JOHNE'S DISEASE RESEARCH CONSORTIUM

ANNUAL REPORT **2015**

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)
NZ	New Zealand
OJD	Ovine Johne's disease
Paratuberculosis	Another name for Johne's disease
PTB	Paratuberculosis
UJV	Unincorporated Joint Venture

The Consortium

The Johne's Disease Research Consortium was established in 2008 as a joint venture between Industry and the Science community to coordinate Johne's disease research in New Zealand. The Consortium will draw to a close in June 2016 after eight years of operation having substantially completed its objective to support the development of cost effective tools for the management of Johne's disease on New Zealand farms.

During its term the JDRC will have invested $10.4 million in Johne's disease research behind the farm gate, looking at diagnostics, genetics, epidemiology and fundamental aspects of Johne's disease, in order to develop and refine practical and cost-effective tools for sheep, cattle and deer. The JDRC has played a key role; investing in the New Zealand research community, supporting the task of understanding the impact of JD in New Zealand and in ensuring that there are tools in place to control the disease for all farmers.

Johne's is a complex disease and combining the resources of major industry associations with research partners through the JDRC was an important step to ensure that research investment was coordinated and focussed on achieving the greatest benefit for the New Zealand livestock industry. The JDRC has also had the benefit and privilege of being able to collaborate with and work alongside other research teams and industry bodies, both within New Zealand and internationally to strengthen the outcomes from its programme and provide the best outcomes for New Zealand farmers.

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. The Ministry of Business, Innovation and Employment (MBIE) provides funding to the Consortium via the Research Partnership funding scheme[1]. Landcorp Farming Limited, Johne's Management Limited (JML) and The New Zealand Merino Company Limited (NZM) are also collaborators.

[1] Formerly the Research Consortia Funding Scheme

The disease

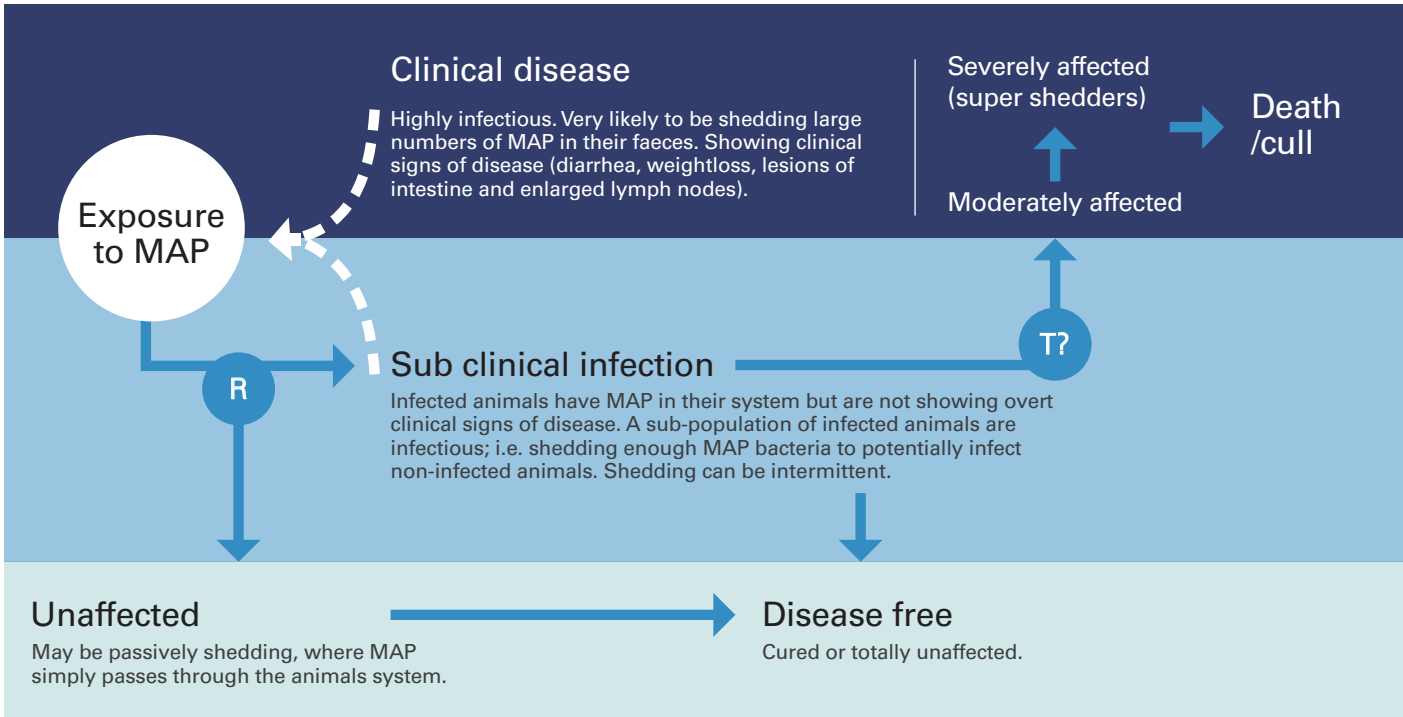
Johne's disease (JD) is a chronic, progressive, contagious and generally fatal infection of cattle, sheep, deer, goats and wildlife caused by the bacterium *Mycobacterium avium* subspecies *paratuberculosis* (or MAP). Infected animals contaminate the environment by shedding large numbers of MAP in their faeces, increasing the risk of infection passing 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.

