Lyme disease in Australia

Patient submission to the Australian Government Department of Health’s ‘Scoping Study to develop a research project(s) to investigate the presence or absence of Lyme disease in Australia’

Lyme Disease Association of Australia

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“Courage is what it takes to stand up and speak: courage is what it takes to sit down and listen”  Winston Churchill
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Executive Summary
The Lyme Disease Association of Australia (LDAA) has prepared this document to reflect the Lyme community’s response to the Scoping Study to Develop a Research Project(s) to investigate the presence or absence of Lyme Disease in Australia commissioned by the Chief Medical Officer (CMO) as part of a process of reviewing Lyme disease in Australia. The LDAA’s response is derived through extensive consultation with the Australian Lyme community since the Study’s release in December 2013.

The Lyme disease topic presents an intractable problem, unique in its ability to polarise the debate in almost every aspect of its complexity and on every continent. The Scoping Study (the Study) appears to mirror this polarisation in its selective use of research representing a sectarian agenda that has historically failed to address the complexities of the problem to the satisfaction of patients wherever it has been applied.

The five research projects presented in the Study are specifically scientific and neglect to include or prioritise patients; this is not a satisfactory situation for the many Australian patients suffering with Lyme disease or a Lyme-like illness. A potential epidemic is not solely the domain of a laboratory based research agenda; it is a people problem. A detailed commentary on the five key research projects recommended in the Study provides the basis for the LDAA’s additional research projects, which advocate for a greater focus on patients.

Throughout the development of this response, the LDAA has been reminded of the cascade of issues that has stalled the recognition in Lyme disease in Australia, including but not limited to: insufficient contemporary research into vector-borne diseases; inadequate and inconsistent testing processes; in combination with, a medical community that is under-educated on Lyme disease and reliant on official government advice stating there is ‘no Lyme here’.

The equivocal science used to justify this position is reinforced in the Study. In its examination and sequential analysis of the Study’s research material as presented, and with the benefit of extensive additional research, the LDAA challenges this and many other troubling suppositions and assertions in its further detailed commentary throughout this response to the Study.

The LDAA recognises the critical and overdue need for accurate information about all aspects of Lyme disease in Australia. Well researched prevention programs, clinical studies, patient support, and appropriate diagnostic and treatment guidelines that address the unique Australian situation will play a key role in changing the current uncertainties and confusion that surround Lyme disease in Australia. Research approaches that are far more aware and encompassing of past barriers and the complexities of this illness are critical to the conduct of effective Lyme disease research. The LDAA and the Lyme community have proposed a patient-focused strategic plan encompassing the research agenda proposed in the Study with the necessary inclusion of more patient-focused outcomes.

Australians now have an opportunity to transcend the sectarian view and, instead, model best practice - if we have the courage to do so.
**Introduction**

The LDAA and the Lyme community embraced the CMO’s announcement for a review into Lyme disease in Australia with enthusiasm. The entire community has placed a great deal of hope and faith in this process and see it as a means by which Lyme disease can be recognised and appropriately treated. The Lyme community values the chance to submit a response to the Study as it is an opportunity for those who experience this illness and all its complexities, to provide valuable insight that may otherwise be neglected.

The LDAA consulted extensively with the Lyme patient community throughout December and January on the content of the Study. Those consultations form the basis of this response with the consolidated input of 125 patients. Although sufferers of Lyme-like illness in Australia face many forms of discrimination, both universally and individually, *the illness itself is non-discriminatory*. The LDAA’s community includes members from all socioeconomic groups and all parts of the country; they comprise patients and the many carers, family and friends of people who are affected by Lyme disease. While some members were so unwell they could only offer encouragement and affirm others’ contributions, previously high achieving members of the community have pushed the limits of their Lyme-imposed disabilities to diligently apply their skills and breadth of experience in working on the research and development of this submission.

Consultations with the patient community raised many areas of concern with the Study and highlighted some of the complexities that will need further consideration if Lyme disease is to be effectively investigated in Australia. The overriding patient response, however, has been that the approach to solving the Lyme disease problem to date, and as reflected in the Study, has been constrained to an extremely narrow ‘scope’ that follows orthodox thinking and established research pathways.

Patients have also expressed concerns that the Study appears to rely heavily on United States (US) sources for its expertise and guidance. Yet the USA is a country in which the Lyme disease problem has not been satisfactorily addressed from any perspective, let alone a patient one. A wholesale importing of US policy directions could result in the replication of political divisions that exist within the American medical profession and the conservative views enthusiastically endorsed by the US health insurance companies. Australian patients deserve better and Australia has the opportunity to benchmark best practice.

The Study fails to consider broad and lateral approaches tailored to Australia’s unique situation. Patients have identified some concerning assumptions, logical flaws and biases in the Study’s approach that could potentially result in more adverse impacts for patients. Patients have provided valuable information and feedback that stems from their first-hand experiences of the current handling, testing, diagnosis and treatment of Lyme disease in Australia.

From the patients’ perspective, the Study appears to lead officials down a highly questionable and well-worn pathway of logic to approach the Lyme disease problem, as described in Table 1: The Lyme Problem Logic.
Table 1: The Lyme Problem logic

<table>
<thead>
<tr>
<th>The Lyme Problem:</th>
<th>Assumption:</th>
</tr>
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<tbody>
<tr>
<td>There is a rapidly expanding group of patients in Australia who believe they</td>
<td>Lyme-like illness = <em>Borrelia</em> and <em>Borrelia</em> can be conveyed by ticks.</td>
</tr>
<tr>
<td>have a Lyme-like illness. This group is becoming increasingly vocal in their</td>
<td>THEREFORE, we search for (a known species of) <em>Borrelia</em> in Australian ticks.</td>
</tr>
<tr>
<td>criticism of the existing public health approach to Lyme disease, which has</td>
<td></td>
</tr>
<tr>
<td>begun to attract adverse publicity.</td>
<td></td>
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</tbody>
</table>

IF we DON’T find *Borrelia* in indigenous ticks.

THEN...
Lyme disease is not here, at all (regardless of other potential modes of transmission or importation).

THEREFORE
Patients who think they have Lyme are deluded (crazy).
Doctors who diagnose Lyme are incompetent and irresponsible (quacks).
Laboratories producing positive Lyme serology lack credibility (dodgy).

ACTIONS
Maintain status quo, that is:
Utilise diagnostic criteria and testing procedures that eliminate the greatest number of patients from the diagnosis.
Declare as ‘false positives’ most contrary lab results.
Educate clinicians that “Lyme doesn’t exist here” and to discount this diagnosis.
Diagnose patients with a condition called ‘anything-but-Lyme’.
Approach as a psychosomatic or psychiatric condition and prescribe psychiatric or antidepressant drugs or medications best-suited for other diagnoses.
Ignore need for disease surveillance and public risk warnings.

IF we DO find *Borrelia* in indigenous ticks

THEN...
we (reluctantly?) acknowledge Lyme disease is here in Australia.

THEREFORE
The patients, doctors and laboratories previously condemned may have been on the right track after all.

ACTIONS
Develop new guidelines based on *Borrelia* in ticks as cause of Lyme-like illness, that is:
Establish ‘tick-focused’ diagnostic criteria and ‘*Borrelia*-focused’ testing pathways likely to exclude a great number of patients from the diagnosis.
Discount clinical and anecdotal evidence indicating other modes of transmission until scientific research is concluded.
Discount co-infections as potential primary infections.
Discount chronic Lyme diagnosis.
Identify short-term treatment protocols - favoured by US pharmaceutical and medical insurance companies - in the (misguided) belief this will reduce burdens on the public purse.

Although this may appear a rather cynical and pessimistic viewpoint, the first scenario describes the logic and approach that currently underpins the official status quo with which patients suffering Lyme-like illness are faced in their dealings with the medical fraternity in Australia at this time and they are not particularly encouraged that the outcomes of the narrowly focused research proposals in the Study will significantly alter their situation.

The current parameters of Lyme in Australia are largely based on one official research study (Russell & Doggett 1994), which failed to find evidence of (a known species of) *Borrelia* in Australian ticks. Patients (regardless of where or how they might have contracted their infections) have been condemned to experience the myriad of destructive manifestations of a status quo that does not recognise their medical condition and discriminates against those who suggest patients might be suffering from Lyme disease. The current situation trivialises and often invalidates the patients’ lived experience of an extremely debilitating and life-destroying condition of Lyme-like illness.
The Study reflects this deeply entrenched attitude. The Lyme patient community can identify some omissions of crucial areas of evidence within the Study’s ‘scope’; most significantly, the omission of consultations with key stakeholders, Australian Lyme and Lyme-like illness patients and the aptly experienced doctors who are diagnosing and treating them successfully.

The Study reports “uncertainty and confusion…fuelled in part by emotive and unsubstantiated reporting by the media…generate substantial public concern.” What is omitted is that the media has gone to considerable lengths to substantiate all claims and seek two sides of the story. It is hardly surprising that when unresponsiveness, dismissal, lengthy misdiagnosis and even discrimination are repeatedly experienced, patients will naturally experience frustration and desperation. Emotive outpouring to the media is a natural consequence; patient stories are alarming to the public, with good reason. Ultimately, where the current medical system has failed those suffering, media has given rise to a population that can ask more questions and find alternate means of assistance.

Patients are often condemned to endure immeasurable suffering because they live within an irredeemable catch-22; a situation where services and support are denied on the basis of insufficient scientific research, even though there is a growing body of anecdotal evidence. This is exacerbated by the fact that there is no scientific evidence because no in-depth research has been conducted, nor relevant data collected. There is no data available to support the growing anecdotal evidence because collection is not currently justified; this again is due to lack of scientific evidence. The most irredeemable statement currently used in regard to the Lyme situation in this country is that “there is no evidence to suggest…… “

Drawing upon the many experiences of living with the manifestations of this logic, the Australian Lyme community suggests avoiding narrowing the scope of the investigations to a focus that would only search for *Borrelia* in ticks alone. It is also of major concern that the Study develops a hypothesis based on assumptions informed by imported knowledge about how Lyme disease and Lyme-like illness occurs in other countries. Considerations for conducting a full and thorough investigation of the unique epidemiology relating to Australian patients’ experience with a Lyme-like illness should be an essential component in the development of the most appropriate hypothesis regarding causes of this illness.

Without this, the Study risks further invalidation and trivialisation of the unique experiences of Australian patients and, in doing this, it risks discarding potential clues that might lead to a more effective solution to the problem. The proposed approach may be likened to solving a jigsaw puzzle by only collecting some of the easier/more identifiable pieces, while throwing all the other pieces into a ‘too hard basket’.

The Lyme community’s priorities in response to the Scoping Study are best summarised in the following statement offered by one patient:

“What is most important to us as patients is not what you call it, where we caught it or what bug spreads it; what is important to us is that the medical fraternity acknowledges we are indeed ill and we need access to appropriate, affordable treatment, as well as protection for the broader public, as a matter of urgency while the science catches up with the reality of our condition”. 
It was most apparent from the LDAA’s consultations that the patient community wishes to see ‘the Lyme problem’ approached from a perspective that is clearly different, particularly outside the narrow focus of the laboratory. On the basis of these consultations, the LDAA presents a Patient-focused Strategy for the Chief Medical Officer’s review at Appendix A.
Comments on the Scoping Study points

The Department of Health (DoH) has asked specifically for comments on the five proposed research projects with consideration of the priority in which they should be undertaken.

For convenience, a summary of the LDAA’s comments on the proposed five projects is provided first, then a further two projects are recommended; research project 6, an epidemiological study and research project 7, the development of a treatment pathway. Each study is addressed following the order presented in the scoping document. Recommendations for how these projects should be prioritised are discussed in the sections that follow.

Following discussion of the projects, a page by paragraph commentary on the Study is discussed. Points of note are highlighted in bold.

Study 1: Experimental program to determine whether there is a *Borrelia* species in ticks in Australia causing Lyme-like disease, or whether another tick-borne pathogen is involved in human Lyme-like disease.

The LDAA agrees in principle to much of the proposed directions in this research project; however there are some necessary considerations as follows:

a) Although the patient community welcomes Study 1, it is worth noting that the LDAA vehemently denies that there is currently insufficient evidence to support the presence of *Borrelia* in Australia. The LDAA also would like to point out that the title of the scoping study report “Scoping study to investigate the presence or absence of Lyme disease in Australia” implies that a negative finding proves there is no *Borrelia* in Australia. This is not true because one cannot prove a negative in this case. Alternatively, the ‘extent’ to which Lyme Borreliosis is present in Australia, either via importation or indigenously, is the issue.

b) The assumption that spirochaetes are easily detected or visualised is incorrect and undermines the need for experienced microbiologists employing state of the art technology to the issue.

c) Samples should be collected from coastal, mountain and desert terrains recognising the vastly different environments in Australia. All areas where people are reported to have a Lyme like illness should not be excluded from scientific inquiry.

d) Collections and studies should not be limited to ticks; samples of all biting insects, fleas, mites, keds (biting flies), lice etc. should be considered, especially where people are reported to have a Lyme-like illness.

e) Other potential pathogens should be included in this study; where ticks are being studied for *Borrelia*, it is imperative to also understand the capacity for Australian ticks to harbour and transmit more than one organisms of infection; *Babesia, Bartonella, Anaplasma, Ehrlichia, Rickettsia* and other pathogens and viruses should not be excluded.

f) *B. Queenslandica* requires acknowledgement.
Study 2: Are Australian ticks competent to maintain and transmit *B. burgdorferi* s.l. genospecies or other *Borrelia* species associated with relapsing fever?

The LDAA agrees in principle to this research project; however there are some necessary considerations as follows:

a) Vector competence studies should not be limited to ticks; where spirochaetal matter is discovered in other insects, their vector competence should be properly investigated.

b) Evidence already exists to indicate that Australians are infected with more than one strain of *Borrelia*. For this reason, research should investigate the multiple strains present within the samples collected and provide transparent calculations of the competence of those vectors to transmit multiple organisms, not simply *Borrelia*. Rates of transmission also necessitate investigation.

c) Research on strains known to cause relapsing fever should be correlated with clinical evidence of patients who are presenting with relapsing fever syndromes, as proposed by the LDAA in research project 4.

d) Native fauna should be considered in the examination of potential reservoirs and should be included to determine whether there is a native Lyme-like organism similar to that detected in Brazil. It is crucial to understand the epidemiology, as there may be more than one vector involved. The Study should be expanded to include identification of native Reservoirs for Lyme and Lyme-like disease and its associated co-infections.
Study 3: Do we have the best reagents for detecting novel Borrelia species, including *B. miyamotoi*, especially in clinical specimens?

