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11:15 am

Q fever: epidemiology, symptoms, diagnosis, treatment and prevention by vaccination.

Dr Stephen R. Graves

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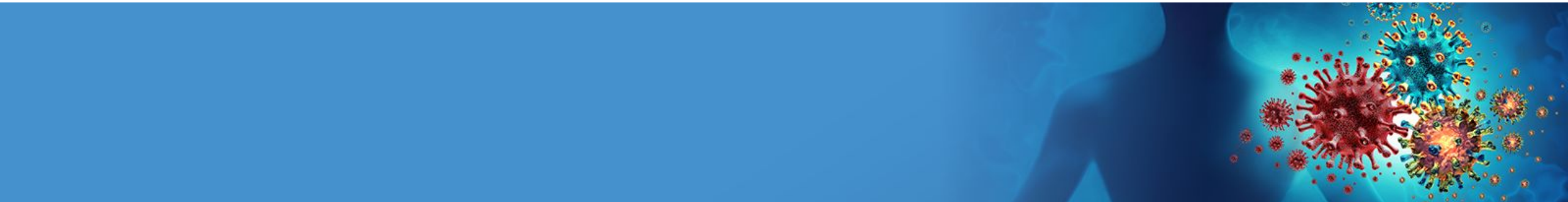
AUSTRALIAN RICKETTSIAL REFERENCE LABORATORY



What is Q fever?

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- An infectious disease
- Transmitted from animals to humans (i.e. it is a zoonosis)
- Caused by the bacterium *Coxiella burnetii*
- Quite common in rural and regional Australia
- Often difficult to diagnose by doctor as it has no unique features
- Relatively easy to treat with appropriate antibiotics
- Can be prevented with Q-VAX® vaccination (vaccine only available in Australia)

Who gets Q fever?

- Q fever is an infection of:

  a) occupation - persons associated with animals

  b) location – persons living in rural and regional parts of the world

- In Australia, the incidence varies:

  Qld > NSW > SA > Vic > WA > TAS

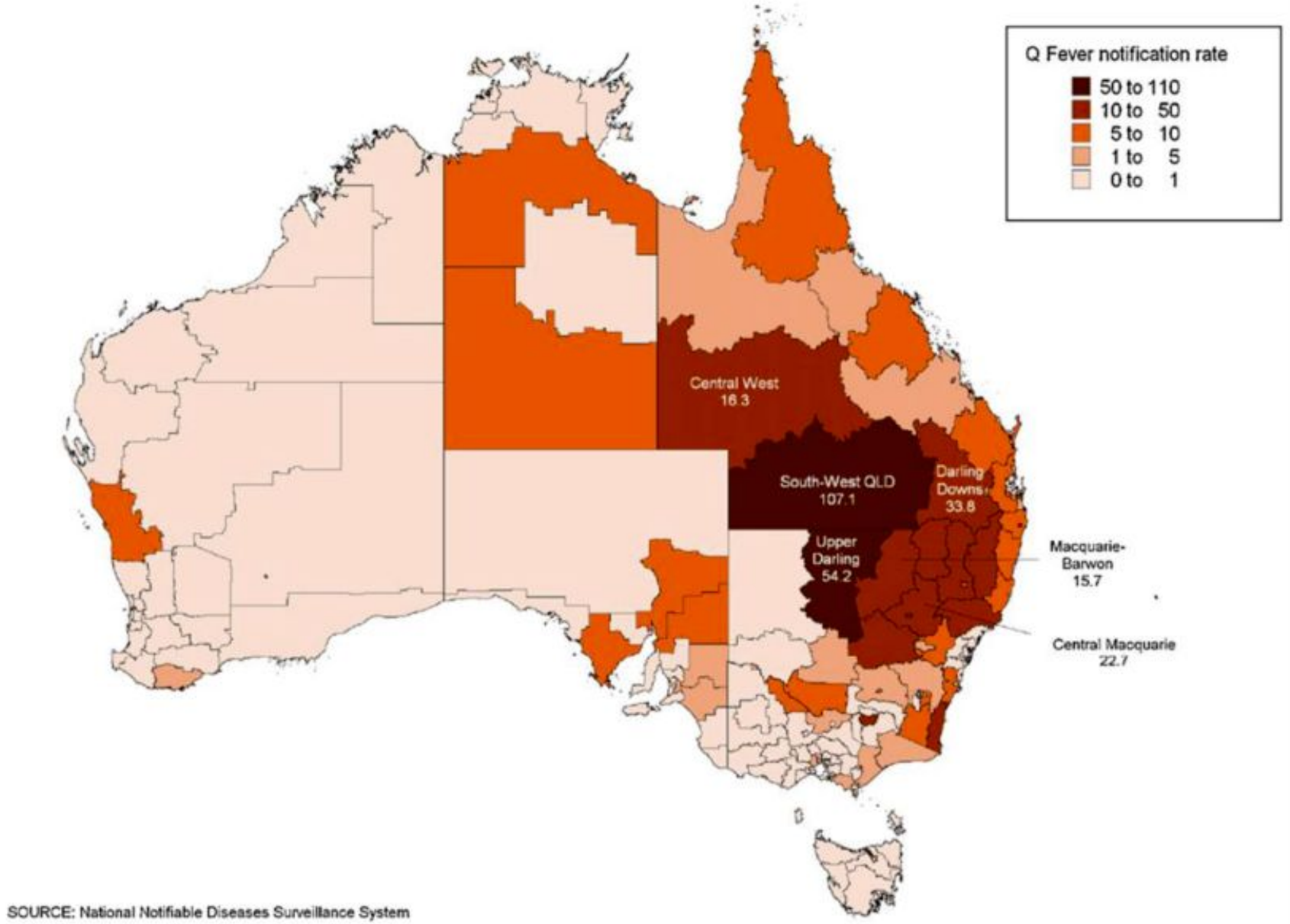