Impacts of the disease on farm

While results from research studies vary, evidence suggests that clinical Johne's disease affects 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 cost of Johne's disease is thought to be minimal on farms without clinical disease, the cost on the worst affected properties can be substantial and not limited to economic impact alone.

The cost of the disease to the livestock industries was estimated to be approximately $40 million per annum in 1998[2], but industry experts considered this to be a significant underestimate of the true cost. Data collected in 2014–15 by JDRC researchers suggests that the cost of Johne's disease to the New Zealand sheep sector is of the order of $75–92 million annually[3]. Updated figures for cost of JD to other sectors are pending the outcome of future JDRC studies.

Pathways of MAP Infection



T?

It is not known what, or if "triggers" result in the progression of infection to clinical disease—but stress is one factor known to influence the manifestation of clinical disease in infected animals.

R

A spectrum of responses can be expected on exposure to MAP. Response will varydepending on species, strain of MAP, age of the host, size of the challenge, degree of stress affecting the host and the innate/acquired resistance of the host (resistance vs susceptibility).

JDRC in 2014-15

JDRC has delivered on a number of its research objectives in 2014–15 as the work programme nears completion. The JDRC has had three major projects designed to generate solutions to improve the control and management of Johne's disease on dairy, sheep and deer farms in the latter stages of the research programme. These projects were developed in conjunction with industry experts to address priority research targets identified by the dairy, beef & sheep and deer sectors in 2011.

A four year study for the dairy sector with Livestock Improvement Corporation to test the practicality and effectiveness of interventions to reduce transmission of disease in a herd is ongoing. This work has been undertaken alongside investment in dairy genetics to provide a selection tool for breeding.

For the Sheep sector, a project team from the Vet Centre Marlborough and Massey University has just completed a study monitoring the cause of ewe death on farms with a high suspected incidence rate of Johne's disease. Data were collected from twenty properties located around New Zealand over two years. This work was carried out in collaboration with The New Zealand Merino Company Limited.

AbacusBio Limited and Johne's Management Limited have almost completed work in a project for the deer sector which assesses the impact of Johne's disease on farm and the use of diagnostic testing. The study involved the sampling and testing of approximately 3000 deer and aligning farmer observation and test results to better understand disease management tools for JD.

[2] DeBrett Report, MAP, 1998

[3] Cord Heuer, January 2014

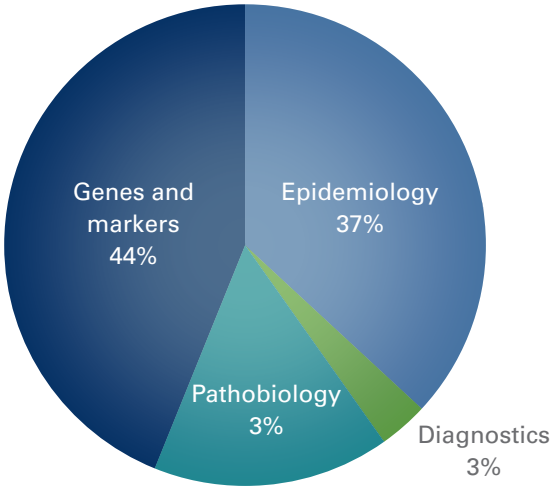
Research programme

The aim of the JDRC research programme is to reduce the impact of Johne's disease on farm, and has involved a number of different approaches to disease minimisation. Johne's disease is complex and MAP a difficult organism to study. The bacteria grow slowly in culture systems, are difficult to detect and their effect on ruminant animals is usually 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.