The LDAA agrees in principle to this research project; however there are also some necessary considerations as follows:

a) Interim testing arrangements and standardisation of testing protocols are urgently required.

b) Some Australian private laboratories are already using sophisticated PCR techniques and isolating *Borrelia* and spirochaetal organisms. Every effort should be made to include any research evidence to continually improve the diagnostic and confirmatory testing protocols.

c) The DoH should immediately conduct a formal review into the current test process in use at the public health laboratories, specifically in light of the sub-optimal testing materials currently in use at Westmead.

d) The DoH should immediately, and formally, liaise with overseas testing laboratories that are providing positive tests to Australian patients. This would aid Australia in gaining an understanding of their test processes, antigens used, primers and sequences. An understanding of the differences in approach is crucial to providing the best possible, and most affordable, testing services in Australia. Patients will continue to demand answers on why Australian public health laboratories cannot find *Borrelia* in their samples. Exemplifying this problem, are cases where the same has been split, sent elsewhere and returns positive results.
**Study 4: Clinical studies of patients presenting with symptoms suggestive of Lyme or Lyme-like disease.**

The LDAA agrees in principle to this research project; however there are also some necessary considerations as follows:

a) Prospective clinical studies of patients must include an inquiry on alternate forms of transmission, for example, from an infected person to a sexual partner, or to a foetus, or via breastfeeding, as well as blood-to-blood contact or via transfusion. While there has been research on these topics internationally that indicates these forms of transmission are possible, further detailed research is required. It is essential for Health officials in Australia to categorically know how this illness is transmitted.

b) Many Australian treating doctors already collect a vast store of symptom-related data on patients by having them complete symptom charts at regular intervals. A program of research needs to commence immediately to gather and collate symptom information to underpin a detailed map of the constellation of symptoms unique to Australian patients.

c) EMs do not occur in many Australian patients. Limiting biopsy samples in Australian studies to EM rashes only is likely to miss more than half of the presenting Australian patients. Many Australian patients report rashes at their bite site other than an EM, or minimal inflammation at the bite site. For these reasons it is fundamental that samples from these patients are not excluded from investigation.

d) It is difficult to understand how the DoH proposes to capture potential patient research subjects and data, especially in regard to the relapsing fever group, while there is no official advice to clinicians about its presence.

e) It would be most beneficial for the DoH to work collaboratively with the patient groups to assist with the annual longitudinal survey of patients.

f) Any clinical study must investigate the manifestations of disease, especially in regard to early and late stages and ‘chronic Lyme’.

g) In clinical studies, it is imperative to include the Indigenous population to ascertain whether there is a history of Lyme-like illness in Australia or if there is a possibility for immunity of these pathogens to develop.

h) All clinical studies must abide by the strictest ethical principles and must be conducted in an open and transparent manner, with full declaration of any conflicts of interest.

i) All clinical studies must recognise the specific impacts that studies will have upon children, who are most at risk and, according to LDAA figures, are an expanding cohort of patients in the Australian demographics of Lyme disease or Lyme-like illness.
Study 5: Retrospective investigation of chronic cases of Lyme borreliosis

The LDAA agrees in principle to this research project; however there are also some necessary considerations as follows:

a) It is difficult to understand how retrospective studies could be populated with patients while the current attitudes and prevailing logic exists; there are a substantial number of patients with negative Australian test results but positive overseas results that are continually denied.

b) Testing processes and considerations outlined in research project 3 must be a precursor to qualifying patients by proving a past infection with *B. burgdorferi*.

c) Testing should not be limited to serological tests (ELISA and IFA), as many studies have shown negative serology in chronic cases with other indications of active infection, such as PCR positive and Elispot positive results.

d) The efficacy of SPECT scans in the diagnostic process.

e) Notwithstanding the criticism of the two-tier testing process in Australia, samples used to qualify patients for any prospective research must meet an agreed criterion and be conducted with the latest scientific knowledge and best laboratory technology available.

f) There is a cohort of patients from every demographic group that would be prepared to share their stories, their medical results and their histories as part of a formal retrospective study. Likewise there is likely a cohort of currently treating doctors that would welcome the opportunity for involvement in independent, well-designed retrospective research which include their patients.

g) Any review of consolidated patient data, as described in research project 4, and further noted for research project 5, should not be limited to infectious diseases experts only. Lyme disease and Lyme-like illness as presenting in Australia crosses several medical specialities and is not the *sole* domain of infectious diseases. Indeed, immunologists, neurologists, endocrinologists, cardiologists and general practitioners all have an interest in the diagnosis and evaluation of patients. To ensure best practice and optimise patient support in such a complex illness, review groups should be comprised of many independent experts.

h) A panel of "experts" requires the inclusion of at least two physicians with extensive experience in diagnosing and treating chronic Lyme disease in Australia, evidenced by a significant case load. This would provide the panel with the opportunity to draw upon valuable Australian-specific knowledge and experience.

i) All clinical studies and retrospective investigations conducted should be carried out with proper ethical approaches where full disclosure of any prior involvement in Lyme disease or Lyme-like illness is made transparent.

j) Acknowledged experts in Lyme disease already provide lectures in Australia as part of the Tick Borne Disease Conference convened by the Karl McManus Foundation; however any further education programs that are fully funded and supported by DoH are welcomed.
Study 6: Epidemiological research

The LDAA recognise that the proposed studies 1-5 comprise components of an epidemiological study however there are two obvious omissions. As a matter of urgency, the LDAA recommends a full epidemiological study that also includes, but is not limited to, the addition of the following:

a) A baseline quantification of Australians with diagnosed Lyme disease or Lyme like illness, to satisfy the Terms of Reference of the Clinical Advisory Committee on Lyme Disease (CACLD). Data collected should include demographics such as prior travel history, geographical location, bite history, disease duration etc.

b) Monitoring of Lyme and Lyme-like cases by the CDNA in light of the emerging incidence of Lyme-like illness occurring in Australians who have never left the country (LDAA 2012). A transparent and open disclosure of the criteria and processes used for monitoring and surveillance of Lyme disease or Lyme-like illness in Australia is required.

Study 7: Development of a treatment options pathway

Importantly, the Study’s eleven Major Gaps omit any reference to the treatment of Lyme disease; as stated earlier, the Study report is largely silent on this critical issue. Therefore the LDAA recommends consideration of the following issues:

a) Immediate authorisation for doctors to treat Lyme disease or patients with Lyme-like illness, irrespective of where they are diagnosed, without repercussions.

b) The development of interim guidelines, potentially based upon European guidelines, seems appropriate for Australia with dissemination to all hospitals, general practitioners and infectious disease doctors in Australia.

c) A standardised Australian ‘criteria’ for diagnosis is required to underpin the development of a diagnostic pathway.

d) Epidemiological studies (Rec 7) and clinical research into the unique Australian presentations of the illness (Rec 4) are required before the development of final treatment guidelines in Australia.

e) Current treating practitioners should be consulted in the development of any Australian treatment guidelines, either interim or final.

f) Co-infections often required a ‘layered’ approach to treatment because the Australian experience has shown that little progress is made until co-infections have been treated.

g) Develop educational material for doctors containing information on:
   - importance of differential diagnosis of Lyme disease;
   - clear articulation of early, late and chronic stages of Lyme with each of these stages requiring different treatment strategies;
   - chronic and relapsing nature of illness, also L-forms, cyst forms, cell wall deficient biofilms and the possibility of co-infections;
   - the Jarisch-Herxheimer reaction following administration of antibacterials;
   - the inappropriate prescription of steroids and /or anti-depressants (especially if the case is differential); and,
   - early intervention treatment strategies following a tick bite.

h) Appropriate specification of the medications required to treat Lyme disease on medical schedules and the Pharmaceutical Benefits Scheme (PBS).
Commentary on Scoping Study

Terms of Reference - Scoping Study paper

Page 2 of the Scoping Study provides a set of Terms of Reference (ToR) for the Study. It references the importance of “consultation with relevant stakeholders” and includes the CACLD, experts on Borrelia and researchers who are currently investigating tick-borne disease in Australia. It does not include the increasing group of Lyme patients who are the ultimate stakeholder in this discussion, nor any group of doctors treating Lyme disease in Australia. Additionally the ToR states that the major outcome of the Study will be the provision of an “outline for a research project to seek whether a causative agent(s) of Lyme disease exists in Australia”; this skews the study specifically to ‘Lyme disease’, not Lyme-like illness which could be representative of a unique or Indigenous disease. Then the ToR further skews the scope of study by constraining the investigation to blood-sucking (haematophagous) arthropods as part of its requirement.

A second required outcome was to provide guidance on a diagnostic pathway, yet the CACLD has established a diagnostic working group to develop a diagnostic pathway. It is unclear why there is a seemingly duplicative piece of work occurring or, if complementary, how the outcomes of the Study will impact upon the already drafted diagnostic pathways guideline.

The LDAA contends that narrowing the focus of the Scoping Study to ‘Lyme disease’ that is transmitted only by blood sucking (haematophagous) arthropods forces researchers to focus on ticks alone. This approach is inconsistent with an open investigation process.

Introduction section Page 3 (para 2) refers to statistics of 65,000 estimated cases of Lyme disease in Europe and 20,000+ cases in the United States and notes that there may be significant underreporting. On August 19 2012, the Centers for Disease Control and Prevention (CDC) in the United States published a media release indicating “that the number of Americans diagnosed with Lyme disease each year is around 300,000.” The Scoping Study misses this crucial news in its review.

The CDC is using digital information from various sources to provide a more realistic indication of the number of patients affected based on their medical claims, surveys of clinical laboratories and through self-reporting of the general public. The CDC also notes that “routine surveillance only gives us part of the picture”.

The Australian Government has similar information available that would also enable a more detailed spatial and temporal analysis of the potential extent of Lyme disease or Lyme-like illness in Australia. The LDAA recommends that proper monitoring of Lyme-like cases be part of the Communicable Diseases Network Australia’s (CDNA) brief in light of the emerging incidence of Lyme-like illness occurring in Australians who have never left the country (LDAA 2012, fig. 4).

There is no data in the Scoping Study that seeks to quantify the number of Australian patients with either Lyme disease, as diagnosed by a medical professional either in Australia or overseas, or of Lyme-like illness. This is disappointing, as the LDAA presented a case folder of 184 people who

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1 CDC provides estimate of Americans diagnosed with Lyme disease each year http://www.cdc.gov/media/releases/2013/p0819-lyme-disease.html
currently suffer from Lyme disease or Lyme like illness to the Chief Medical Officer (CMO) in March 2013. Furthermore a report about the Australian patient experience based on a survey of Lyme patients in Australia in 2012 was published (LDAA 2012). The most recent survey collected data from patients indicating over 800 cases of Lyme or Lyme-like illness in Australia. In fact, reference to the LDAA’s report is notably absent from the entire Study and may have been useful on many occasions to illustrate experiences here in Australia. These issues are further explored and discussed in the research project 5 – Epidemiological study.

It is also important to note that the LDAA sought amendment to the CACLD’s proposed Terms of Reference (ToR) Item 1. They were successful in obtaining an amendment to require the formal review of Lyme disease in Australia to investigate ‘the extent of Lyme disease’. Formal measurement of the incidence of Lyme disease is a major omission from the Study’s research projects and this is contrary to the CACLD’s own ToR’s.

Furthermore there are numerous findings relating to the incidence of Lyme and *Borrelia* in Australia, not limited to the following:

- Mackerras (1959) reported the isolation of *Borrelia* from Australian fauna including kangaroos, wallabies and bandicoots.
- McCrossin (1986) reported on ‘Lyme disease on the NSW South Coast’ in a letter to the Medical Journal of Australia.
- Rothwell et al. (1989) also reported on ‘Suspected Lyme disease in a cow’ in the Australian Veterinary Journal.
- Carley and Pope (1962) identified an Australian strain of *Borrelia* they named *Borrelia queenslandica* isolated from wild rats.
- Wills and Barry (1991) assert more than a dozen Australians on the northern beaches of Sydney and in the Hunter Valley have acquired Lyme disease, as reported in a letter to the Medical Journal of Australia. In addition, it found 70 of 167 of Australian ticks were culture positive for *Borrelia*-like spirochaetes
- Mayne (2011) reported on the *Emerging Incidence of Lyme Borreliosis, Babesiosis, Bartonellosis and Granulocytic Ehrlichiosis in Australia*.
- Mayne (2012) also provided evidence of *Borrelia burgdorferi* genotypes in Australia obtained from erythema migrans tissue.

In 1994 researchers Michelle Wills and Bernie Hudson proposed existence of an Indigenous form of Lyme disease based on data collected since 1991 (Hudson et al. 1994). They describe the clinical presentations of erythema migrans rash, arthritis and radiculopathy in candidate Lyme Borreliosis cases in Australia. When they tested the blood of these candidate patients, they discovered antibodies to European strains of *Borrelia - Borrelia garinii and Borrelia afzelii*, while antibodies to *Borrelia burgdorferi* were uncommon.
The LDAA recommends that a full and thorough investigation of all information be conducted to establish a baseline quantification of Australians with diagnosed Lyme disease or Lyme-like illness.

Page 3 (para 3) makes reference to the clinical presentation of Lyme disease and asserts that signs and symptoms resolve after antibiotic treatment of two-four weeks. The cited research (Murray and Shapiro 2010) is not referenced in the Scoping Study and, in fact, refers to two studies conducted by Klempner et al. (2001) (also not referenced). The study relates to two clinical trials of 78 and 51 patients respectively; this hardly qualifies as representative of the majority of patients (Klempner et al. 2001).

The LDAA’s Australian patient experience survey sought information from patients about the effectiveness of the guidelines for treating Lyme disease made by the Infectious Disease Society of America (IDSA). These guidelines recommend two-four weeks of antibiotic treatment. More than 200 Australian patients reported in this survey that significant improvement occurred with treatment beyond 30 days (LDAA 2012). The survey response provides a very strong indication that the IDSA guidelines for treatment, and those currently being recommended by the NSW Department of Health, are ineffective for Australian patients. It is critical to consider that this could indicate a more resistant strain that is resulting from a sub-curative course of antibiotics.

A 2007 article discusses the persistence of spirochaetes within macrophages after antibiotics (Stricker 2007). Dogs, mice and monkeys treated for 30 days failed to eliminate infection. It summarises that the animal models provide “credible scientific evidence” for persistent infection of Lyme disease. Further issues regarding early, late and chronic treatment issues are discussed in research project 7.

It is noted that the Study mentions treatment seven times throughout the document. This highlights a major omission from the paper and it leaves patients currently affected by Lyme disease or Lyme-like illness with little certainty or confidence. Without significantly more focus on both the interim and long-term treatment of Lyme disease and Lyme-like illness, the research process will not identify and resolve the many complex and current issues associated with treating Lyme disease or Lyme-like illness, irrespective of the affordability of that treatment.

The LDAA questions what the goal of the Scoping Study is, if it’s not to assist patients in returning to wellness? Omitting the essential discussions around possible treatment guidelines for patients is not conducive to the ultimate health outcomes for Australians suffering from the Lyme-like illness. There are many cases being reported from multiple doctors all over Australia and there is a very real and growing need, from doctors and patients alike, for treatment guidelines. In its current state, this report does not set appropriate parameters for an open-minded investigation.

Research that is neither holistic nor patient-focused, will not address the concerns of the Australian Lyme community. Lyme disease treatment guidelines are already an internationally contentious issue and an increasing source of frustration for Australian doctors treating Australian patients, so treatment issues should be properly investigated. As there is no plan in the Study on effective treatment protocols, the Australian patient community needs clarification on how this will be addressed.
Treatment pathways will be complex because Australian patients are presenting with different infections and different manifestations. Individual clinical assessment will need to play a major role in determining the most appropriate treatment for patients. For clinical assessment to be an effective diagnostic tool, practitioners will need further education on Lyme disease and Lyme-like illness.

Page 5, para 1 reports that the uncertainty about Lyme disease in Australia has caused confusion that has ‘fuelled ... emotive and unsubstantiated reporting by the media, and has resulted in substantial public concern’. The LDAA contends that Lyme disease and Lyme-like illness has been a public concern for more than 20 years in Australia and the media, in turn, have picked up on the discriminatory situation in which patients find themselves.

The same paragraph asserts that the ‘current accepted knowledge of Lyme as it occurs in the United States, Europe and Asia’ should provide the basis of Australian studies on the topic. The LDAA counters that current knowledge is far from ‘accepted’ and is largely in dispute. To infer otherwise is a disservice to Australian patients. Furthermore, if the issue of Lyme disease was globally ‘accepted’ there would be no need for a Scoping Study to underpin what can only be described as a significant research agenda on this very topic.

Background: Brief review of Lyme Borreliosis
Borrelia species in Lyme disease and their vectors, reservoirs and genomes Page 6, para 2 notes that Lyme Borrelia complexes are being recognised yearly and that if a concerted effort were made more would be found; it cites examples from Canada and Uruguay and Brazil. Incidentally, in the 20 years since the highly controversial Russell and Doggett (1994) study, six more pathogenic Borrelia genospecies have been discovered ².

The LDAA questions what efforts the Australian Government has made to understand how other Governments are dealing with the identification of vector diseases and how they are responding to such impacts upon human health. In a policy context, it is imperative to understand how research is being conducted into vector pathogens in geographic areas with a similar climate and topography to Australia.

Page 6, para 3 focuses on the ‘transmission of Lyme Borreliosis through injection of tick saliva during feeding’. It is important to highlight here that, to date, it has never been proven beyond a doubt that this is the ONLY form of possible transmission of Lyme disease. The LDAA Patient Experience reports that 39% of patients offered alternate explanations for their acquisition of Lyme disease, ranging from congenital and possible sexual transmission to bites from animals other than arthropods. (LDAA 2012, p.14).