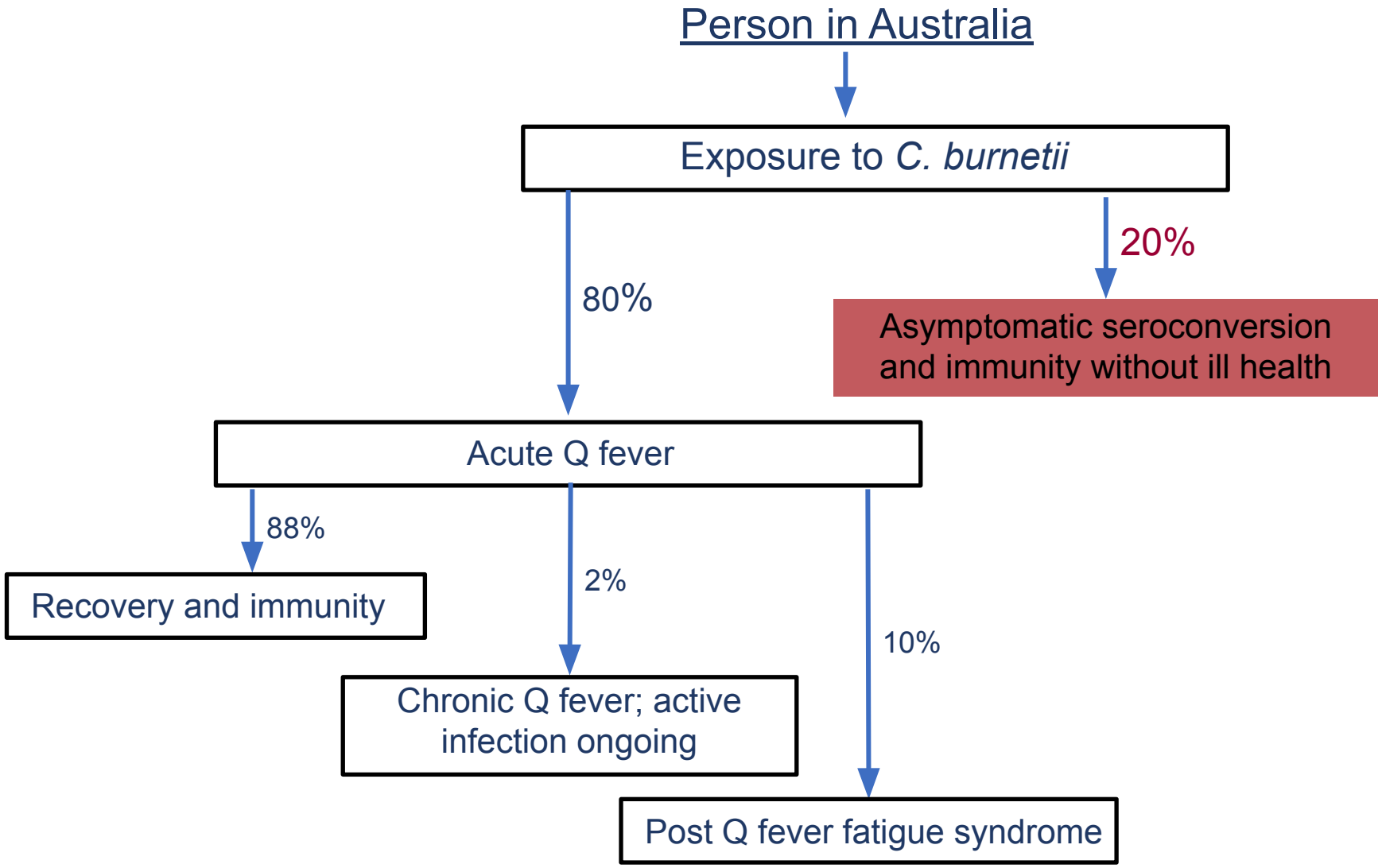