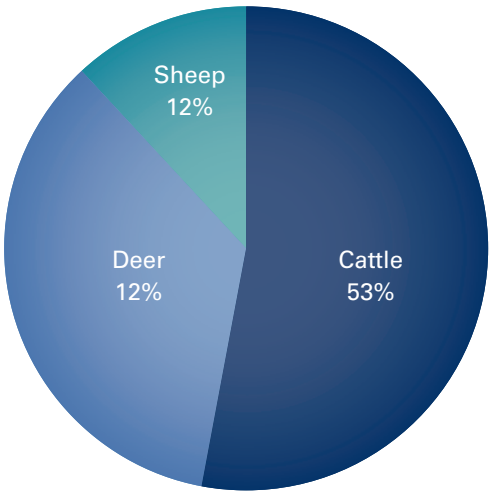
The JDRC programme has invested research and development funds in four major areas:

- Diagnostics
- Pathobiology
- Genes and markers
- Epidemiology

Science funding by objective



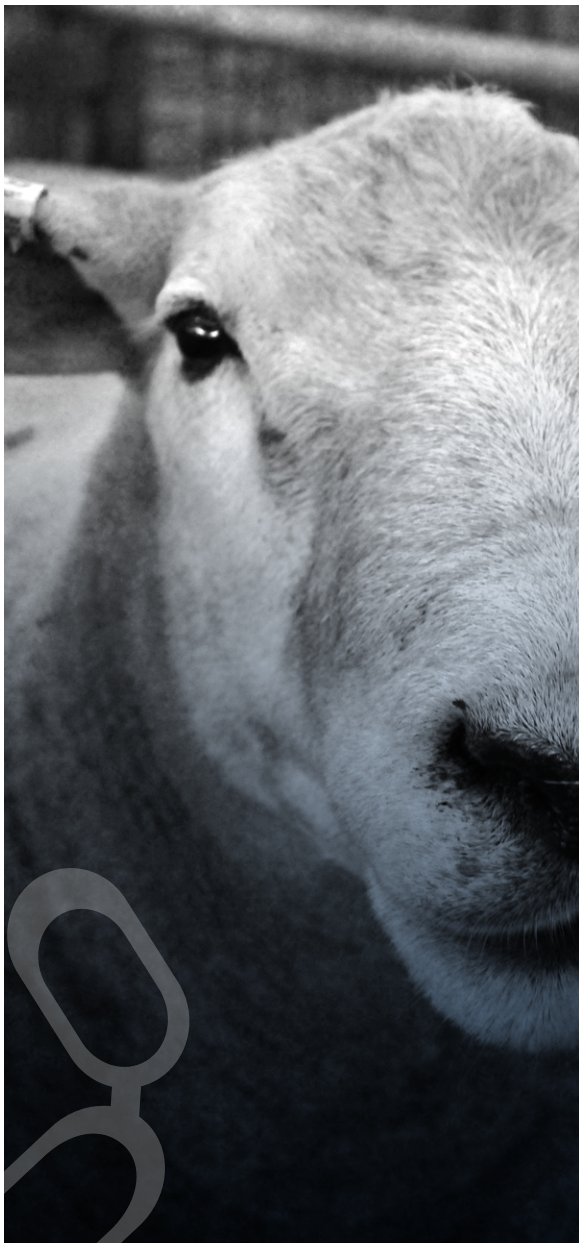
Species funding allocation



Sheep and beef sector

The Ovine Johne's Disease study, investigating the cause of ewe death on farms reported to have a "high prevalence" of Johne's disease, was completed in 2015.