Research has shown B. burgdorferi spirochaetes can be transmitted transplacentally from mother to foetus (MacDonald, Benach & Burgdorfer 1987). While a causal link is yet to be established, maternal Lyme disease has also been implicated in miscarriage after first trimester, still births and birth defects (Gardner 2001). Furthermore, newly published research also provides evidence that Borrelia burgdorferi may be transmittable through both vaginal secretions and seminal fluid, raising the very real issue of sexual transmission (Middleveen et al,2014). In an interview on this research,

² See http://www.ezbiocloud.net/search?k=all&v=borrelia
Australia’s Dr Mayne said “the presence of the Lyme spirochete in genital secretions and identical strains in married couples strongly suggests that sexual transmission of the disease occurs³.” The LDAA recommends this field is included in researching alternate modes of transmission and that it also includes animals other than arthropods.

Page 6 omits to reference *B. queenslandica* (Carley and Pope 1962) along with the 18 other *Borrelia* species specifically named. This strain (*B. queenslandica*) would be particularly relevant, given it is a native species; as such the quote in relation to Barbieri et al. (2013), identifying it as “the first isolation of indigenous *B. burgdorferi* s.l. in the Southern Hemisphere,” is incorrect.

Page 7, para 2 refers to an outdated reference (Piesman and Sinsky 1988; Ryder et al 1992) in the report. In this reference, the Lone Star tick was shown to be unable to transmit Lyme *Borrelia* yet more recent data indicates a contrary view (Clark, Leydet & Hartman 2013). The contemporary research notes that they “identified *Borrelia burgdorferi* sensu lato DNA in samples of blood and skin. They also identified this DNA in Lone Star ticks (*Amblyomma americanum*) removed from several patients who either reside or were exposed to ticks in Florida or Georgia”.

Furthermore, the same research indicates that PCR testing was performed on all patients, yet their serological results (using antibodies interpreted using the CDC surveillance criteria) indicated that “nearly all results would be considered negative. Four of six patients had equivocal or positive EIA or IFA screening tests, but only Patient 10 in our study may have met the current two-tier testing standard criteria for Lyme “seropositivity”” (Clark, Leydet & Hartman 2013). Like the situation that exists in Australia, it is possible that people in the southern part of the USA are infected with a different form of *Borrelia (Borrelia lonestari)* and this highlights some substantially different requirements for interpreting test results in these areas. The LDAA maintains that these types of research results need further consideration and exploration to better understand blood testing for Lyme disease in Australia.

Page 7, para 3 discusses birds as biological carriers of Lyme disease and transporters of affected ticks. It should be noted that many Australian patients report being bitten by non-arthropod insects including but not limited to, fleas, lice, leaches and bird mites (LDAA 2012, p. 12).

Pages 6-8 disregard the possibility of agents other than ticks and mites and, in fact, limit tick involvement to the Ixodes ticks, despite evidence to the contrary. There is a brief mention of *Ornithodoros* genus, but this does not appear to be deemed significant, despite “New species of *Borrelia (B. queenslandica)* from *Rattus villosissimus* in Queensland” stating “many species of *Borrelia* are transmitted by ticks of the genus *Ornithodoros*, the presence of *O. gurneyi* in inland Australia, including north-western Queensland, is of interest in the present study” (Carley and Pope 1962).

*The natural reservoirs of Lyme Borrelia species*

Page 8, para 3 (b) *The natural reservoirs of Lyme Borrelia species*, indicates that there are few potential hosts, yet later in the Study (under Section (f)) the author refers to the Mackerras (1959) study that isolated *Borrelia* on Australian fauna (Kangaroos, Wallabies and Bandicoots).

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In fact, a number of Australian articles indicate that Kangaroos may indeed be a key host to the ever-increasing risk of tick-borne pathogens not limited to Lyme Borrelia (Waudby, Petit & Weber 2008). There are more than 50 articles relating to tick-transmitted disease in Australia on the now defunct TAGS website reference list. We note that few of these references have been incorporated as part of the review underpinning the Scoping Study report and many refer to the possibility of alternate hosts.

The articles quoted in the Study about reservoirs refer to a very narrow field of review. Indeed an article on host biodiversity (Levy, 2013), indicates there are a range of reservoir hosts, some more competent than others. It also refers to some reservoirs being ‘amplification hosts’ whereby they complement the Borrelia transmission cycle, and others are ‘dilution hosts’ where the reservoir can pass it on to a new tick but with much less reliability.

Levy (2013) presents a valuable argument on the amplification efficiency of the White Footed Mouse in Borrelia transmission. Levy also makes a strong case for a “better understanding [of] the fundamental processes underlying the role of biodiversity in ecosystem functions”, especially in respect to Lyme disease. From China, researchers reported on the competence of Rodents, whose infection rate was 22.86% and were also found to maintain more than one strain of Borrelia (Zhang et al. 2010).

The LDAA highlights that identifying any potential reservoir(s) for Lyme disease and their competence of transmission is paramount in future Australian research. An understanding of our potential hosts, reservoirs, amplification hosts and dilution hosts and the habitats they occupy is a prerequisite that is essential for mounting an appropriate policy response for the prevention of Lyme disease or Lyme-like illness in Australia. It is only then that Australia could be in a position to make verifiable calculations of the risk to human health.

Page 9, para 1 refers to the potential for Passerines to carry various strains of Borrelia and so become part of the Borrelia dispersal cycle. Para 2 extends this possibility to Procellariiformes (seabirds) and notes that migrating seabirds could play a significant role in the transmission of Borrelia between the northern and southern hemispheres. Indeed any resident of an east coast stretch of beach could attest to the increasing incidence of Shearwater (Muttonbird) washing up during migratory periods.

Pages 8 and 9 do not consider the possibility that reservoirs introduced to this country by humans, as well as migratory birds, may be significant in that infected ticks may fall off these animals and then either bite humans directly or bite other effective reservoirs, thereby participating in the Lyme disease cycle.

In the author’s own paper on Responding to emerging diseases: reducing the risks through understanding the mechanisms of emergence (Mackenzie 2011), he notes that many factors contribute to disease emergence and suggests international travel should never be under-emphasised. “This includes the movement of infectious agents between countries and continents and the transportation of vector species to establish in new habitats and ecological niches far from

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4https://sites.google.com/site/ticktransmitteddiseasesaust/references
their origins, resulting in countries and areas becoming receptive to exotic diseases." Yet in Australia we are faced with the recurring discriminatory position that there is ‘no Lyme here’ making it extremely difficult for patients who have legitimately acquired Lyme disease overseas to obtain treatment. Furthermore there is complete silence on alternate methods of importation.

The LDAA recommends a serious investigation and thorough epidemiological study of Borrelia occurrence in Australia as a matter of urgency. Until formal recognition of a native Borrelia or Lyme-like illness exists in Australia, the true extent of Australians suffering will be significantly diluted due to ongoing differential diagnoses or misdiagnosis.

Lyme Borrelia and human disease

Page 8, para 2 (d) Lyme Borrelia and human disease refers predominately to the commonality of the clinical manifestations of Lyme disease in Europe and North America and notes the presence of an EM skin lesion occurring at the bite site in 90% of cases. While this may be the case in some studies carried out in the Northern Hemisphere, there are also several articles that refute this claim. For example, in his paper ‘What You Should Know About Lyme Disease’, Harris states that a “characteristic red bulls-eye rash (EM) at the site of the bite is present in less than 40% of patients”⁵. Similarly, Utah’s Department of Health’s ‘Clinical Information for Lyme Disease Diagnosis’ pamphlet states that “Lyme disease diagnosis can be difficult because the symptoms can be vague, especially with the absence of erythema migrans”⁶.

Indeed the statement is contrary to the Australian patient reports captured in the LDAA survey (LDAA 2012). The LDAA study examined the presence of a rash and asked participants to describe their rashes. All respondents answered the question with only 50% reporting they had a rash. Of those who reported a rash, only a third (31%) reported their rash to be a typical bulls-eye EM and nearly 40% reported a red raised circular rash. As such, the LDAA contends that the lack of an EM rash does not omit the possibility of Lyme disease or Lyme-like illness.

The LDAA recommends the diagnostic pathway criteria should not solely require the inclusion of an EM for diagnosis as it would automatically exclude 50% of Australian patients, based on the current data. Significantly, an EM rash is considered a definite indication of infection. It is also important to note here that most doctors around Australia are not treating patients upon presentation of EM rashes as they are not aware of the diagnostic significance of these. Evidence of this problem can be found in the growing reports of such incidences (often with photos attached) to the LDAA through various means (i.e. Patient experience survey, collection of patient experiences projects and through the email enquiry service). This indicates an urgent need for General Practitioners to be educated in identifying key diagnostic symptoms as a precursor to delivering early intervention treatment protocols. Refer to Patient-focused Action Plan (Appendix A).

Observation of the global discussion on this topic also notes there is some recognition that different geographical areas often produce different symptoms among patients. This is further supported later in discussion on the Baggio-Yoshinari Syndrome (BYS) case reported from Brazil. It is, therefore, highly likely that an indigenous strain of Borrelia or Borrelia-like organism could cause different manifestations in Australian patients. While these concerns exist, it would be most

⁵ See [http://www.ilads.org/lyme_research/lyme_articles6.html](http://www.ilads.org/lyme_research/lyme_articles6.html)
appropriate to exercise caution in comparing Australian symptoms to those incurred in other geographical areas.

The LDAA recommends that Stanek’s (2012) articulation of common differential diagnosis symptoms should be revised for Australia once clinical studies have determined the most common aspects of Australian Lyme disease or Lyme-like illness. Currently a reference many patients and Lyme doctors find useful for symptom identification is the Comparison Chart of Lyme Disease and Co-infections Symptoms7 maintained by the www.Lyme-Symptoms.com website published by L. Jenner.

Page 9, para 3, asserts that the IgM and IgG response follows a typical pattern witnessed in “all” infectious diseases, where the IgM response is detected first followed by an IgG, which may remain for decades. It must be emphasised that Lyme disease causes immune dysfunction; therefore isotype switching from IgM to IgG does not occur in all patients. According to Dr McManus in her article, Assessment of Research into immune response to Borrelia (yet to be published), IgM is not a very high affinity antibody and it does not participate in antibody mediated /cell mediated immunity. In Lyme disease, T-cell immunity is impaired and the body does not launch a typical response as in other infectious disease processes. Indeed, many Australian Lyme patients are able to produce IgM and IgG positive tests results over a number of years.

Franke, Heldebrandt and Dorn (2013) note that false-negative and false-positive tests frequently occur. They agree that Borrelia-specific antibodies often fail, especially in early illness, because a specific immune response has not occurred.

The LDAA contends that, in any diagnostic pathway development, the issue of conversion from IgM to IgG must first be properly understood.

Page 9, para 4, refers to the Brazilian experience of Lyme-like illness and provides three references. The Brazilian government have adopted the name ‘Baggio-Yoshinari Syndrome’ (BYS) to refer to their Brazilian Lyme disease-like syndrome. A 2009 paper about BYS, not quoted in the scoping paper, concludes that “BYS is considered a new tick borne disease in Brazil that differs from classical Lyme disease observed in the Northern hemisphere. BYS replicates most of the neurological symptoms observed in Lyme disease, except for the additional presence of relapsing episodes and the tendency to cause chronic neurological and articular manifestations” (Shinjo et al. 2009).

This paper also notes ten significant differences of BYS from Lyme disease experiences in the northern hemisphere. The paper mentions significant differences in laboratory reactivity during diagnostic testing. It further notes that the name Baggio-Yoshinari Syndrome was proposed to substitute all the previous nomenclatures given to Brazilian Lyme disease like illness or syndromes (BLDLS). Furthermore, due to many particularities, this disease was considered an original tick borne disease, indicating that inappropriate comparisons with Lyme disease should be avoided. In this sense, low serological immune response to B. burgdorferi sensu lato or repeated negative PCR assays observed in BYS patients could represent laboratorial hallmarks of BLDLS, despite mistakes due to technical flaws” (Shinjo et al. 2009).

7 http://www.lyme-symptoms.com/LymeCoinfectionChart.html
From the patient community’s perspective, there are many parallels that can be drawn from the Brazilian experience. As such, consideration should be given to the inappropriate use of, and comparison with, typical Lyme disease as it occurs in the northern hemisphere. This is particularly necessary in discussions about laboratory diagnosis and in the development of diagnostic pathways. In Brazil’s case, diagnosis of BYS is based upon two major and two minor criteria, only one of which relates to positive serology (see section on LDAA’s further recommendations.)

Page 12, para 1, uses the term ‘late Lyme disease’ with an inferred definition that Lyme disease is not actually diagnosed until it is ‘late’ in its progression and having already had significant health impact on a patient. The Study suggests that this is a rarity, then asserts a ‘few months’ for full resolution. These statements do not reflect the current patient experience and could be considered rarely evident for many patients in Australia. There are a number of patient-focused studies\(^8\) that refute this point entirely and demonstrate verified persistent infection, even after antibiotic treatment.

Similarly, the use of the term ‘chronic Lyme disease’ is mentioned in the following para 2 with the added assertion that the ‘jury is out’, indicating the contentious issue of Lyme disease persisting beyond prescribed short course of antibiotics is an unknown. Indeed the paper notes that ‘chronic Lyme disease’ is a poorly-defined term and the patient community agrees. It is important to get these two definitions correct, as it is a critical issue for patients suffering long-term manifestations of this illness.

According to the CDC, the term ‘Chronic Lyme disease’ is properly known as ‘Post Treatment Lyme Disease Syndrome (PTLDS)\(^9\) and is meant to occur after the patient has received initial antibiotic treatment that is currently recommended by the IDSA for up to 30 days. On the other hand, the International Lyme and Associated Diseases Society (ILADS) uses the term ‘chronic Lyme disease’ to describe symptoms that occur within six months of a tick bite and which last for more than six months. A universally accepted definition of these terms is needed.

A highly recommended discourse on these opposing viewpoints is available in the article Chronic Lyme Disease and the “Axis of Evil” (Stricker & Johnson 2008). The article asserts there is growing evidence that chronic Lyme disease exists and is the result of a persistent infection with Borrelia burgdorferi as shown by microbiological and molecular studies. There are more than 77 peer reviewed studies\(^10\) indicating the persistence of Lyme disease after antibiotic treatment and increasing evidence suggesting that Borrelia may participate in “quorum sensing, biofilm-like behaviour, and persister cell induction”, which helps explain its ability to survive not just initial antibiotic therapy, but ongoing aggressive antibiotic therapy as well (Bernston 2013).

In another article, German scientists modelling Borrelia found that it “recovers from a strong initial immune response by the regrowth of an immune-resistant sub-population of the bacteria”. As such, the chronic phase “appears as an equilibration of bacterial growth and adaptive immunity”. They concluded that their findings have major implications for the development of the chronic phase

\(^8\) ILADS- Chronic Lyme and Evidenced based review
\(^10\) [http://www.lymeinfo.net/medical/LDPersist.pdf](http://www.lymeinfo.net/medical/LDPersist.pdf)
of Borrelia infections as well as on potential protective clinical interventions (Binder, Telschow & Meyer-Hermann 2012).

For most Australian patients, the construct of ‘chronic Lyme disease’, or more appropriately PTLDs, is a rarer issue. Until recently, dogged lack of recognition of this illness in Australia has meant that very few patients have been afforded the benefit of early intervention treatment and the vast majority are in late stages of the illness before they are diagnosed. The LDAA’s Australian patient survey reported the average time from bite to diagnosis was six and a half years (LDAA 2012, p. 20). It was concluded from the results that 80% of Australians acquiring Lyme disease, or Lyme-like illness, are currently progressing to the late stage before treatment even commences.

As Bernston notes in his conclusion, “the question is no longer whether LD (Lyme disease) can survive an antibiotic challenge in order to become a persistent infection. High quality studies show not only that it happens, but they also show how it happens” (Bernston 2013). His argument lays the foundations for future research suggesting that the task is now “to determine which patients suffer from persistent LD, and to keep pressing for evidence-based wisdom to guide the physicians called upon to treat them”.