Image from: Marks S & Olenski M. Trop. Med. Infect. Dis. 2019, 4(2), 90; https://doi.org/10.3390/tropicalmed4020090

Q fever: the disease

Several presentations/stages of Q fever

- Asymptomatic seroconversion
- Acute Q fever
- Chronic (focal, persistent) Q fever
- Post Q fever fatigue syndrome
- Past Q fever, now immune

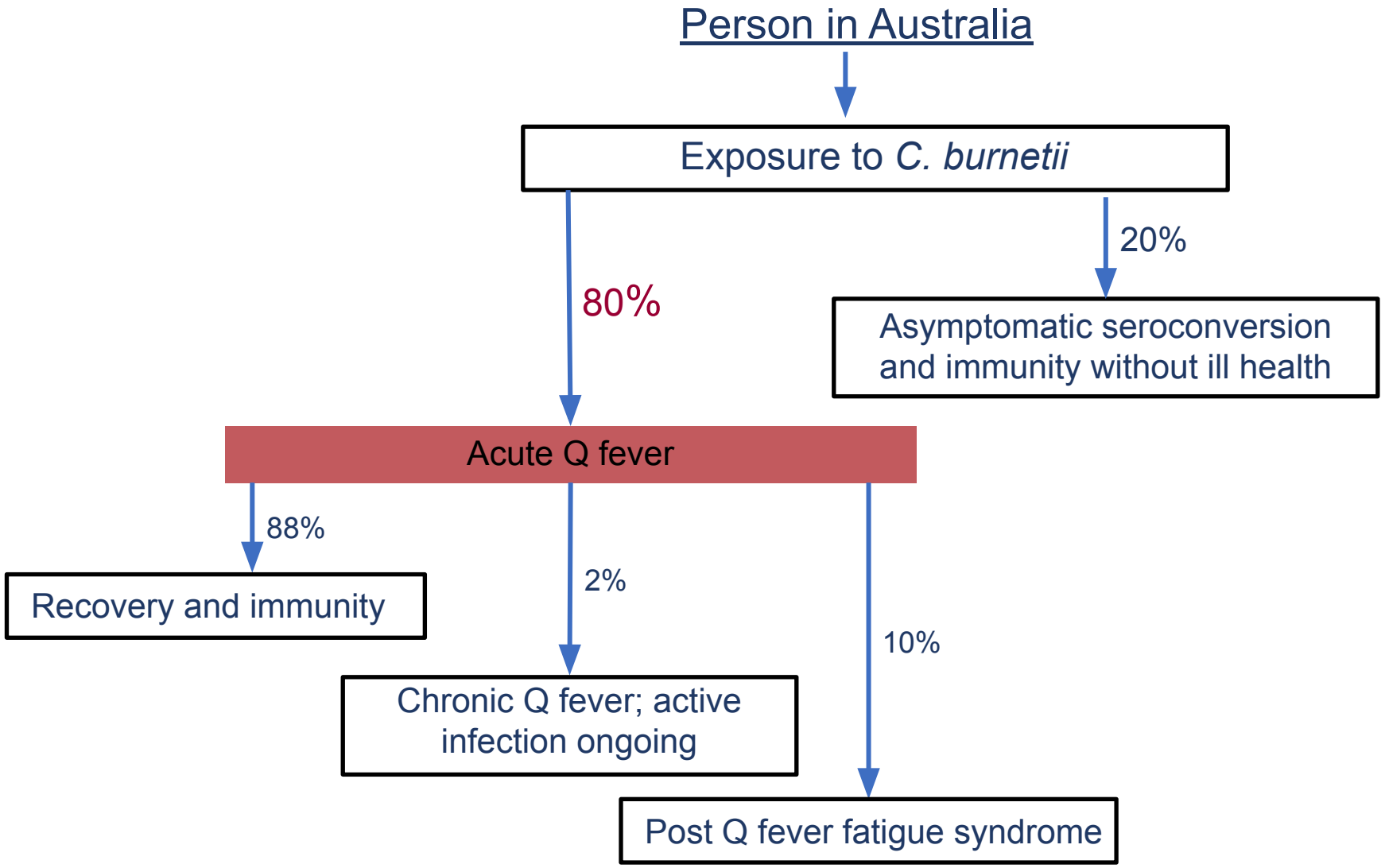

Person in Australia
Exposure to C. burnetii
20%
80%
Asymptomatic seroconversion and immunity without ill health
Acute Q fever
88%
2%
10%
Recovery and immunity
Chronic Q fever; active infection ongoing
Post Q fever fatigue syndrome

Asymptomatic seroconversion

- Percentage can vary in an outbreak
  - Meredith, Victoria (2015): 20% asymptomatic
  - Netherlands (2007-2010): 90% asymptomatic

    Healthy Dutch persons were tested by the health authority as they were deemed to be part of a large outbreak. They were not sick.

