be used to screen dairy herds for Johne's disease, but screening should not be attempted in late lactation as raised antibody levels in milk interfere with test performance
Dairy cattle are most likely to test positive to Johne's disease between lactations 3-6		Screening programmes using a milk ELISA test have indicated that the prevalence of JD in Jersey cows is three times greater than that observed in the "Holstein-Friesian" population
A reliable challenge model for inducing MAP infection in dairy cattle has been developed, traditionally an area of difficulty for researchers worldwide		There is limited value in testing for JD infection in young cattle as both culture and serology can fail to detect infected animals
A DNA bank from ~2000 Johne's affected dairy cows has been established and DNA genotyped to find genes that may be related to resistance and susceptibility to Johne's disease		In dairy cattle with severe JD, MAP bacteria survive in the gut because the immune system fails to recognise that MAP is a threat and does not respond as it should
Guidelines have been published for the management of Johne's disease in dairy herds	2012 - 13	Johne's disease reduces the productivity of dairy cattle both seasonally and across the lifetime of a cow. Milk, fat and protein yields can be significantly lower in JD positive cows

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DEER

Trials have proven that young deer are more likely to develop clinical disease on exposure to challenge with MAP than older animals	On-farm trials suggest that a proportion of deer with histopathological signs (lesions) caused by Johne's disease can self-cure
Whole herd test and cull, applied over 3 years can effectively reduce the incidence of deer testing Paralisa® positive for Johne's disease	Typing of MAP strains found in lymph node lesions of deer at slaughter show that all of the common MAP strains frequently cause clinical disease
Genetic parameters for measure of Johne's susceptibility in deer are moderate (0.16 to 0.26) and highly genetically correlated (0.85 to 0.94) in red deer. Heritability's are low in Wapiti	2012 - 13: A module has been created for DEERSelect, to aid in the selection of JD resistant stock for breeding; however the module has not been implemented as the expected genetic gains do not currently merit removing selection pressure from other valuable traits
A bank of DNA from Johne's affected deer has been created and is available for future genetic studies	A list of genes which potentially may be markers for signalling resistance or susceptibility to JD in deer has been identified
Resistant and susceptible phenotypes in deer may be distinguished by the nature of their gene expression response to MAP challenge in vitro	Several key genes have been found related to MAP infection in deer. Their function suggests that susceptible animals develop severe disease due to uncontrolled inflammation and cell death processes. Resistant animals appear to be able to control cell death.
Analysis suggests that both pooled faecal culture and serology may not be suitable tests for determining "freedom from disease" in deer herds due to a high rate of false-positive diagnoses.	2012 - 13: Computer models in deer predict that rotational grazing is preferred for disease control in deer over permanent grazing to minimise bacterial loads on pasture

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