Results have been correlated from a two year study monitoring the cause of death in ewes on 20 farms from across New Zealand[4]. The surveyed farms were made up of a range of breeds including Romney, Corriedale, Cross-breed and Merino flocks. Researchers used both pre- and post mortem testing to quantify the contribution of Ovine Johne's disease (OJD) to ill-thrift and mortality and estimate the impact of OJD in these flocks.



Researchers found that the average annual mortality rate of mixed aged ewes on these farms was between 7-8%, of which up to 2.8% of deaths were caused by Johne's disease itself. Therefore while OJD morality rates were high, a number of other conditions were also causing wasting and ewe death on these properties, including parasites, poor molars, poor legs or feet, enteric and respiratory disease. There was a large variation in the rates of OJD seen farm to farm, but the overall mortality rates were similar on each property.

Vaccination is currently the most practical intervention for control of OJD in sheep in New Zealand. Cost-benefit calculations from this phase of the study have confirmed that vaccination is likely to be an attractive intervention in flocks with a high observed incidence of OJD mortality (>1%).

This study was completed in collaboration with The New Zealand Merino Company and was partially supported by funding from the Primary Growth Partnership fund.

[4] Peter Anderson, Marlborough Veterinary Centre, Cord Heuer, Massey University

Dairy sector

Two significant tools developed by the JDRC have been released for the control of JD in dairy cattle in 2015.

The first edition of the Dairy Toolbox for the control Johne's disease in Dairy cattle was published by DairyNZ in 2015. The Toolbox was rolled out to Farmers and Veterinary practitioners at a series of regional events in key "high risk" Johne's disease areas in February-March 2015. The toolbox provides advice about how to minimise the impact of JD by focussing on calf health and minimising the transmission of JD infection to the most vulnerable animals in a herd.

The toolbox was developed by Livestock Improvement Corporation as a part of a four year study that is being run on 20 farms from across New Zealand. These farms are trialling the practices recommended in the toolbox to ensure they are both practical and effective in real farming situations. Farms participating in the study have seen dramatic and immediate improvements in the number of cows being culled as a result of Johne's disease. The toolbox recognises that all farming systems are different and the advice provided gives options that allow a farmer to tailor a control programme suitable to the needs of their herd and farming environment. As well as describing best practice the toolbox also highlights high risk practices that should be avoided. The implementation of good management practice is the backbone of control for JD and the best tool farmers have to minimise the impact of JD in their herds.

A copy of the Dairy toolbox can be downloaded from the DairyNZ website (www.dairynz.co.nz/animal/health-conditions/johnes-disease).

The second tool developed and released by researchers at LIC in 2015 is a genetic based test which can be used to calculate breeding values for Johne's disease. The Johne's Disease Susceptibity Index (JDS) was developed as a result of the analysis of DNA from approximately 2000 dairy cattle infected with Johne's disease. The set of genetic markers found in that analysis make up the JDS and are used to indicate an animal's susceptibility to the disease. Low JDS values indicate that an animal is less likely to contract JD than an animal that has a higher JDS and therefore that animal might be preferred for breeding.

While breeding for resistance is an attractive means of controlling disease, having good animal genetics is only a small part of reducing the impact of Johne's disease in a herd. Relying only on genetics and sires with a low JDS to control disease is not recommended. Breeding strategies must be used in combination with good management practices (as described in the Dairy Toolbox) to ensure the best results on farm.

The JDS is currently available to farmers via the LIC 2015 Precision Breeding, Alpha Sire Catalogue.

[5]Hinrich Voges, Geoff Corbett; Livestock Improvement Corporation

Deer sector

A study to provide a better understanding of the use of diagnostic tools in the deer industry, has been substantially completed in 2015.