- Normally background (endemic), asymptomatic seroconversion is unlikely to be detected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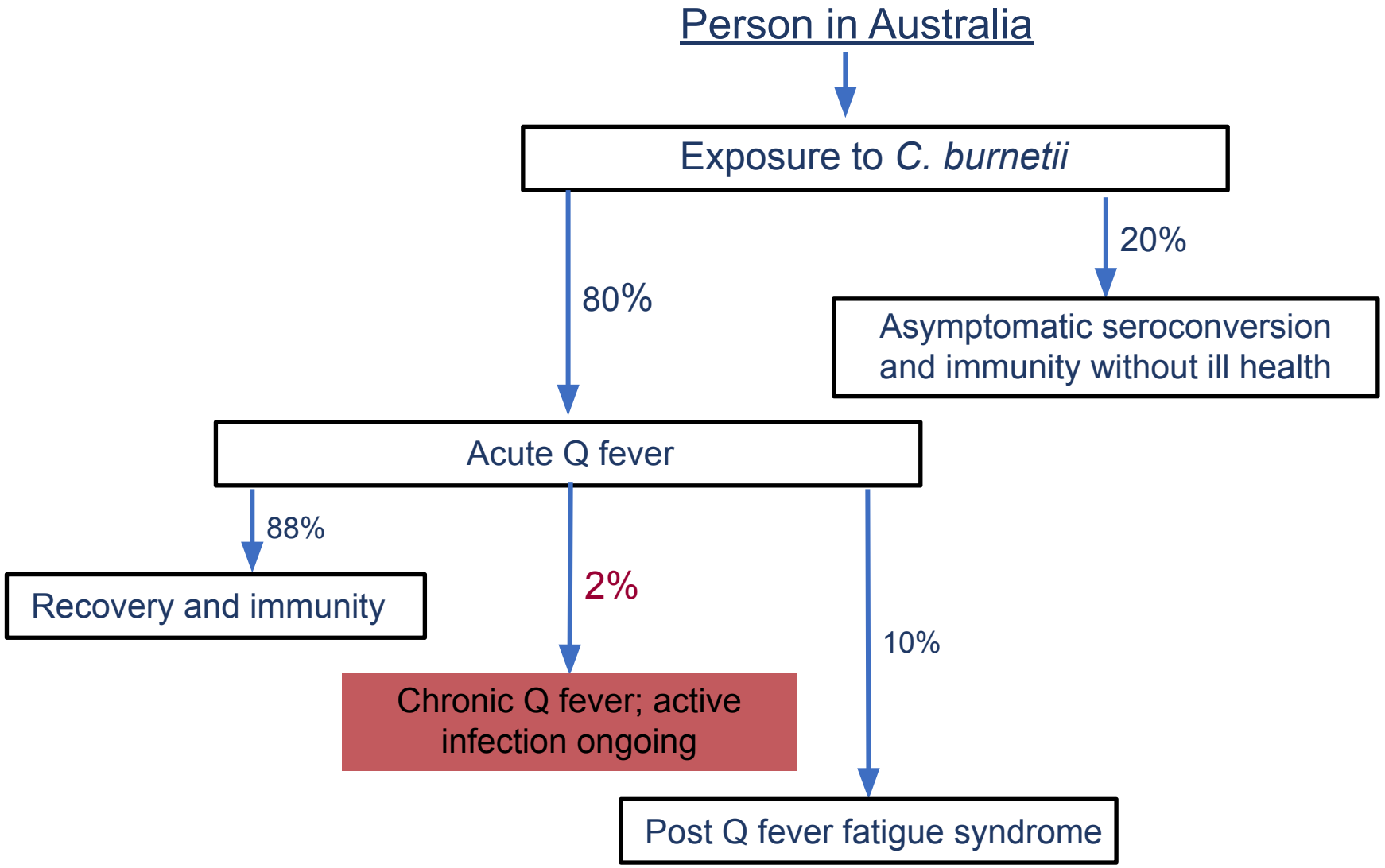
Acute Q fever