Perhaps in light of the Australian patient experience, a more apt description for the condition facing patients might be ‘entrenched Lyme-like illness’. This terminology more accurately describes a situation in which, without early treatment intervention, the pathogens have had years to disseminate, impacting on random sites within the body, potentially causing significant damage to multiple infection sites and necessitating more extensive and extended treatment strategies to eradicate.

Page12, para 3 cites references of Australian cases of Lyme disease noting that the ‘vast majority’ of cases were from patients who had travelled overseas. It is noted that there is no articulation, nor confirmation, of the diagnostic criteria applied to the reported cases via personal communications with the author. It is also noted that, as the referenced ‘personal communication’ originates from a co-author and researcher of the controversial Russell and Doggett (1994) study, its use is hardly impartial, or independent. The LDAA Australian patient situation report reveals a very different story. There were 66 patients who reported a local tick bite and who had not left the country prior to becoming ill (LDAA 2012, fig. 4) and half of those reported they have never left the country. In addition, there are 35 more patients who report being bitten while travelling overseas. This demonstrates that while there is indeed a cohort of patients in Australia with ‘overseas-acquired’ Lyme disease that needs to be further addressed, there are also many more cases that suggest there is an Australian-acquired Lyme-like illness.

Page 12, para 3 states that confirmatory testing of patients who had never travelled should be carried out in a NATA accredited laboratory. It infers the processes used in the previously cited references (e.g. Mayne 2011; Hudson et al 1998) are questionable because they do not conform to ‘international standards’ for Lyme diagnosis. The section on Laboratory diagnosis deals specifically with the testing controversy, however it is important to acknowledge that ‘international standards’ for Lyme diagnosis DO NOT exist. Standards per se do not exist for individual diseases, only diagnostic criteria. In the case of Lyme disease, there are many diagnostic guidelines and all are voluntary, so it is important to qualify the context and method of classification of any claim citing an
‘international standard’. To what ‘international standard’ is the author inferring Australian Lyme disease tests should comply?

The LDAA notes it is neither prudent nor defensible to adopt either officially, or by default, the diagnostic criteria set out in other Lyme-endemic countries. The importance of avoiding this form of action until there is a better understanding of the epidemiology, etiology and manifestations of the native disease must be carefully considered. Furthermore, better understanding needs to be obtained through endorsed clinical studies of patients, to determine the specific Australian peculiarities.

The LDAA recommends that Australian-specific criteria be established for the diagnosis of Lyme disease, or Lyme-like illness following proper clinical evaluation of Australian patients.

Page 12, para 2 (e) Other Borrelia species associated with disease states that “louse-borne and tick-borne relapsing fevers have not been reported in Australia”. The LDAA asserts that there is ambiguity in this statement. Medical professionals are not trained to recognise tick-borne diseases in Australia and where they are suspected, current official advice implies that Lyme disease does not exist here.

Instead in Australia we see many cases of alternative diagnosis being made for other fever syndromes where Lyme disease was not considered a differential diagnosis. This has even been noted in cases where the patients had reported a recent tick bite. The summary of a pathology report on a specimen of tonsils and a lymph node of a two year old female Australian patient who has never left the country, indicating a diagnosis of ‘Marshalls Syndrome (recurrent fevers)(PFAPA)’ is at Appendix B. The same patient was later diagnosed with Lyme disease by an experienced and Lyme trained physician; she is four and now lives with a Lyme-like illness.

Also accompanying Appendix B is a consultation summary for a three year old female who had history of a ‘bite’ with expanding rash and sore joints who was treated with steroids for an allergic reaction. Nine days later the child attended a hospital following 5+ days of high fevers, extreme lethargy and joint pains. She was subsequently diagnosed with Tonsillitis and a differential diagnosis of glandular fever (EBV) / Strep Infection pending further tests. Six months later, Hunter Area Pathology detected Lyme antibodies, three B. burgdorferi bands, one B. afzelii band, and stated, “This does not suggest infection”. The child progressed to have a Lyme-like illness with ongoing widespread joint pains, cognitive impairment, twitching, fatigue and relapsing fevers. A bullseye rash was noted and photographed by the mother who attests that no doctor ever asked about the possibility of a tick bite. The five-year-old child now lives with a Lyme-like illness.

Appendix B also includes the referral note for a middle-aged patient whose doctor acknowledges recurrent fever for more than a year. Although only two examples are provided here, there are many more patients stories presented to the LDAA which demonstrate patients living with the consequences of ‘alternate’ diagnosis of a fever syndrome, or worse still, patients who remain undiagnosed. Further exploration in this area is needed and would certainly highlight many cases.

Page 14, para 3 discussion on (f) Borrelia species in Australia, refers to Dr Mayne’s (2012) work outlined in the previous paragraph. It implies questionable scientific rigour and casts doubts about

11 Periodic Fever, Aphthous Stomatitis, Pharyngitis, Adenitis Syndrome (PFAPA) (Juvenile)
the methods used by Mayne. It suggests that confirmatory evidence of the presence of *Borrelia* should be obtained in a second [Australian] laboratory that is NATA accredited.

**The LDAA has serious concerns about the NATA accredited laboratories equipped to test for Lyme disease in Australia.** The current concerns exist in regard to the differing standards used and these **require urgent resolution.** A further discussion on testing is included in the next section. This highlights an interim opportunity for the Chief Medical Officer to identify other laboratories that are equipped with state of the art testing facilities that comply with the standards for Medical Laboratories set out in AS ISO 15189:2009. These labs are obtaining positive results, which validate the significant suffering that Australians with Lyme disease or Lyme-like illness face.

The overall discussion included on [Page 14, Part (f)] appears to be unnecessarily biased. While it mentions some limitation with the studies that found evidence of locally acquired Lyme in Australia, the same treatment is not applied to studies that did not find evidence, despite significant flaws. For example, in the Russell and Doggett (1994) study of the NSW coast, approximately 6000 of the studied ticks had not had a blood meal, including larvae. It is reported elsewhere that larvae infection rates are less than 1%, and so they are typically not used in studies to determine the infection rates of ticks. The Russell and Doggett (1994) study has been legitimately criticised as having seen evidence of *Borrelia*-like objects under the microscope and discounting them as artefact based on the false and discounted premise of a US study in Mississippi. The appearance of spirochaete-like objects in this study should have attracted a full and thorough explanation.

Furthermore, the ticks were only tested for *B. burgdorferi*, and not for others such as *B. garinii* and *B. afzelii*, despite the fact that given the heritage of modern Australia, it is likely large numbers of animals were imported from Europe. Further discussion on testing issues is included at research project 3.

**Laboratory diagnosis**

[Page 15, para 1 (g) Laboratory diagnosis] states that laboratory support is an ‘essential’ component of a Lyme diagnosis. The LDAA counters that it is globally accepted that the presence of an EM rash following a tick bite does provide sufficient clinical evidence for a Lyme diagnosis. Laboratory support may be an ‘essential’ component, but it should **NOT** be stated as an absolute. It would be remiss of doctors to subject their EM-presenting patients with a recent history of tick bite to unnecessary pathology procedures and their subsequent costs.

One of the most serious challenges in Lyme disease or Lyme-like illness is obtaining correct diagnosis. In an article published in early 2013 (which was not included in the Study), researchers present a simple and reliable process for the detection of live spirochaetes and cysts in the blood by the use of classic techniques in microscopy (Laane & Mysterud 2013).

Their paper implies there may be a symbiotic relationship between a spirochaete and a human host, wherein lifelong chronic infection may occur with recurring and relapsing infections dependant on the quality of the patients’ immune system. The diagnostic test proposed is a simple technique with a negligible cost and could be performed in almost any contemporary laboratory with an experienced microbiologist who is trained in identifying spirochaetes in their various forms. This method would obviate the need for expensive two-tiered antibody related testing and potentially
omit the controversy surrounding false negative / false positive test results, which rely upon the body mounting an appropriate immune response. Exploration into adopting such a test certainly has some merit for improving Lyme disease testing in Australia.

**Page 15, para 1** discussed methods of isolation of *Borrelia* via PCR, lamenting the long incubation times and low numbers of spirochaetes. The author neglects to mention that some recent researchers have developed a modified culture method that has had excellent success with culturing *B. burgdorferi*, even from a single spirochaete (Sapi et al. 2013). Given this, the LDAA suggests that culturing samples from existing patients with Lyme-like illness could be an important tool in identifying the etiological agent in Australia. When used in this way, the long culture times would not pose a significant issue.

**Page 15, para 2** in discussing the most sensitive methods for detecting *Borrelia*, the author acknowledges that “direct detection of *B. burgdorferi* s.l. by PCR is much more desirable than serology if the method can be developed to be reliable, easy-to-perform, economical, and sensitive”. A method has been described whereby *B. burgdorferi* are detected using nested PCR, combined with “gold standard” DNA sequencing and can offer excellent sensitivity and specificity (Lee et al. 2010b). Development of such methods could offer the ability to detect spirochaetes following a tick bite and offer appropriate treatment without delay. This provides a distinct benefit in diagnosis and treatment of acute Lyme compared to two-tier testing, which is unreliable during the early stages of the disease (Steere et al. 2008). Rapid administration of treatment will improve long-term outcomes and avoid the problems associated with antibiotic treatment impacting on the development of antibodies in two-tier testing.

The Scoping Study fails to recognise that some Australian specialty laboratories are already capable of detecting *Borrelia* by PCR in Australian patients in a way that is affordable and repeatable. Their testing methods could be duplicated to promote efficient and more sensitive tests in other laboratories.

**Page 15, para 2** this paragraph notes the widespread use of serological assays for antibodies in Lyme disease laboratory diagnosis. It also acknowledges that the sensitivity and specificity of serological tests are less than optimal and highlights the added complications of a weak, or absent, antibody response due to poor seroconversion. When testing for European-acquired infection, two-tier testing using US test kits had an overall sensitivity and specificity of 52% and 100% respectively (Branda et al. 2013). The LDAA asserts this is completely inadequate and equates to coin-toss odds of a positive test being correctly identified. *Borrelia* strains identified in Australia using PCR include genospecies other than *B. burgdorferi* s.s (Mayne 2012), yet the ELISA screening test performed at Westmead uses only *B. burgdorferi* s.s. (Figure 2). It is therefore likely that the sensitivity of Westmead’s ELISA is unacceptably low for use as a screening test.

The paragraph also notes that the use of newer recombinant antigens rather than whole cell lysates have substantially improved test reliability. However it fails to mention that the serological tests performed at Westmead12 (our primary specialist Lyme test laboratory) and potentially many other pathology laboratories performing first tier testing, are using the outdated and less sensitive whole cell lysate method. It appears that the Australian laboratory testing system is weighted against

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sufferers of Lyme-like illness in Australia. Sadly many patients have already been exposed to this inadequate situation and will continue to be, unless a review of laboratory testing processes is prioritised as part of this research process.

Page 15, para 2 also reports on the two-tier testing processes adopted by the USA and Europe, where a screening assay, either ELISA or IFAT is processed first and if positive, a Western Blot (WB) follows. It provides a continuing commentary on how the two-tier system works in both locations and describes the different approaches to interpreting WBs due to the differing geno species of the countries. It is best summarised in the Figure 1: CDC Two-tier Testing Diagram.

The discussion on laboratory diagnosis neglects to report on the current testing process in Australia, which is outlined in the NSW Government publication Lyme disease – testing advice for NSW clinicians, and appears to be the primary reference for most jurisdictions in Australia. The two specialist laboratories (Institute for Clinical Pathology and Medical Research (ICPMR) at Westmead and Pacific Laboratory Medicine Services (PaLMS)) responsible for confirmatory immunoblot tests do not follow a standardised process in the criteria by which they assess their results; see Figure 2: Comparison of test processes.

To add to the complexity of the issue, the NSW Government recommends that clinicians ‘send their first tier test to their usual pathology service for a screening immunoassay’. This means that there are an unquantified number of pathology labs performing screening assays for Lyme disease and they are likely doing so with outdated test processes against a reduced range of identified strains.

The clinician advice also states that "if the IgG screening test is negative, and recently acquired Lyme disease is clinically suspected, a second serum specimen should be collected 4-8 weeks later". Analysis of the data in the Westmead evaluation suggests the recommendation for retesting is not occurring very often, if at all.

Tier 1

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Pathology Service (100+)</th>
<th>Westmead Primary reference lab</th>
<th>PaLMS</th>
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</thead>
<tbody>
<tr>
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<td>ELISA / IFAT</td>
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<td>ELISA</td>
</tr>
<tr>
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<td>- MarDx (Sonic)/ Vidas</td>
<td>- MarDx (Trinity Biotech)</td>
<td></td>
</tr>
<tr>
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<td>(BioMerieux)</td>
<td>- B. burgdorferi</td>
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<td>- B. afzelii</td>
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<tr>
<td></td>
<td></td>
<td></td>
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Tier 2

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<tr>
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<tr>
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<td>- In-house whole cell</td>
<td>- EU Lyme + ViSE IgG(Trinity</td>
<td></td>
</tr>
<tr>
<td>- Strain</td>
<td>lysate</td>
<td>BioTech)</td>
<td></td>
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<tr>
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<td>- B. burgdorferi</td>
<td>- B. burgdorferi</td>
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<tr>
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<td>- B. afzelii</td>
<td>- B. afzelii</td>
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<tr>
<td></td>
<td>- B. garinii</td>
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<table>
<thead>
<tr>
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<th>CDC Surveillance criteria</th>
<th>European guidelines</th>
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<tbody>
<tr>
<td></td>
<td>5 bands</td>
<td>3 bands</td>
<td></td>
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</tbody>
</table>

Figure 2: Comparison of test processes

Following a highly unlikely positive in an immunoassay, the advice to clinicians requires that a "confirmatory immunoblot for antigens from *Borrelia burgdorferi* sensu lato genospecies (including *B. afzelii, B. garinii*)" be conducted. According to two major labs, referrals are made exclusively to Westmead, where it should be noted that Westmead is not testing for *B. garinii*.

As noted earlier, in the 20 years since the Westmead testing methods were developed, six more pathogenic *Borrelia* s.l. genospecies have been discovered\(^1\)\(^5\).

The LDAA recommends an immediate update to the NSW Government’s clinician advice to better reflect the actual testing process. The immediate rollout of European test kits to the Westmead laboratory to enable the extension of their testing to include *B. garinii* is highly recommended.

In the second tier of the process, samples are once again subject to outdated testing processes and then assessed against differing criteria in each of the labs. Immunoblot testing performed at Westmead applies the stricter CDC criteria, noting that these criteria were developed for surveillance purposes in the United States, despite the fact that the CDC has clearly indicated these are not to be used for diagnostic purposes. As such, it is statistically more likely that a patient will obtain a positive test from PaLMS because they are testing against a wider range of strains and applying a 3 band criteria for a positive result. An illustration of the effect of this ambiguity on patient test results is included at Appendix B.

The LDAA recommends that, in developing a diagnostic pathway, it would be useful to analyse historic test data showing the bands present in patients with Lyme-like illness acquired in Australia. For example, researchers in China have proposed that band 58 is important diagnostically in that country in detecting *B. garinii* strain PD91 (Jiang et al. 2010).

Until further research determines the causative agent for Lyme-like illness is Australia, the European guidelines must be applied simply because they cover both the US and European strains of *Borrelia*.

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\(^5\) See [http://www.ezbiocloud.net/search?k=all&v=borrelia](http://www.ezbiocloud.net/search?k=all&v=borrelia)
Through application of the European guidelines, whereby two or three bands denote a positive (depending on which bands are shown), it would be evident that up to eight times more patients would have tested positive on the Westmead immunoblot.

Drawing from the Westmead data, between 1994 and 2012, the LDAA calculated that this would represent between 300 and 690 patients who may have tested positive by applying the more relevant European guidelines. In a 2012 paper, Westmead acknowledges that over 900 samples might have been classified positive, but quote 71 (or 4% of total specimens) are reported as positive because of the ‘required five or more specific IgG bands’¹⁶. This does not take into account false negatives as a result of Westmead testing not considering B. garinii.

The same paper states that “of these patients all were bitten by ticks in northern hemisphere countries except for two with no history of travel”. The LDAA contends it is pertinent to note that the US CDC guidelines¹⁷ consider that two or more locally acquired cases will be considered endemic for Lyme disease.