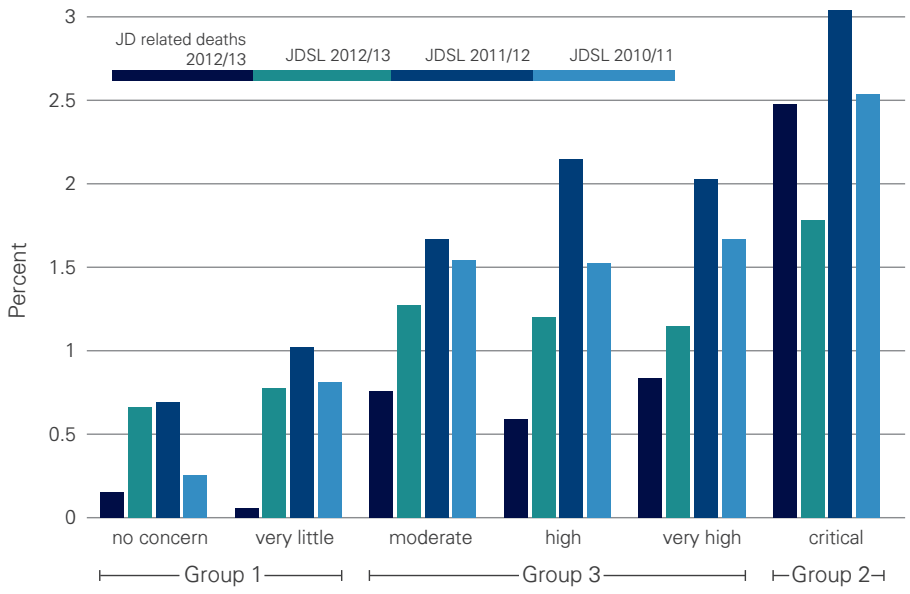
The on-farm deer study, run by AbacusBio Limited[6], in collaboration with Johne's Management Limited (JML)[7], has compared the performance of the Paralisa® and Parachek® serum ELISA tests against quantitative faecal PCR. It has also compared JD-suspect lesion rates recorded in the JML national surveillance database with the JD-related death rate on-farm and farmer concern regarding the disease. The study is collating these findings into a number of case studies for industry to demonstrate the management of Johne's disease using the tools currently available to deer farmers.

The JML component of the deer study was completed in late 2014. Responses to a survey from 151 deer farmers were compared with the JD-suspect lesion rate for their deer. The research confirmed that there is a strong link between JD-suspect lesion rate, on-farm impact of Johne's disease and farmer concern about Johne's disease.

This result provides support for the methodologies that JML uses to prioritise resources for controlling JD in New Zealand deer herds.

The second component of the deer study was a comparison of the ability of two serum ELISA tests to detect highly infectious deer. These deer will inevitably be shedding high levels of MAP in their faeces and spreading infection in a herd. The study focussed on herds with a high death or high JDSLN rate and involved repeat testing of rising two-year old females at scanning. The results confirm that ELISA tests are most effective at detecting infection in animals that are high shedders. Final data from the study are being used to formulate a set of best practice guidelines for the use of diagnostics on deer farms that will be published, along with a number of case studies on the control of JD, later in 2015.

Lesion rate in farmed deer



[6] Peter Fennessy, Neville Jopson; AbacusBio Limited
[7] Solis Norton; Johne's Management Limited

Sector wide developments

Alongside science delivery the secondary mandate of the JDRC has been to build a platform for the management and provision of JD information for industry. The Consortium has worked with its industry partners to both identify what resources, information and research the industry required and then, where possible, has provided support to fill the gap where a need was identified. With the end of the Consortium term approaching the JDRC is working to ensure that any outstanding issues around the management of JD have been scoped and documented so that industry is well informed regarding issues and opportunities in the Johne's area, prior to the JDRC closing.

Industry resources

JDRC continues to work with its industry shareholders to develop and refine best practice guidelines for the management of Johne's disease in livestock. With the publication of the dairy toolbox, best practice guidelines are now available for dairy cattle, sheep and deer. Guidelines for the management of livestock are based on three major factors; controlling on-farm transmission, preventing entry of the disease into the herd and maximising herd/flock health. Current work includes steps to standardise the format of all JD resources in New Zealand to ensure there are clear and consistent messages around the fundamental principles of disease management for all sectors.

Vaccination review

Vaccination is an effective tool for reducing the impact of Johne's disease in livestock. While not preventing disease, vaccination has been shown to reduce shedding and disease transmission and therefore the incidence of disease in herds and flocks. Vaccines are available for cattle, deer and sheep, but only the sheep vaccine is registered for use in New Zealand. Vaccination is not used in cattle and deer due to a number of regulatory and practical issues, including the fact that vaccinated animals can give rise to false positive tests for tuberculosis.