- “flu-like” illness
- “fever with mild respiratory symptoms”
- No pathognomic features
- Difficult to diagnose clinically without good history and epidemiological clues
- Main symptoms:
  - Fever, myalgia, headache, hepatitis (granulomatous), arthralgia, acute and severe fatigue
- Many rarer manifestations:
  - Including cholycystitis, haemophagocytic syndrome, disseminated intravascular coagulation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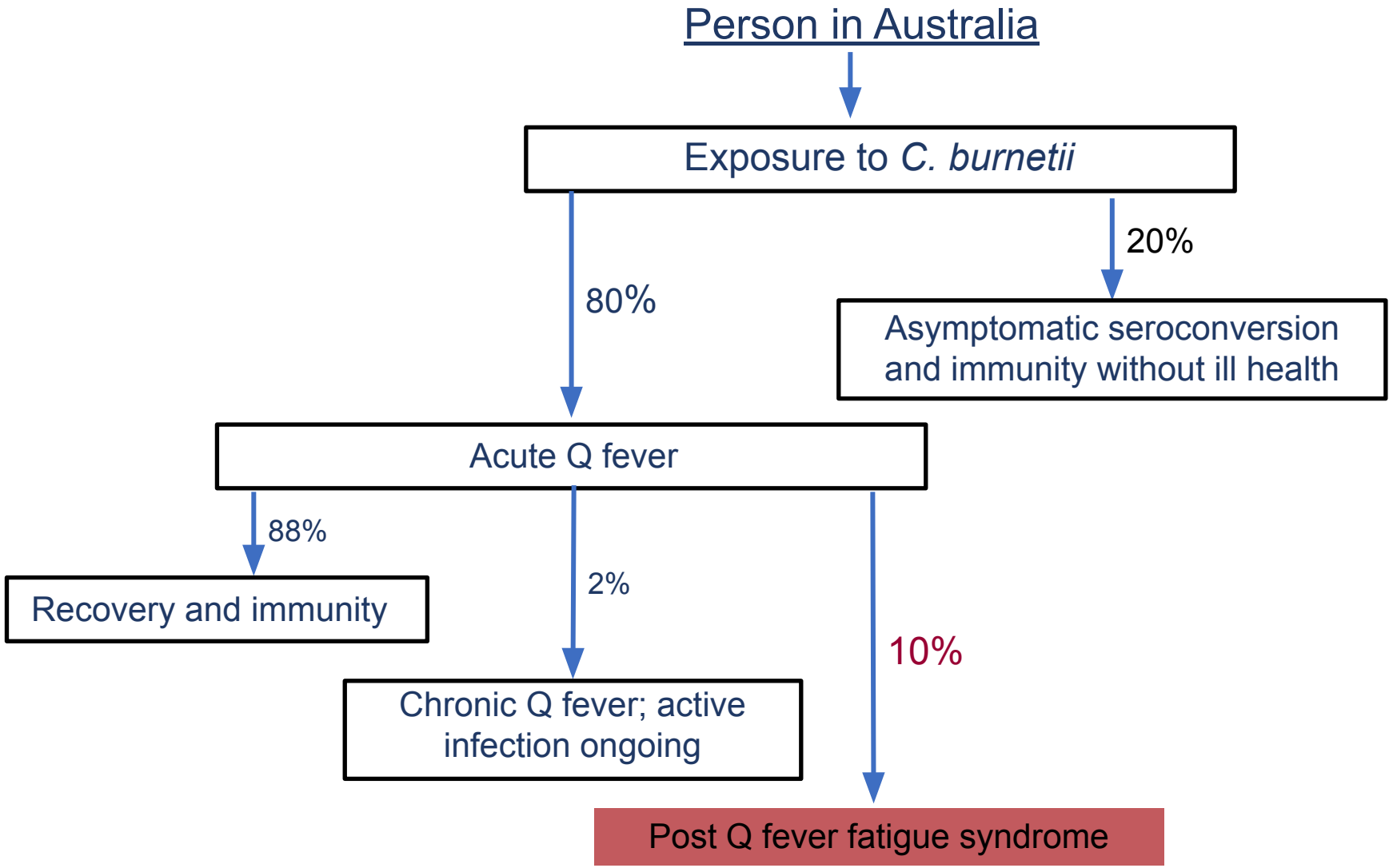
Chronic (focal, persistent) Q fever

Occurs months to years after the initial infection (which may have been mild or even asymptomatic)

Due to persistence of a focus of viable C. burnetii somewhere in the patient's body, due to inadequate immune response or inadequate antibiotic therapy. The bacteria start growing again later.

Clinical features

- Gradual onset of increasing poor health in patient
- Endocarditis, cardiac failure (especially with infected artificial valve)
- Vasculitis (especially if aneurysm or vascular prosthesis present)
- Osteomyelitis, discitis
- Hepatitis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Post Q fever fatigue

- Occurs in approx. 10% of persons who are infected with *C. burnetii*
- A chronic fatigue syndrome that is present 12 months after acute Q fever onset
- Very debilitating,
  - often in hard-working, conscientious patients who are very keen to get well and get on with their lives
- **NOT** like the “classic” CFS patient who has been unwell for years

Laboratory Diagnosis of Q fever

First week of acute illness

- Molecular (PCR) (EDTA blood) positive but serology (serum antibody) negative

Second week of acute illness

- Request both PCR and serology, as either may be positive or negative

Third week (and later) of acute illness

- Serology positive but PCR negative

Prevention of Q fever

- Reduce exposure to infected/carrier animals and contaminated environments
- Respiratory protection (e.g. N95 marks)
- **Vaccination** (Q-VAX®)