Assessing testing at PaLMS and using a prevalence of 15% (the number of positives Westmead would have given if using 3 bands), provides a positive predictive value of 77%. If a patient received a positive result, there’s a good chance it’s a true positive. Hence, unless the patient is known to have syphilis or a condition with known cross-reactivity, laboratories should not be discounting positives as "false".

The LDAA contends that there is major systemic failure in the testing processes that surround Lyme disease and Lyme-like illness in this country. On a single lab’s testing figures there are likely to be hundreds, if not thousands, of patients whose serum has been subjected to inadequate testing procedures. This is especially in regard to tests with low sensitivity and using outdated solutions or employing inaccurate commercial test kits. To highlight further diagnostic hurdles, any positive results are then subject to further degradation because they are measured against stringent surveillance criteria designed for another country.

Page 16, para 2 advocates the importance of the two-tier test protocol and notes that without it there is likely to be a reduction in the specificity of the testing leading to misdiagnosis. The LDAA counters that view, asserting that with the two-tier test protocol there is already an unacceptable level of sensitivity if the Westmead results are to be relied upon.

The majority of Australian patients are presenting with late Lyme disease or Lyme-like illness, taking an average of 6.6 years to diagnose (LDAA, 2012). In these cases, their conditions have never been treated and the pathogens have often disseminated throughout their systems indicating effective immune suppression as a consequence of Borrelia infection. As such, it is vital that this patient cohort is provided with the most specific and highly sensitive methods to detect the pathogens infecting them so that they are able to access effective treatment for their debilitating symptoms.

For patients who have been suffering for years, the question becomes one of economics; a more expensive Western Blot performed in the course of laboratory diagnoses is likely to lead to earlier

¹⁷ See http://www.cdc.gov/lyme/faq/#endemic
This approach would enable immediate treatment instead of prolonging the endless course of investigations for any number of misdiagnosed diseases without resolution. In the current fiscal crisis, it is in the best interests of the public purse to effectively diagnose and treat these long-term chronically ill patients. Experienced Lyme-treating doctors should be trusted to determine the appropriateness of the two-tier test process and be allowed to specifically order a Western Blot test when attempting to assist their chronically ill patients.

A 2006 paper on the Economics of Lyme Disease (Zhang et al. 2006) reviewed the burden of disease (BOD). The Study noted that in patients where Lyme disease was accurately diagnosed and treated early, the BOD was less than $1500. In cases where patients were not diagnosed early and had become progressively sicker, the BOD was calculated at more than $16,000 per year, every year. There are Australia patients who can attest to these insurmountable costs, with many being left financially devastated by the disease and many others losing not only their health and livelihoods but also their homes (see Patient Impacts section of LDAA’s Australian patient situation report (LDAA 2012)).

Page 16, para 3 introduces the more contemporary C6 peptide ELLISA test and its higher sensitivity and specificity especially for specimens of patients in acute, convalescent and late phase of Lyme disease or Lyme-like illness. While initial studies developing the C6 peptide ELISA showed benefits over two-tiered testing, a prospective study performed in 2008 showed no statistical difference between the specificity and sensitivity of these two test methods. In addition, the test only detected *Borrelia* in one third of patients with EM rash (Steere et al. 2008 referenced in the Scoping Study); this is certainly not excellent sensitivity as suggested. Page 16, para 4 acknowledges that the accuracy and reproducibility of commercially-produced Lyme kits is generally poor and provides several references to support this point. What it omits to note is the polarised argument often substantiated by the fact that more positive Lyme disease tests originate from so-called ‘specialised’ laboratories, which incidentally do not use these inaccurate commercial test kits.

Furthermore it is not well known that the in vitro diagnostic (IVD) testing devices used in laboratory testing for Lyme disease fall into the Class IV ‘high public health risk’ category, as specified in Regulation 3.1 of the Therapeutic Goods (Medical Devices) Regulations 2002\(^\text{18}\). Under our own system, these devices are classified at the highest level of risk, which is determined by an assessment of the risk of an incorrect result arising from the use of an IVD. Sadly many Australian patients are living with the results of these inaccurate and poorly designed testing processes. Which begs the question who bears the liability for the inefficient, ineffective and inaccurate testing processes? For now it is patients who are paying with their health; however, if these issues are not quickly resolved, the laboratories and governments that advocate for these processes (in full knowledge of their limitations) may well be found to be legally liable.

It should be noted that the ‘class’ is partly determined by the “manufacturer’s intended use of the device”. The product data accompanying the commercial test kits states that “Negative results

\(^{18}\) http://www.tga.gov.au/industry/ivd-classification.htm#UteEz_Lxvcc
(either first or second-tier) should not be used to exclude Lyme disease\textsuperscript{19}\textsuperscript{19} (from the MarDX ELISA test kit used at Westmead) and “the diagnosis of Lyme Disease must include careful clinical evaluation and should not be based upon the detection of antibodies to \textit{B. afzelii/garinii/burgdorferi} alone; a negative interpretation does not exclude the possibility of infection with \textit{B. afzelii/garinii/burgdorferi}\textsuperscript{20}\textsuperscript{20} (from the Trinity Biotech Western Blot test kit used at PaLMS).

\textbf{Page 16, para 4} also asserts that commercial laboratories must use validated testing kits, but provides no commentary on the particular standards for validation. The LDAA requests a formal briefing about the current process and standards for validation and to be kept informed of any changes to this assurance process.

\textbf{Page 16, para 5} notes the limitations of the current commercial testing kits; other major limitations of immunoblot assays include the visual scoring and subjective interpretation of band intensity (Lee et al. 2010a).

Another testing method that should be investigated for use in Australia is the lymphocyte transformation test (LTT). These measure the T-cellular activity in the blood against \textit{B. burgdorferi} (von Baehr et al. 2012). The LTT method can be effectively used to assess the success of treatment, with levels returning to normal once active infection is no longer present in the patient.

The Study author’s own paper, ‘\textit{Responding to emerging diseases: reducing the risks through understanding the mechanisms of emergence},’ states that the “development of new, more sensitive technologies can also provide improved detection and diagnostic procedures allowing a new dimension to pathogen discovery, thus detecting new or cryptic agents for known diseases” (Mackenzie 2011).

The LDAA contends that there are extensive limitations in the current testing process, which places a greater emphasis on the need for better education of doctors to enable clinical diagnosis of Lyme disease or Lyme-like illness in the absence of any certainty in the testing process. The LDAA recommends that interim diagnostic guidelines be developed for medical practitioners while the laboratory testing issues are resolved. These guidelines should be transparent about the lack of specificity and sensitivity in the testing process and reinforce the need for differential diagnosis, especially where there is a high probability of those laboratory tests being returned negative.

In particular there is a critical need to direct significant training, education and treatment guidelines specifically to Australian Infectious Disease Specialists (IDS). Through several recent projects, the LDAA has received numerous patient stories that reflect a strong adverse opinion towards Lyme disease from this profession. This current widespread position within the IDS field is being reinforced and maintained by a very strong emphasis on laboratory results. These are the medical specialists who should be at the forefront of Lyme disease diagnosis and involved in specialist referrals for patients with Lyme-like illness; however patients often find them to hold intractable views that exclude the possibility of Lyme disease. Interim guidelines placing a much stronger


\textsuperscript{20} http://www.trinitybiotech.com/Product%20Documents/44-2020GV-29EN%20EU%20Lyme%20VLS%20IgG%20WB.pdf
emphasis on clinical presentations and differential diagnosis are urgently required. Further education issues are discussed in research projects 4, 5 and 7 and in the Patient-focused Action Plan at Appendix A.

**Co-transmission of tick-borne organisms**

Page 17, para 2 discusses the (h) co-transmission of tick-borne organisms and notes that ticks are able to transmit more than one pathogen per blood meal. The LDAA Australian patient report indicates that 55% of Australian patients reported they have been diagnosed with one or more co-infections (LDAA 2012, p. 18). The most common co-infection reported was Babesiosis, followed by Bartonellosis, Chlamydia Pneumoniae, Mycoplasmosis and Ehrlichiosis. Compared to patient data in the US, this report indicates that Australian figures for co-infection are much higher than those reported in the US.

The discussion about co-infections is particularly interesting given that many Australian patients are testing positive to myriad infections that are claimed to not exist in Australia - like Borreliosis. This suggests that more effort must be directed at understanding the commonalities of co-infections and their combined impact on patients and the unique presentation of Lyme-like illness in Australia.

Page 18, para 2 on Bartonella, claims “there has been no record of co-infection of Bartonella species with B. burgdorferi s.l. overseas.” The LDAA asserts that this statement is incorrect. It is noted that this contradicts the author’s earlier notation that “only information on Australian examples of these organisms is shown, unless the organism is yet to be reported in Australia” (see page 17, para 2). As early as 2001, there are research articles on the concurrent infection of Lyme disease and Bartonella (Eskow, Rao & Mordechai 2001) There is also recent published research reporting on Australian patients who are infected with Lyme disease and Bartonella as well as Babesia and granulocytic Ehrlichia (Mayne 2011).

Page 18, para 5 on Ehrlichia, the Study states that “Ehrlichia species have not been recognised in Australia”. The LDAA asserts this statement is incorrect; Ehrlichia platys was found in 46% of dogs tested in central Australia (Brown et al. 2001). The LDAA Australian patient situation report found that 10% of Lyme patients report being diagnosed with Ehrlichia (LDAA 2012, p. 18). Interesting to also note is a recent article on a boy who acquired Ehrlichia from a blood transfusion (Regan et al. 2013) (see further discussion on risks of transmission via blood transfusion in points of contention section).

Lyme disease on its own is difficult to treat, particularly in its later stages, however it has been repeatedly found that “Lyme disease patients who are co-infected with other tick–borne infections have a more prolonged and severe illness than those who are infected with Lyme disease only” (Krause 1996). For this reason the LDAA recommends that research into Lyme disease diagnosis and treatment cannot stand alone without a proper examination of the potential co-infections. In 2013, Franke, Heldebrandt and Dorn (referenced in the Study) reviewed the current scientific literature and found that “co-infections with Borrelia and other pathogens, such as Babesia spp., Rickettsia spp., A. phagocytophilum, or tick-borne-encephalitis-virus (TBEV) often lead to more severe or atypical clinical outcomes of LB and problems in diagnosis and treatment occur” (Franke, Heldebrandt and Dorn 2013).
The LDAA notes that the experience of Lyme disease patients in Australia is that the vast majority of them are not only infected with Lyme disease but also other co-infections. The LDAA’s Australian patient experience report also reflected that, due to treatment difficulties and/or lack of financial resources, patients are often not adequately treated for the co-infections and their Lyme disease. This frequently produces experiences of a more severe illness and debilitation. Eminent Lyme disease specialist, Dr Richard Horowitz, recommends that patients be diagnosed with Multiple Systemic Infectious Disease Syndrome (MSIDS) so that the patient can be properly treated for all their infections concurrently (Horowitz, 2103).

Dr Joseph Burrascano’s paper “Advanced Topics in Lyme Disease21”, states that “a huge body of research and clinical experience has demonstrated the nearly universal phenomenon in chronic Lyme patients of co-infection with multiple tick-borne pathogens. These patients have been shown to potentially carry Babesia species, Bartonella-like organisms, Ehrlichia, Anaplasma, Mycoplasma, and viruses.” It is encouraging that the Study report recognises that co-infections are often under-diagnosed, but do occur frequently and that it recommends, “concurrent infections should be considered in a patient with unusually severe or atypical features of Lyme disease”. However it is of concern, given the high rate of co-infection in Australian Lyme disease patients, that none of the research projects proposed in the Study address the problem of patients infected with more than one pathogen.

**Major gaps in our knowledge of Lyme disease in Australia**

Page 21, para 4 asserts once again that the ‘jury is out’ in respect to an ‘evidence-based’ answer on Lyme disease. Interestingly the author uses the same term in his introduction regarding the contentious issue of Lyme disease persisting beyond prescribed short courses of antibiotics.

The paragraph also refers to ‘evidence-based’ answers. While the focus is understandably on ‘evidence-based’ answers, will the CACLD acknowledge that it’s possible that currently the knowledge and resources to provide evidence-based results in all aspects of the research may not be available? Even the International Lyme and Associated Diseases Society (ILADS), for example, acknowledge that pathology for Lyme and co-infections is currently imperfect and therefore Lyme should be considered a clinical diagnosis. The LDAA recommends Lyme disease and Lyme-like illness should primarily be a clinical diagnoses, and treatment methodologies should follow guidelines being produced by Australian Lyme doctors and those of ILADS.

The same paragraph also states that evidence-based answers must ‘fulfil the criteria’ of Lyme disease or otherwise, but neglects to mention that there are NO such criteria established in Australia. It is assumed that the author is referring to the criteria for the effective diagnosis of Lyme disease. Even in jurisdictions where ‘criteria’ have been developed, they are a contentious topic, resulting in significant polarisation of discussion and research is available to support both sides of the debate. To import criteria surrounded by such controversy is undesirable and it is preferable to develop criteria based on observing local research, including thorough epidemiological studies to first ascertain whether Borrelia (or Lyme disease) is the cause of Australian patients’ Lyme-like illness.

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21 Available at [www.ilads.org/files/burrascano_0905.pdf](http://www.ilads.org/files/burrascano_0905.pdf)
Importantly the eleven key questions also omit any reference to the treatment of Lyme disease and, as stated earlier, the Study report is largely silent on this critical issue. Once the Australian ‘criteria’ for diagnosis have been developed and agreed, a diagnostic pathway requires development and treatment becomes the next primary issue. As there is no plan in the Study on effective treatment protocols, the Australian patient community need clarification on how this will be addressed.

Page 21, para 4 also proposes two actions that must occur in all research carried out on Lyme disease. It proposes that specimens must be shared and that confirmatory testing of any positive results should occur. The Lyme patient community agrees wholly with this notion but maintains that these need to be verifiable ‘conditions’ that are the pre-requisite to any research undertaken in this process, and that rhetorical agreement to them is insufficient.

The statement as quoted on page 22 notes that confirmatory testing must take place using a ‘NATA accredited laboratory’. The LDAA Australian patient report provides some insight into the laboratories that Australian patients have used to conduct their Lyme disease testing (LDAA Australian patient report 2012, p. 25). The table reports the laboratory and the test result; either positive or negative. From the results, it is clearly evident that Australian tests conducted by the two NATA accredited laboratories return significantly fewer positive results than those performed in other private laboratories that are overseas and in Australia.

If this process was immediately implemented and performed only between Westmead and PaLMS, the two specified laboratories, they would have difficulty confirming each other’s results because of the different testing methods and different diagnostic criteria employed in each lab. Requiring a private laboratory like Australian Biologics, who are already using superior testing methods and successfully detecting *Borrelia*, to refer their positive specimens to a lab specified as NATA accredited, for confirmatory testing is argued to be a highly contestable suggestion. It is a suggestion that reinforces the circular nature of the logic being proffered upon us as part of this Study.

The significant flaws and limitations in the current test processes, outlined earlier and the indefensible differences between the diagnostic criteria used in these laboratories provide little confidence in a ‘NATA accredited only’ strategy. Lyme-aware doctors are relying upon these results to support their clinical finding, General Practitioners are using these results as a binary measure of diagnosis (if it’s not positive, it’s not Lyme) and patients are bearing the burden of ongoing undiagnosed or misdiagnosed illness.

The LDAA recommends that, until the issues regarding testing in Australia are resolved, the Department of Health should investigate the potential for using an overseas reference laboratory, or the private Australian laboratory in performing all referred specimens for Lyme disease testing.

The Department of Health might consider adopting strategies that are used in other jurisdictions. For example, in Scotland regular audits of laboratory diagnosis of Lyme disease are conducted. On a number of occasions this has resulted in modifications to the criteria for interpretation of the Western blot scoring system (Evans et al 2005, Evans et al 2010). This has allowed a better understanding of the characteristics of local strains of *B. burgdorferi*. 
The LDAA recommends regular audits of laboratory diagnosis of Lyme disease in Australian laboratories to help identify bands specific to a ‘local strain’ of *Borrelia*.

In addition, it is imperative that patients with Lyme-like illness are informed which laboratory has performed their testing so that they are aware of the limitations of their result.