A review of vaccination was commissioned by the JDRC Board in 2014 as a number of recent changes have meant that these issues might no longer be barriers to implementing vaccination for cattle and deer. Findings from the review suggest that while there are still barriers, these have reduced in number and impact in recent years.

"It should be possible and in some cases would be advantageous to overcome these so that vaccination could be implemented as a management tool for those herds and flocks most affected by the Johne's disease".

This report is being reviewed by industry stakeholders prior to general release on the JDRC website.

Johne's Advisory Group

The JDRC established the Johne's Advisory Group (JAG) in 2013 to provide advice to the JDRC Board regarding the science and management of Johne's disease both within New Zealand and internationally. The JAG is appointed by the JDRC Board and 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.

In 2014-15 the JAG reviewed international media and scientific publications for data relevant to New Zealand and reviewed the status and content of industry resources for the management of JD in livestock. Both sets of reviews have confirmed that JD information in use in New Zealand is up to date and reflects the best information currently available worldwide.

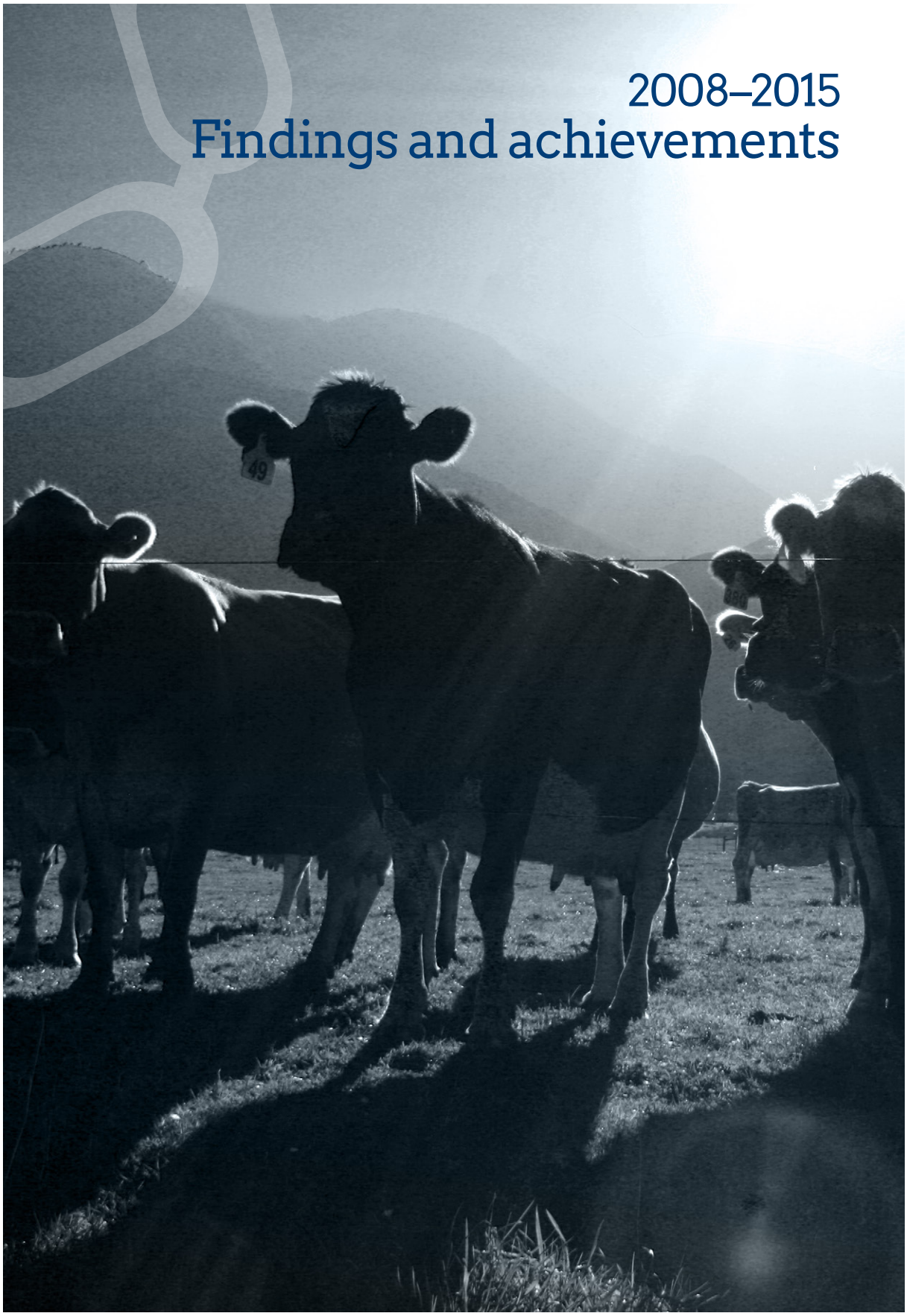
The ongoing work of the JAG to oversee both the national and international JD information will ensure that gains from the JDRC collaboration remain and are built on in the future for the benefit of the livestock industry.