The LDAA would also like to have clarification on whether the ‘condition’ of sharing specimens will result in further impost upon patients. If the condition is likely to result in higher quantity blood draws, then children must be considered in that scenario. While adult patients might be amenable to providing a higher quantity of blood to enable confirmatory testing, for many Lyme families obtaining *any* blood for serological testing on behalf of a child is difficult and unpleasant. To require a double sample of children may not be justifiable, especially under the current test regime.

**Page 22, para 2** suggests that greater involvement with European experts on Lyme disease could be pursued. The LDAA agrees with this statement and acknowledges the inclusion of a European expert on the CACLD. The LDAA also agrees with the proposals to hold a panel of reference sera. The LDAA asserts that it is necessary to recognise that Australians travel to all continents. For this reason, it is proposed that the reference resources need to be extended to include samples and reference information from the US, Japan and Canada to cater for northern hemisphere pathogens, and from South Africa, Asia and Brazil to cater for southern hemisphere peculiarities. Furthermore, it is essential that the Department of Health consult with all other jurisdictions to gain an understanding of the policy context on how they are approaching Lyme disease and Lyme-like illness (as was referred to in the earlier discussion on the Brazilian approach to BYS).

**Page 22, para 3** advocates the establishment of a ‘reference laboratory(s)’ for Lyme Borreliosis. It then inappropriately suggests that ICPMR (Westmead) and PaLMS are the ‘obvious’ contenders and further adds the currently private Australian Rickettsial Laboratory in Geelong and PathWest lab in Perth to the mix. While the dispersed locations are noted, the LDAA is unclear on the justification for four Reference Laboratories; whether for independent verification of results or for reference purposes. Furthermore, in light of the critical assessment of the current testing processes adopted by ICPMR, in particular, this hardly qualifies these labs as contemporary leaders in their field.

It is inappropriate that the Study should recommend the laboratories to be unilaterally nominated as Reference labs. Rather, it is more appropriate for the scoping study to recommend the ‘qualities’ that a laboratory would be required to have to qualify as a Reference Lab; in this instance, it should:

- require the laboratories to have the latest in laboratory technology;
- contain the specified equipment;
- meet the conditional requirements of the proposed research projects and agreements that their processes and results will be subject to verification;
- have a quality assurance program in place; and,
- be a laboratory with demonstrated experience in isolating vector-borne organisms.

Any laboratory that can fulfil these requirements should be appropriately considered for the role of a Reference Laboratory. Only then will the Australian Lyme community have confidence and assurance in the testing processes to which they are subjected. Any public funding, either via direct
procurement or via grant, provided to establish a Reference Laboratory, must uphold the highest standards for the best patient outcomes in laboratory testing.

Furthermore the LDAA highlights a conflict of interest in the research project 3 put forward in the Study. The Public Health Laboratory Network (PHLN) is represented on the CACLD by staff either employed in, or associated with, three of the four laboratories recommended to be reference laboratories. If the DOH intends to pursue this project it should require full Conflict of Interest statements from staff involved in those laboratories who have published research material on Lyme disease, Lyme-like illness or ticks, so that there is transparency in the scientific research process.

The LDAA require that ethical conduct and proper declaration of conflicts of interests must be a core component of all Australian work on Lyme disease and Lyme-like illness.

Page 26 (para 4) suggests an invitation be made to an acknowledged international expert to assist in assessing projects and be part of an educational program for doctors. It ignores that professional invitation for acknowledged experts in Lyme disease occurs yearly in Australia via the Karl McManus Foundation’s Tick-Borne Diseases Conference which is wholly funded by donations made to the organisation.

The conferences are conducted as satellite programs of the Australian Integrative Medicine Association, who are the current organisation supporting the collaborative educational efforts between many Australian doctors treating Lyme-like illness. The recommendation, currently demonstrates a lack of awareness of this privately funded education agenda, it indicates poor consultation; and can be thought to imply these events are not significant or to be taken seriously because they do not come under the domain of mainstream medicine defined as communicable diseases, infectious diseases or Microbiology (which are all streams of medicine who have in the past colluded to deny the disease exists in Australia).
LDAA’s General Recommendations

a) The LDAA requires clarification regarding the efforts the Australian Government has made to understand how other Governments deal with the identification of vector diseases and how they are responding to such impacts upon human health.

b) The LDAA recommends the Australia Department of Health invite discussions with Brazilian health officials to determine how they have dealt with tick-borne disease in a policy context and what research, diagnostic, educational and preventative programs they have activated in response to BYS.

c) The LDAA proposes that consideration be given to the inappropriate use of the term Lyme disease and comparisons with its typical manifestations as experienced in the northern hemisphere until the Australian situation is better understood.

d) The LDAA proposes ongoing consultation with the Lyme community, including current treating doctors, in the research arising from the Study.

Lyme community priorities

The Lyme patient community proposes concurrent activities are prioritised for Australia. Delaying investigations into clinical presentations and epidemiological factors of Lyme disease cannot be justified, as increasing numbers of people come forward with Lyme-like illness. Conducting investigations in a linear fashion also misses the opportunity for cross pollination of hypotheses and findings which may be essential components required to inform other studies.

As noted earlier, the LDAA contends that the two proposed actions (Page 21, para 4) on research for Lyme disease must be verifiable conditions and a pre-requisite to any research undertaken in this process.

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<td>Treatment guidelines (Study 7)</td>
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Additional considerations

The patient community recognises the CACLD is a clinical advisory committee comprising experts and that this Study has been prepared to assist in informing the CMO. However, there are numerous clinical issues relating to patients that have been excluded from consideration in the Study and the LDAA raises these issues in the following section.

Notifiable disease status

Apart from inaccurate references to the number of Lyme disease cases in other countries, there is no discussion on monitoring and surveillance of Lyme disease or Lyme-like illness in Australia. The LDAA understand that the Communicable Disease Network Australia (CDNA) has recently assessed and discounted the need to add Lyme disease to its surveillance actions or to consider it for the National Notifiable Disease List (NNDL) because it did not meet the ‘criteria’ for inclusion. In yet another catch-22 situation, the criteria for inclusion are neither open nor transparent and the LDAA currently pursues a Freedom of Information request to obtain this innocuous data.

Patients report inquiring through their local MP’s or Ministers about disease surveillance; invariably they are met with the standard reply, included below.

The Communicable Diseases Network Australia, in coordinating communicable disease surveillance, prevention and control, will continue to monitor this issue.

The formal efforts of the LDAA to understand the monitoring and surveillance process have been met with significant resistance. It is evident that Australia is many years behind similar jurisdictions in recognising Lyme disease and mounting a proper and effective public health response to the issue. An excerpt from a European study on emerging health risks associated with climate change provided the Figure 3: European risk of Lyme disease classification (Lindgren et al. 2012)

![Figure 3: European risk of Lyme disease classification (Lindgren et al. 2012)](image_url)
Using the risk profile of contemporary infectious diseases and their potential severity of consequence, as described by Europe, the LDAA conducted an analysis of the diseases that currently qualify for the National Notifiable Disease List in Australia; Figure 4: Australian notifiable diseases against European risk rating illustrates the dilemma for Australians. Of the common co-infections experienced in Australian patients, only Brucellosis is notifiable on the national list and Yersiniosis is reportable in only WA, TAS, SA, QLD, NSW and the ACT.

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<td>States NT, WA, TAS</td>
</tr>
<tr>
<td>High / Medium</td>
<td>Visceral leishmaniasis</td>
<td>N</td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>Campylobacteriosis</td>
<td>Y (2004)</td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>Chikungunya fever</td>
<td>Pending since 2010</td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>Cryptosporidosis</td>
<td>Y (2004)</td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>Giadiasis</td>
<td>States ACT, TAS, VIC, WA</td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>Hantavirus</td>
<td></td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>Rift Valley Fever</td>
<td></td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>Salmonellosis</td>
<td>Y (2004)</td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>Shigellosis</td>
<td>Y (2004)</td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>VTEC</td>
<td></td>
</tr>
<tr>
<td>Medium/Medium</td>
<td>West Nile fever</td>
<td>Y (2010)</td>
</tr>
</tbody>
</table>

Figure 4: Australian notifiable diseases against European risk rating

In the LDAA’s rudimentary examination of surveillance in other jurisdictions, it was noted that Hong Kong (a place of low Lyme prevalence but significantly higher population) has a more contemporary way of addressing the discovery of Lyme disease in their country. While Lyme disease is not a notifiable disease in Hong Kong, there are stringent public health measures that have been set out by the government in the event of a doctor suspecting a case of Lyme disease. Even a suspicious case will trigger government intervention and epidemiological investigations, together with surveillance and control programs.

The author of the Study report quite readily recognises the importance of surveillance. In his own work he states that early detection and rapid responses are key to reducing the risks from emerging diseases (Mackenzie 2011). It is recommended that achieving high levels of surveillance and an “ability to respond rapidly and effectively to infectious disease threats also requires a strong political commitment by policy-makers and governments, and by a cadre of well trained and committed health workers in relevant disciplines.” The LDAA fully agrees with this and adds that open minds must also be part of a best practice policy response.

The LDAA recommends an immediate review of the CDNA’s decision to omit Lyme disease from the National Notifiable Diseases list. It further requests transparent and open disclosure of the criteria and processes used for the monitoring and surveillance of Lyme disease or Lyme-like illness in Australia.

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Use of SPECT scans in the diagnostic pathway
The Study neglects to recognise that Lyme disease is primarily diagnosed clinically with serology used to support the clinician’s findings. It also fails to mention the growing use of Single Photon Emission Computed Tomography (SPECT) scans in the diagnosis of Lyme disease for many patients, especially those with neurological manifestations and inconclusive or equivocal serology.

A study undertaken in 1994 revealed that MRI results of late stage Lyme sufferers were generally found to be normal; however, SPECT scans returned hypo perfusion in cerebral white matter in these patients (Fallon et al, 1994). This study was later supported by additional research noting that 51.4% of suspected Lyme patients had significant perfusion abnormalities (Fallon et al, 1997). These abnormalities were found primarily in the frontal and temporal lobes of 75% of the patients with researchers concluding that ‘these scans can be used to provide objective evidence in support of the clinical diagnosis’ (Donta et al, 2012).

A reported 75% of Lyme patients were found to return abnormal SPECT results. These abnormal results were found to be consistent whether a suspected Lyme patient had previously returned seropositive or seronegative results under CDC criteria (Donta et al, 2012).

In addition, it was found that intracellular antibiotic treatment administered over 1-2 years yielded an improvement in 70% of Lyme patients (Donta et al, 2012). Profusion improvement through antibiotic treatment was also concluded by Logigian (1994).

These findings suggest that SPECT scans should be considered as a diagnostic tool for Lyme disease. More importantly, with the debate currently surrounding the accuracy of serology testing in Australia, SPECT scans would be beneficial in supporting a current clinical diagnosis. However, it follows that if SPECT scans were adopted doctors and radiologists would need to be appropriately informed and educated regarding SPECT investigations appropriate to Lyme disease. In line with the above findings SPECT scans can also be used to monitor improvements. Consideration should also be given to initial diagnostic use, if a patient is already undergoing antibiotic treatment.

Risk of transmission through blood transfusion
There is a growing body of evidence suggesting that Lyme disease and also other vector borne pathogens and bacterial infections can be spread through blood transfusion. Significantly, it is noted that *B. burgdorferi* survive storage under blood banking conditions and that transfusion-related Lyme disease is theoretically possible (Nadelman et al. 1990). A recent case reported that a nine-year old boy was infected with *Ehrlichia* after a blood transfusion (Regan et al. 2013).

A number of other studies in the US indicate there were 159 known cases of Babesiosis caused by transfusions where blood bank officials were able to trace back to 136 donors (Herwaldt et al. 2011; Leiby 2011). Alarming 30 of the cases reported were able to be traced to only 12 donors because blood supplies were split and used in multiple recipients. In the last ten years, 77% of reported cases of Babesiosis have occurred and this indicates the risk is increasing. Further issues on the risk of infection via blood transmission are covered in the Additional considerations section.

In light of the growing awareness, many Australian patients have contacted the Australian Red Cross seeking information about donation eligibility and received replies stating “unfortunately as Lyme
disease is a chronic condition we are unable to accept blood donations if someone has been
diagnosed with this condition, to protect their health and safety”. These issues are of primary
concern to public health and require formal recognition by DoH. Blood donation criteria regarding
Lyme-like illness have not been considered as part of the Study, nor included in any research project.

Fortunately, Australian patients already diagnosed with Lyme disease or Lyme-like illness have been
conscientious in voluntarily withdrawing from not only transfusion-related donation but also organ
donation lists. However, there remains considerable public health risk for the many recipients as
there are likely many donors with Lyme disease or Lyme-like illness who are as yet undiagnosed or
potentially misdiagnosed. To date, patients have been unable to successfully communicate these
risks to those operating placental cord blood banks.

**Ethical conduct & conflicts of interest**

Many patients are given the inadequate and ambiguous label of ‘crazy’ by the medical fraternity. As
evidenced in the Study and further discussed in this document, patient’s attempts at raising public
awareness are largely viewed by mainstream medicine and officials as ‘emotive’. This is a particularly
disrespectful generalisation and difficult to defend as ethical by any standard.

There has been substantial evidence, specifically in the US, of blatant bias and perceived corruption
in the Lyme disease debate. In one state of the US it has culminated in the Attorney-General
launching his own inquiry into the biased practices of authoring committees and openly criticising
the seemingly common, and little questioned, practice of appointing ‘likeminded’ researchers while
blocking the appointment of scientists with divergent views. The Attorney-General’s investigation
found that the “IDSA failed to screen for conflicts of interest on the part of the guidelines panel."

It is evident the Australian Scoping Study report itself has been biased in its approach with selective
use of journal articles. Lyme disease in Australia requires a review of literature and research from all
perspectives, it requires a full evaluation of its most current issues and it must ensure that it
encompasses the intricacies of this current health problem. It is fundamental to ensure
investigations and enquiries into Lyme disease are free from conflicts of interest. The literature
review could be argued to be far too rudimentary in contrast to the complexities of the current Lyme
disease problems.

In addition, it is alarming to the patient community to learn that experts associated with, quoted
within, or referred to, in this Study, hold previous positions that are perceived as conflicting. This
highlights the need to carefully review the selection of material and to absolutely ensure there are
no conflicts of interest. In the absence of any declarations in respect to the Study, patients can only
assume there are none; however, this now requires clarification.

The LDAA require that ethical conduct and full declaration of conflicts of interests be a core
component of all Australian work on Lyme disease and Lyme-like illness.
Appendices
Appendix A – Patient focused strategic approach to the Lyme problem

Patients scope the problem as follows:

- There is a rapidly increasing cohort of patients experiencing Lyme-like illness in Australia.
- More than a thousand patients have already been clinically diagnosed with a Lyme-like illness by reputable and knowledgeable GPs; there are potentially many thousands more who remain undiagnosed.
- The majority of the clinically diagnosed patients have also had positive *Borrelia* spp. serology results via overseas laboratories and some in Australian labs.
- Most of these patients have also been diagnosed with a selection of Lyme-related co-infections, such as Babesiosis, Bartonellosis, Ehrlichiosis, Rickettsiosis, Mycoplasmosis, Chlamydiophila pneumoniae.
- Some patients have travelled overseas; some have never left Australia.
- Some patients can confirm a history of tick bites; many cannot.
- There is sufficient anecdotal evidence among this cohort to suggest other modes of transmission, which warrant further scientific investigation.
- Many patients who have been receiving treatment based on protocols recommended by Lyme-aware GPs have already experienced significant health improvements.
- There are no formal policies for the proactive medical treatment of Lyme disease and Lyme-like illness in Australia.
- Most patients have experienced difficulties in readily accessing affordable, reliable diagnosis and treatment by Australian clinicians who are receptive and appropriately educated to treat their condition.
- Most patients have experienced significant impediments and many have experienced discrimination due to a lack of public awareness of Lyme-like illness and an official position that Lyme disease cannot exist here (since it was not located in a 1994 study of east coast ticks).
- There are no formal policies in place to ensure the protection of the Australian public as a whole from the possible spread of Lyme-like illness via various potential means of transmission.

Patients asked these questions:

1. What can be done to assist patients who are already infected with Lyme-like illness?
2. What are the impediments to accessing appropriate testing and treatment?
3. What can be done to prevent further infection among the general public?
4. What might be causing this illness (with totally open parameters, not focused only on ticks)?
Patients identified these Key Issues & Objectives:

1. Australian Patients experience difficulties obtaining a reliable diagnosis for Lyme-like illness in Australia.

   Objective: Ensure patients can readily access affordable and reliable diagnosis and ‘best practice’ laboratory testing by 2016.

2. Australian patients with Lyme-like illness experience difficulties accessing appropriate and affordable medical treatment for their condition(s) and often encounter discrimination.

   Objective: Ensure patients with Lyme-like illness are able to access appropriate and affordable treatment by 2016.

3. The Australian public has not been made aware of the potential risks of exposure to Lyme-like illness from ticks and other possible vectors nor has a national health policy been developed to address treatment issues.

   Objective: Reduce the risk of an epidemic of late stage Lyme-like illness by ensuring the Australian public is aware of the potential risks of exposure to possible transmission(s) and by improving access to early intervention treatment protocols throughout Australia by 2016.

4. Patients with Lyme-like illness experience discrimination because their medical condition is not formally recognised.

   Objective: Ensure an end to discrimination by raising public awareness of Lyme-like illness by 2016.

Patients identified these Priority Strategies:

1. Chief Medical Officer to issue a public statement acknowledging the existence of Lyme-like illness in Australia and ensure widespread dissemination throughout medical and public agencies, as well as through mass media.

2. Implement a broad scale Public Education Program, targeting medical community and sectors of the public identified as ‘at risk’.

3. Implement an Interim Treatment Strategy for existing patients while further research into causative factors is conducted.

4. Review Australian laboratory testing processes to ensure reliability of testing.

5. Conduct a study of the unique patterns (epidemiology) of Lyme-like illness in Australia before making assumptions about its causes.

6. Pursue research into ‘causative factors’ ensuring an open focus to consider all potential sources of transmission.
**Patient focused Strategic Action Plan**

1. **Diagnosis and Testing**

**Major Issue:** Patients experience difficulties obtaining a reliable diagnosis for Lyme-like illness in Australia.

**Objective:** Ensure Australians experiencing Lyme-like illness can readily access affordable and reliable diagnosis and ‘best practice’ laboratory testing by 2016.

<table>
<thead>
<tr>
<th>Target for Change</th>
<th>Impediments</th>
<th>Strategies</th>
<th>Refer to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australian clinicians GPs &amp; Specialists</td>
<td>Clinicians discount the possibility of Lyme disease in their diagnoses because an entrenched scientific position, based on a single study of indigenous ticks, leads them to conclude Lyme disease cannot exist in Australia, regardless of travel history and symptom presentation in their patients. They are also reluctant to consider diagnosing Lyme disease because of the controversy surrounding the disease.</td>
<td>1.1 CMO re-issue official statement regarding the existence of Lyme-like illness and the possibility of <em>Borrelia</em> or similar pathogen causing illness in Australia. Revise dissemination strategy to be more effective in reaching GPs.</td>
<td></td>
</tr>
<tr>
<td>Australian clinicians GPs &amp; Specialists</td>
<td>Clinicians frequently misdiagnose and recommend inappropriate treatment protocols.</td>
<td>1.3 Develop educational guidelines. 1.4 Develop training program for clinicians in diagnosis of Lyme-like illness.</td>
<td>See Education Action Plan</td>
</tr>
<tr>
<td>ICPMR, PaLMS and referring laboratories</td>
<td>Australian laboratory tests appear biased towards a high false negative rate (when compared to same-sample overseas testing). Positive test results are often dismissed as being erroneous.</td>
<td>1.5 Conduct a thorough review of current Australian testing procedures. 1.6 Study laboratory practices in all countries testing for Lyme-like illness to ascertain ‘best practice’.</td>
<td>See Diagnosis &amp; Testing Action Plan</td>
</tr>
<tr>
<td>CMO CACLD</td>
<td>Uncertainty about the causative factors for Lyme-like illness in Australia has meant most clinicians rule out Lyme disease as a differential diagnosis.</td>
<td>1.7 Conduct epidemiological research based on current patients with Lyme-like illness. 1.8 Conduct retrospective research. 1.9 Conduct clinical research.</td>
<td>See Research Action Plan</td>
</tr>
<tr>
<td>CMO CACLD</td>
<td>Research into Lyme disease appears to falter once simplistic causative factors have been identified, leaving many questions unanswered as to alternate potential causes of Lyme-like illness, and patients can be excluded when their presentations of the condition fall outside narrow definitions endorsed for diagnosis and treatment.</td>
<td>1.10 Study the unique presentations of Lyme-like illness in Australia before conducting research based on assumptions from other locations where Lyme disease and Lyme-like illness occurs.</td>
<td>See Research Action Plan</td>
</tr>
</tbody>
</table>
2. Treatment

**Major Issue:** Australian patients with Lyme-like illness experience difficulties accessing appropriate and affordable medical treatment for their condition(s) and often encounter discrimination.

**Objective:** Ensure all Australian patients with Lyme-like illness are able to access appropriate and affordable treatment by 2016.

<table>
<thead>
<tr>
<th>Target for Change</th>
<th>Impediments</th>
<th>Strategies</th>
<th>Refer to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMO/CACLD</td>
<td>Attention to developing treatment protocols for existing patients has been delayed due to scientific focus on identifying causative agents before acknowledging medical condition.</td>
<td>2.1 Consult with clinicians with most experience treating Lyme-like illness in Australia and overseas. Identify ‘best practice’.&lt;br&gt;2.2 Develop interim treatment guidelines endorsed by CMO. &lt;br&gt;2.3 Ensure thorough dissemination of treatment protocols to all Australian clinicians. &lt;br&gt;2.4 Develop training for clinicians.</td>
<td>See Treatment Action Plan for detail. See Education Action Plan for detail.</td>
</tr>
<tr>
<td>Australian clinicians GPs &amp; specialists</td>
<td>Patients attending GPs &amp; specialists are prescribed inappropriate treatments, particularly antidepressants and steroids.</td>
<td>See Strategy 1.1 See Strategy 2.3</td>
<td>See Treatment Action Plan for detail.</td>
</tr>
<tr>
<td>Public hospitals</td>
<td>Patients attending public hospitals (particularly emergency departments) have been refused treatment when revealing a Lyme diagnosis in their medical history.</td>
<td>See Strategy 1.1 See Strategy 2.3</td>
<td>See Education Action Plan for detail.</td>
</tr>
<tr>
<td>GPs &amp; Public hospitals</td>
<td>Patients presenting with a recent tick bite have been refused early intervention treatment with antibiotics, or incorrect antibiotics.</td>
<td>2.6 Implement early intervention strategy where infection is suspected. Administer antibiotic treatment (6 weeks minimum).</td>
<td>See Treatment Action Plan for detail.</td>
</tr>
<tr>
<td>PBS</td>
<td>Patients treating Lyme disease bear unsustainable expenses because many of the prescribed medicines they require are not covered under Pharmaceutical Benefits Scheme (PBS).</td>
<td>2.7 Authorise inclusion of pharmaceuticals regularly used in Lyme treatment protocols on PBS.</td>
<td>See Treatment Action Plan</td>
</tr>
<tr>
<td>Medical community</td>
<td>There is an acute shortage of Lyme-aware doctors available to treat patients with Lyme-like illness in Australia.</td>
<td>Implement Strategy 1.1 to reduce controversy and stigma associated with Lyme-like illness. Implement Strategy 2.5 - training for clinicians.</td>
<td>See Treatment Action Plan</td>
</tr>
</tbody>
</table>
3. Public awareness/Risk protection

**Major Issue:** The Australian public has not been made aware of the potential risks of exposure to Lyme-like illness from ticks and other possible vectors nor has a national health policy been developed to address treatment issues.

**Objective:** Reduce the risk of an epidemic of late stage Lyme-like illness by ensuring the Australian public is aware of the potential risks of exposure to possible transmission and by improving access to early intervention treatment protocols throughout Australia by 2016.

<table>
<thead>
<tr>
<th>Target for Change</th>
<th>Impediments</th>
<th>Strategies</th>
<th>Refs/Timeframe</th>
</tr>
</thead>
</table>
| DoH CDNA         | There are currently no formal mechanisms in place to measure the incidence of Lyme disease or Lyme-like illness in Australia. | 3.1 Monitor incidence of Lyme disease in the Australian population.  
                   |                                                                              | 3.2 Initiate a national surveillance program.                               | See Education Action Plan for detail.    |
| The Australian Public | Australians are generally unaware of the potential sources of and risks associated with transmission of Lyme-like illness. | 3.3 Develop and disseminate public awareness campaign.  
                   |                                                                              | 3.4 Erect warning signage in areas of potential high risk exposure.        |                                          |
| GPs & Public hospitals | There is no early intervention strategy in place for people being bitten by arthropods known to be potential vectors for Lyme-like illness. | 3.5 Ensure all GPs are aware of risks and ready to administer appropriate treatment for early intervention. | See Treatment Action Plan for detail.    |
| Red Cross & Organ Donation agencies | There is a risk of transmission through blood banks and organ donation, as opting out is voluntary and only an option for those who have been correctly diagnosed. | 3.6 Screening of blood for *Borrelia, Babesia* and other known co-infections.  
                   |                                                                              | 3.7 Notification to organ donors to withdraw from program after suspected tick bites. |                                          |
| GPs, public health facilities. | Mothers may be transmitting pathogens to babies during pregnancy and breast-feeding. | 3.8 Issue public health warnings to prospective parents and treat expectant mothers to minimise transmission risk. | See Education Action Plan for detail.    |
| Public Health Education Programs, Clinicians. | The general public is unaware of the possibility of sexual transmission of Lyme disease, particularly from partners who remain undiagnosed. | 3.9 Issue public health warnings regarding potential risks of LD along with other safe sex warnings.  
                   |                                                                              | 3.10 Warn patients diagnosed with Lyme-like illness of potential risks to sexual partners. | See Education Action Plan for detail.    |
4. Social welfare & discrimination issues

**MAJOR ISSUE:** Patients with Lyme-like illness experience discrimination because their medical condition is not formally recognised.

**Objective:** Ensure an end to discrimination by raising public awareness of Lyme-like illness by 2016.

<table>
<thead>
<tr>
<th>Target for Change</th>
<th>Impediments</th>
<th>Strategies</th>
<th>Refs/Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australian clinicians GPs, Specialists &amp; Public Hospitals</td>
<td>Patients attending GPs, specialists and public hospitals (particularly emergency departments) have been subjected to humiliation and refused treatment when revealing a Lyme diagnosis in their medical history.</td>
<td>See Strategy 1.1.</td>
<td>See Education Action Plan for detail.</td>
</tr>
<tr>
<td>Department of Human Services / Centrelink</td>
<td>Patients have been denied welfare income payments, as Lyme-like illness is not recognised as an official medical condition. Children are denied disability supports because their illness is not currently listed for consideration on Centrelink paperwork.</td>
<td>4.1 Raise awareness of Lyme-like illness in public institutions including the relapsing recurring nature of manifestations</td>
<td>See Education Action Plan for detail.</td>
</tr>
<tr>
<td>GP, Public hospitals, DCD, Child welfare agencies</td>
<td>Parents have been threatened with losing custody of their children due to school non-attendance and/or told their children’s obvious symptoms are psychosomatic when revealing they are suffering from Lyme-like illness, or are accused of Munchausen’s syndrome by proxy.</td>
<td>As per 4.1</td>
<td>See Education Action Plan for detail.</td>
</tr>
<tr>
<td>Schools</td>
<td>Children suffering from Lyme-like illness are unable to perform to their potential and are frequently unable to attend school.</td>
<td>4.2 Open up pathways for partial homeschooling options. 4.3 Provide additional in-school support options.</td>
<td>See Education Action Plan for detail.</td>
</tr>
<tr>
<td>Workers’ comp &amp; Insurance companies</td>
<td>Workers’ compensation and income protection insurance claims are frequently rejected due to official ambiguity over existence of Lyme disease in Australia.</td>
<td>4.4 See Strategy 1.1. Improve diagnosis and testing.</td>
<td>See Education Action Plan for detail.</td>
</tr>
<tr>
<td>CMO/Medicare</td>
<td>Disparity of costs between patients in tests available to them for diagnosing and testing Lyme disease.</td>
<td>4.5 Implement diagnostic guidelines</td>
<td>See Diagnosis &amp; Testing Actions Plan</td>
</tr>
</tbody>
</table>
### 5. Education Action Plan – in further detail

<table>
<thead>
<tr>
<th>Target audiences</th>
<th>Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Australians</td>
<td>CMO to make a formal announcement to the Australian public regarding the existence of Lyme-like illness among Australian patients and the need to take precautions while research into potential transmission sources are further researched.</td>
</tr>
<tr>
<td>All Australian clinicians</td>
<td>Develop and disseminate educational packages on the background, diagnosis and treatment of Lyme-like illness. (Refer to 7. Treatment Action Plan for further details.)</td>
</tr>
<tr>
<td>Radiologists, IDS, Neurologists, private and public practices of specialists</td>
<td>Develop and disseminate specialist diagnostic and treatment guidelines for clinicians involved in differential diagnosis.</td>
</tr>
<tr>
<td>Government agencies, Educational institutions, public health centres, Centrelink, DCS</td>
<td>Develop and disseminate education packages providing medical background, care considerations and risk protection information regarding Lyme-like illness.</td>
</tr>
<tr>
<td>General public Private health centres, National Parks, State forests, coastal recreation areas, public and private camping areas, school camps</td>
<td>Develop public risk awareness campaign identifying arthropods suspected as sources of infection. Including: print and electronic media packages; signage in public areas; advertising and media stories.</td>
</tr>
<tr>
<td>Public, including prospective parents via GPs &amp; Public Hospitals, sex education programs.</td>
<td>Develop awareness information brochures to advise of ‘potential risk’ via sexual and in utero transmission.</td>
</tr>
</tbody>
</table>
### 6. Diagnosis and Testing Action Plan – in further detail

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate</td>
<td>CMO to establish Review committees/working groups for Diagnosis and Testing.</td>
</tr>
<tr>
<td>Interim step</td>
<td>Develop interim diagnostic guidelines in consultation with Australian doctors treating Lyme-like illness and based on local disease presentations.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Research Brazil’s diagnostic tools for BYS in the development of a diagnostic pathway.</td>
</tr>
<tr>
<td>By 2016</td>
<td>Common differential diagnosis symptoms should be developed for Australia once clinical studies have determined the most common aspects of Australian Lyme disease or Lyme-like illness.</td>
</tr>
<tr>
<td>By 2016</td>
<td>Develop guidelines for diagnosis of the most common Australian co-infections.</td>
</tr>
<tr>
<td>Medium</td>
<td>Full review of all Australian laboratories conducting Lyme disease testing to determine test method used, genospecies tested, actual testing practices compared to test kit guidelines.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Study laboratory practices of all countries testing for Lyme-like illness to ascertain ‘best practice’.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Establish criteria for eligibility and standarise testing process for all Australian laboratories involved in testing for Lyme disease.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Reference labs to be established based on a statement of requirement.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Only reference labs testing for <em>B. burgdorferi, garinii and afzelii</em> will perform two-tier testing (ELISA and immunoblot).</td>
</tr>
<tr>
<td>Interim step</td>
<td>Local pathology laboratories cease performing screening ELISA tests until standardised testing processes are established.</td>
</tr>
<tr>
<td>Immediate</td>
<td>Testing process to outline steps to ensure samples are analysed within 3 days of collection.</td>
</tr>
<tr>
<td>Immediate</td>
<td>Changeover of ICPMR Lyme disease testing to European ELISA and immunoblot test kits.</td>
</tr>
<tr>
<td>Interim step</td>
<td>All Lyme disease testing to be performed by Australian Biologics or PaLMS until ICPMR has updated and verified their new testing procedures. Standardisation of criteria used to determine positivity on Western Blots.</td>
</tr>
<tr>
<td>Immediate</td>
<td>Patients and clinicians to be provided with details of which laboratory has performed their testing and the full results (showing species tested and bands detected).</td>
</tr>
<tr>
<td>Immediate</td>
<td>CMO to provide national clinician advice to reflect the testing process (revise the NSW Government version).</td>
</tr>
<tr>
<td>By 2015</td>
<td>Analyse historic immunoblot results to determine characteristic bands in patients with Lyme-like illness acquired in Australia and use to refine immunoblot interpretation guidelines.</td>
</tr>
<tr>
<td>By 2016</td>
<td>Testing capability to be developed for potential co-infections.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Conduct studies into other diagnostic tools, including, but not limited to:</td>
</tr>
</tbody>
</table>
| By 2015 | - microscopy tests for detection of spirochaetes  
| By 2015 | - latest culture methods  
| By 2015 | - nested PCR in conjunction with DNA sequencing tools  
| By 2015 | - lymphocyte transformation test (LTT)  
| By 2015 | - SPECT scans  |
| By 2015 | Review /recall Westmead tests results in which ‘false positive’ result was given on basis of 5-bands requirement. Request these patients retest once processes are revised and refined. |
### 7. Treatment Action Plan – in further detail