[8] www.dairynz.co.nz/animal/health-conditions/johnes-disease/

[9] www.beeflambnz.com/Documents/Farm/Johne's%20disease%20guidelines%20for%20NZ%20sheep%20farmers.pdf

[10] www.johnes.org.nz/publications

[11] An Assessment of Vaccination as a Control Tool for the Management of Johne's Disease in New Zealand. Terry Ryan, 2014



2008–2015
Findings and achievements

Across the 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 eight 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		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 and 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		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
	The annual cost of Ovine Johne's disease has been estimated at $2.2–3.2 per adult ewe. With 75% of the 38 million adult sheep estimated to be affected with OJD, the costs at a national level are in the order of $75–92 million		Data collected on farm suggests that ewes with Johne's disease die at least six months earlier than their flock mates
	Modelling data suggests vaccination could be expected to reduce ewe mortality in a flock from 2. 75% to zero over nine years by continuous vaccination		Guidelines have been published for the management of Johne's disease in sheep flocks
	Modelling data predicts that vaccination would be cost effective in flocks where OJD mortality is ≥1.8%, but is not cost effective below 1% mortality		
	A number of other conditions (including include parasites, poor molars, poor legs or feet, enteric and respiratory disease) contribute to mortality on farms with a high OJD prevalence rate	2014-15	Annual mortality due to OJD on farms suspected of having a high prevalence of JD has been found to be between 0.7–2.8%. Overall mortality on these farms was between 7–8%

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		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		Jersey cows are three times more susceptible to Johne's disease than Holstein-Friesians
	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		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
	A survey of 1750 dairy herds has indicated that 23% of herds rank their concern about JD as serious or moderate, 48% had suspected or diagnosed JD on farm in the past five years and 39% had a management plan in place for JD		Survey data indicates that herds are more likely to be JD positive with increasing herd size and if replacement heifers are transported off farm at ≥5 months of age or calves are raised on the property of birth for at least one month post-weaning
	Publication of best practice guidelines for management of JD in dairy herds	2014-15	Predictive test for determining resistance/ susceptibility to JD developed and commercialised for dairy cattle

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 (i.e. lose visible signs of the infection)
	Whole herd test and cull, applied over three 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		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 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.		Computer models in deer predict that rotational grazing is preferred for disease control in deer over permanent grazing to minimise bacterial loads on pasture
	Survey data suggests farmers rate losses due to JD culling as having more impact on farm than weaning losses		Farmers that use consultants and participate in discussion groups are more likely to recognise the true impact of JD than others
	Survey data indicates a strong link between lesion rate and on-farm impact of JD. 70-80% of farms with a low or zero lesion rate had a JD suspect death rate of less than 1%.		Survey data indicates that 77% of farmers feel JD is either declining or already at low levels in their deer, while only 23% rank the disease as a serious production limiting issue.
	Average annual loss rate due to JD on deer farms is $1.33 per stock unit	2014-15	Elisa and qPCR tests are useful in the control of JD and will show a positive cost benefit ratio when used appropriately. Testing achieves the best results when integrated with a whole herd health and farm management plan
	Paralisa® and Parachek® Elisa tests show comparable performance across a range of shedding rates in deer		Sensitivity of ELISA tests increase with increasing shedding rates (~73% at $\geq 10^3$ to 100% at $\geq 10^6$ in the JDRC study)

JDRC Board

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JOHNE'S DISEASE
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