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immediate</strong></td>
<td>Formally authorise doctors to treat Lyme disease or patients with Lyme-like illness, irrespective of where they are diagnosed, without repercussions.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Develop interim guidelines, potentially based upon European guidelines, and disseminate to all hospitals, general practitioners and infectious disease doctors in Australia.</td>
</tr>
<tr>
<td><strong>Immediate</strong></td>
<td>Consult current treating practitioners in the development of any Australian treatment guidelines, either interim or final.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Develop a standardised Australian ‘criteria’ for diagnosis to underpin the development of a diagnostic pathway.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Develop educational material for doctors containing information on:</td>
</tr>
<tr>
<td></td>
<td>• importance of differential diagnosis of Lyme disease and clear articulation of early, late and chronic stages of Lyme requiring different treatment strategies;</td>
</tr>
<tr>
<td></td>
<td>• the Jarisch-Herxheimer reaction following administration of antibacterials;</td>
</tr>
<tr>
<td></td>
<td>• chronic and relapsing nature of illness, also L-forms, cyst forms, cell wall deficient biofilms and the possibility of co-infections;</td>
</tr>
<tr>
<td></td>
<td>• treatment of co-infections, where a ‘layered’ approach to treatment may be required, and non-bacterial co-infections (Babesiosis) require alternate treatment protocols;</td>
</tr>
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<td></td>
<td>• the inappropriate prescription of steroids and /or anti-depressants (especially if the case is differential); and,</td>
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<tr>
<td></td>
<td>• early intervention treatment strategies following a tick bite.</td>
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<tr>
<td>By 2015</td>
<td>Develop appropriate specification of the medications required to treat Lyme disease on medical schedules and the PBS.</td>
</tr>
<tr>
<td>By 2016</td>
<td>Conduct epidemiological studies (Rec 7) and clinical research into the unique Australian presentations of the illness (Rec 4) before developing final treatment guidelines in Australia.</td>
</tr>
<tr>
<td>By 2015</td>
<td>Review the range of complementary therapies currently being used in the treatment of Lyme-like illness to evaluate which may be efficacious and worthy of inclusion in recommended treatment protocols. For example, diet, detoxification, herbal, vitamin or mineral supplementation protocols.</td>
</tr>
</tbody>
</table>
7. Research Action Plan – in further detail

Patient community’s priorities for research projects proposed in response to the Scoping Study.

<table>
<thead>
<tr>
<th>Priority</th>
<th>Etiology</th>
<th>Patients</th>
<th>Pathogen</th>
<th>Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Epidemiological study (Rec 6)</td>
<td>Clinical study (Rec 4)</td>
<td><em>Borrelia</em> search (Rec 1)</td>
<td><strong>Interim solution</strong> for pathology testing &amp; Treatment</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td><em>Tick competence</em> (Rec 2)</td>
<td>Testing (Rec 3)</td>
</tr>
<tr>
<td>3</td>
<td>Retrospective investigation (Rec 5)</td>
<td>Treatment guidelines (Rec 7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The LDAA agrees in principle to the research projects proposed in the Study and proposed two additional research proposals (at Rec 6 & 7). What follows is a summary of the noted considerations the LDAA would like to see implemented in research projects on behalf of patients:

**Study 1: Experimental program to determine whether there is a Borrelia species in ticks in Australia causing Lyme-like disease, or whether another tick-borne pathogen is involved in human Lyme-like disease.**

1. Samples should be collected from coastal, mountain and desert terrains and from areas where people are reported to have a Lyme-like illness.
2. Collections and studies should not be limited to ticks; samples of all biting insects, fleas, mites, keds (biting flies), lice etc. should be considered.
3. Other potential pathogens should be included in this study; *Babesia, Bartonella, Anaplasma, Ehrlichia, Rickettsia* and other pathogens and viruses should be included in the study along with *Borrelia*.
4. *B. Queenslandica* should be acknowledged as a potential strain.
### Study 2: Are Australian ticks competent to maintain and transmit B. burgdorferi s.l. genospecies or other Borrelia species associated with relapsing fever?

1. Vector competence studies should not be limited to ticks; where spirochaetal matter is discovered in other insects, their vector competence should be properly investigated.

2. Evidence already exists to indicate that Australians are infected with more than one strain of *Borrelia*; research should investigate the multiple strains present within the samples collected and provide transparent calculations of the competence of those vectors to transmit multiple organisms, not simply *Borrelia*. Rates of transmission also necessitate investigation.

3. Research on strains known to cause relapsing fever should be correlated with clinical evidence of patients who are presenting with relapsing fever syndromes.

4. Native fauna should be considered in the examination of potential reservoirs and should be included to determine whether there is a native Lyme-like organism; it is important to understand the epidemiology, as there may be more than one vector involved. The Study should include identification of native Reservoirs for Lyme and Lyme-like disease and associated co-infections.

### Study 3: Do we have the best reagents for detecting novel Borrelia species, including B. miyamotoi, especially in clinical specimens?

1. Interim testing arrangements and standardisation of testing protocols are urgently required.

2. Some Australian private laboratories are already using sophisticated PCR techniques and isolating *Borrelia* and spirochaetal organisms. Every effort should be made to include any research evidence to continually improve the diagnostic and confirmatory testing protocols.

3. The DoH should immediately conduct a formal review into the current test process in use at the public health laboratories, specifically in light of the sub-optimal testing materials currently in use at Westmead.

4. The DoH should immediately, and formally, liaise with overseas testing laboratories that are providing positive tests to Australian patients to gain an understanding of their test processes, antigens used, primers and sequences.
### Study 4: Clinical studies of patients presenting with symptoms suggestive of Lyme or Lyme-like disease.

| 1. | Prospective clinical studies of patients must include an inquiry on alternate forms of transmission, for example, from an infected person to a sexual partner, or to a foetus, or via breastfeeding, as well as blood-to-blood contact or via transfusion. |
| 2. | A program of research needs to commence immediately to gather and collate symptom information from Australian treating doctors to underpin a detailed map of the constellation of symptoms unique to Australian patients. |
| 3. | Samples from patients not presenting with an EM rash should not be excluded from investigation. |
| 4. | The DoH should work collaboratively with the patient groups to assist with the longitudinal survey of patients conducted annually. |
| 5. | Any clinical study must investigate the manifestations of disease, especially in regard to early and late stages and ‘chronic Lyme’. |
| 6. | The Indigenous population should be studied to ascertain whether there is a history of Lyme-like illness in Australia or possibility for immunity to develop. |
| 7. | All clinical studies must abide by the strictest ethical principles, be conducted in an open and transparent manner, with full declaration of any conflicts of interest. |
| 8. | All clinical studies must recognise the specific impacts that studies will have upon children, who are most at risk. |

### Study 5: Retrospective investigation of chronic cases of Lyme borreliosis

| 1. | Testing processes and considerations outlined in research project 3 must be a precursor to qualifying patients. |
| 2. | Testing should not be limited to serological tests (ELISA and IFA), as many studies have shown negative serology in chronic cases with other indications of active infection, such as PCR positive and Elispot positive results. |
| 3. | Evaluate the efficacy of SPECT scans in the diagnostic process. |
| 4. | Samples used to qualify patients for any prospective studies must meet an agreed criterion and be conducted with the latest scientific knowledge and best laboratory technology available. |
| 5. | Research should include patients from every demographic group who can share their stories, their medical results and their histories as part of a formal retrospective study as well as currently treating doctors who are prepared share their records. |
| 6. | Any review of consolidated patient data, should not be limited to infectious diseases experts only and should include other independent experts. |
| 7. | A panel of “experts” should include at least two physicians with extensive experience in diagnosing and treating chronic Lyme disease in Australia. |
| 8. | All clinical studies and retrospective investigations conducted should be carried out with proper ethical approaches where full disclosure of any prior involvement in Lyme disease or Lyme-like illness is made transparent. |
**Study 6: Epidemiological research**

1. As a matter of urgency, the LDAA recommends a full epidemiological study that also includes, but is not limited to, the addition of the following:

   a) A baseline quantification of Australians with diagnosed Lyme disease or Lyme like illness, to satisfy the Terms of Reference of the Clinical Advisory Committee on Lyme Disease (CACLD). Data collected should include demographics such as prior travel history, geographical location, bite history, disease duration etc.

   b) Monitoring of Lyme and Lyme-like cases by the CDNA in light of the emerging incidence of Lyme-like illness occurring in Australians who have never left the country (LDAA 2012). A transparent and open disclosure of the criteria and processes used for monitoring and surveillance of Lyme disease or Lyme-like illness in Australia is required.

**Study 7: Development of a treatment options pathway** - is included in the Treatment Action Plan of this section.
Appendix B - Patient Test Results

Lab #: 2011T012745

NATURE OF SPECIMEN
TONSILS AND LYMPH NODE

HISTORY
1. A and L tonsil. 2. Lymph gland from L occipital area. Two year- old female with Marshall’s Syndrome (recurrent fevers) [PFAPA]. For histo/chemistry/cyto/flow. Please note that Dr Silva/ENT also requested extended TB panel and to retain some of the specimen for frozen as well as flow cytometry.

Dr Lavinia Hallam contacted Dr Matthew Cook on 26 July at 11.15 am. The instructions were as follows: For Specimen A which included ‘ght and left tonsils each required histology, flow cytometry,

_ lecular pathology, microbiology cultures including TB and fungus as well as a fresh tissue to be collected for Dr Jalilia Al Shekaili, Immunology Registrar for freezing. For Specimen B which was the post auricular biopsy instructions were to submit half for histology, a quarter for flow cytometry and a quarter for molecular pathology.

MACROSCOPIC DESCRIPTION
A. "TONSILS (RT PLUS LT)"
Two fresh tonsils received in one container. One measures 24x17x10mm. The other tonsil measures 29x18x13mm. Two Diff-Quik smears were made from each tonsil and samples were sent as per detailed instruction in the history from each lymph node. Cut surface of both nodes are pale, tan and solid.

Key to blocks:
-1,2 = sections from one tonsil
-3,4 = sections from other tonsil
4-N AE

B. "POSTAURICULAR LEFT"
A fresh reddish tan nodule measuring 10x7x4mm. Half of the specimen was submitted for formalin fixation ie histology, a quarter was sent for flow cytometry and a quarter was sent for molecular pathology. 1-2 AE [SAJ]

MICROSCOPIC
A. RIGHT AND LEFT TONSILS
Sections show floridly reactive tonsils. There is intimate association of lymphoid tissue with the surface and crypt squamous epithelium. The lymphoid tissue shows large prominent but apparently benign follicles. There appears to be bands of fibrosis crossing the tissue. There is no evidence of malignancy in this material.

B. LEFT OCCIPITAL LYMPH NODE
Sections show lymph node. There are bands of fibrous tissue crossing the node. The intervening lymphoid tissue shows prominent lymphoid follicles and irregular mantles however there is no obvious evidence of malignancy.

DIAGNOSIS
A. RIGHT AND LEFT TONSILS: FLORIDLY REACTIVE TONSILS.

B. LEFT OCCIPITAL LYMPH NODE: FLORID REACTIVE CHANGES.

Reported by DR L. HALLAM
Phone: (02) 6244 2877
Dear

I would value your opinion and assessment of this unfortunate patient of mine. She has a 12-month history of recurrent fevers and malaise of unknown cause. I have investigated her via blood tests, chest x-ray, echo-cardiogram, and micro urine. Her bloods including for autoimmune disease, inflammatory markers, thyroid etc are all normal as are other investigations except for a weakly positive hep c titre with no evidence of viral load. She is convinced her symptoms followed a tick bite but lyme serology was negative. She has a chronic regional pain syndrome of 12 years standing, being managed via the pain clinic.

I am at a loss to know what to do with her and her quality of life is greatly affected by her symptoms.

Current Medications

Endone 5 mg Tablets 1 bd
Durogesic 25 mcg/hour 4.2 mg Patches 1 every second day
Valium 5 mg Tablets 1 nocte pm
Colgout 500 mcg Tablets 1 bd
Catapres 100 1 bd

Current Problems
chronic regional pain syndrome

18 years - May 94
402 years - August 2000

Kind Regards
22 Sep 2011

Nurse
RN SMC
Mum noted rash on left thigh and back of shoulders at 1600 today. Itchy. Given zyrtec and stingoos, rash now spread down legs, and arms, hands and feet, abdomen also complaining of sore t and left wrist sore.

Hx allergic rhinitis Meds beconase nasal spray prn

T 36.4 HR 110 spo2 99% in ED

Hist / Exam
Hx- bite on left leg then noticed rash spreading further
O/e large welts on legs between legs and on feet, now also on arms and hand, face spared, breathing normal
Wt 17.1kg

Dx / Mx
Mx steroid dose tonight and Friday am
3.5ml now and in am

Dx: Allergic reaction (A92007)
Rx: 1 - Redipred (Oral solution) 5 mg/1 mL 30 mL
Measurement: Origin (O) - Triage
Measurement: Disposition (D) - Home
Medical Warning: (NKA)

Attention:
Fax:

Seen By: Signed:

Consent given to share medical details with other health providers: Yes

Please note - For your pathology test and xray results you should contact your own GP.

The selected message transfer option for this doctor is Electronic

This facsimile is intended only for the use of the addressee named above and may contain privileged and confidential information. If you are not the intended recipient of this facsimile you must not disseminate, copy or take any action based upon it. If you receive this facsimile in error please notify the GPAccess After Hours immediately (+61 02 4925 2259).
Address: [REDACTED]
Referred by: [REDACTED]
Collected: 13/03/2012
Specimen:
Test name: Arbovirus-Zoonosis
Copies to:
Requested: 12/03/2012
Performed: 13/03/2012
Test name: ARBOVIRUS-ZOONOSIS
Provider name: HAPS

Hunter Area Pathology Service - VIROLOGY REPORT 10:42 24-Apr-12

Collected: 10:10 13-Mar-12 MRN: H1675444 Specimen Type: Blood
Clinical Notes: Unwell 4-5 mths. Mother has recent Rickettsial serology pos
spotted

Rickettsia (spotted fever) <128 (< 128)
Rickettsia (murine typhus) <128 (< 128)
Rickettsia (scrub typhus) <128 (< 128)

Lyme Antibodies SCOM (< 1.0)

COMMENT
ICPMM Comment: Lyme Confirmation
B burgdorferi Bands 3
B afzelii Bands 1

These results do not suggest infection.

Lyme serology was referred to the Institute of Clinical Pathology and Medical Research (ICPMM), Westmead Hospital, Sydney, NSW. Tel: 1800-639412. ICPMM MRN: 9353786

ARRL Rickettsia comment: No evidence of exposure to any of the rickettsial strains tested. If this was an acute phase specimen please submit a convalescent specimen collected 10-14 days later to test for a change in antibody titre.

Rickettsia serology was referred to the Australian Rickettsial Reference Laboratory, Douglas Hocking Research Institute, The Geelong Hospital, Bellarine Street, Geelong, VIC. 3220. Tel: (03) 5226-7521. ARRL Ref Lab No: 44328

No additional report copies requested

HAPS Enquiries: Phone 1800 801949 Fax: 02 49 214400 Web Site: wwwhaps.nsw.gov.au
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LDAA – see Lyme Disease Association of Australia


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