Vaccination against Q fever with Q-VAX®

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- Q-VAX® is a **whole cell, killed** vaccine
- Comprises the Herzerling (Italian) strain of *Coxiella burnetii*
- Made by Seqirus (part of CSL) in Melbourne
- Only available in Australia (since 1989)
- Very effective vaccine
  - 95-99% protective
  - only a few known vaccine failures (10 in 20 years in Victoria)
- Dosage: 0.5 ml (25 µg) Q-VAX injected subcutaneously
- Immunity takes 2/52 to develop. Recommend patient is NOT exposed to *Coxiella burnetii* in this interim period as they are not yet immune and may get Q fever

Pre-testing patient before administering Q-VAX®

- Very safe if given to persons without prior contact with *Coxiella burnetii*
- Must screen patients (skin test and serology) before vaccination

On Day 7 after pre-testing:

Positive Serology	✗	Don't vaccinate
Positive Skin Test*	✗	Don't vaccinate
Negative Serology **and** Negative Skin Test	✓	Vaccinate

* Any induration in skin at inoculation site is positive, but ignore colour changes.

Thus, Q-VAX® more difficult to use than most vaccines

Adverse events reported after administering Q-VAX®

A range of adverse reactions have been reported with clinical use of Q-VAX® as outlined in the table:

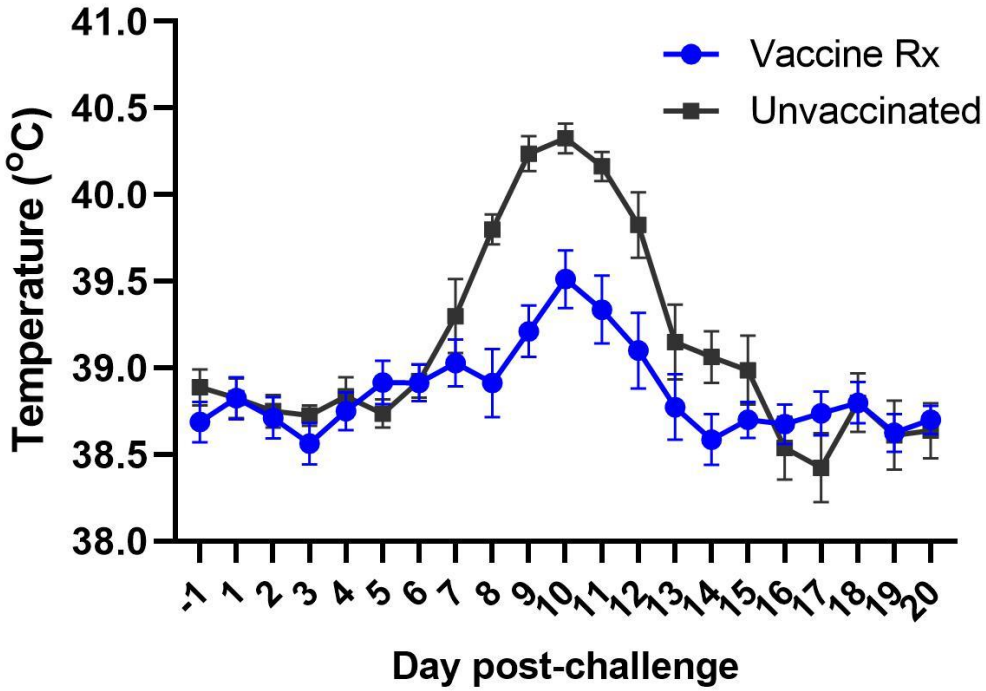
Frequency of adverse event	Adverse event
Very common (≥ 1/10)	• Injection site inflammation (e.g. erythema, pain, warmth and swelling)
Common (<1/10 and and ≥ 1/100)	• Headache • Delayed skin reaction (presenting up to 6 months after vaccination) at injection site (either vaccination and/or skin test site)
Uncommon (<1/100 and ≥ 1/1000)	• Nausea, vomiting and diarrhoea • Hyperhidrosis • Myalgia • Injection site induration and/or oedema, pyrexia, malaise, fatigue
Rare (<1/1000 and ≥ 1/10000)	• Injection site abscess formation, granuloma
Very rare (<1/10 000)	• Lymphadenopathy • Dizziness • Arthralgia • Chills, chronic fatigue syndrome

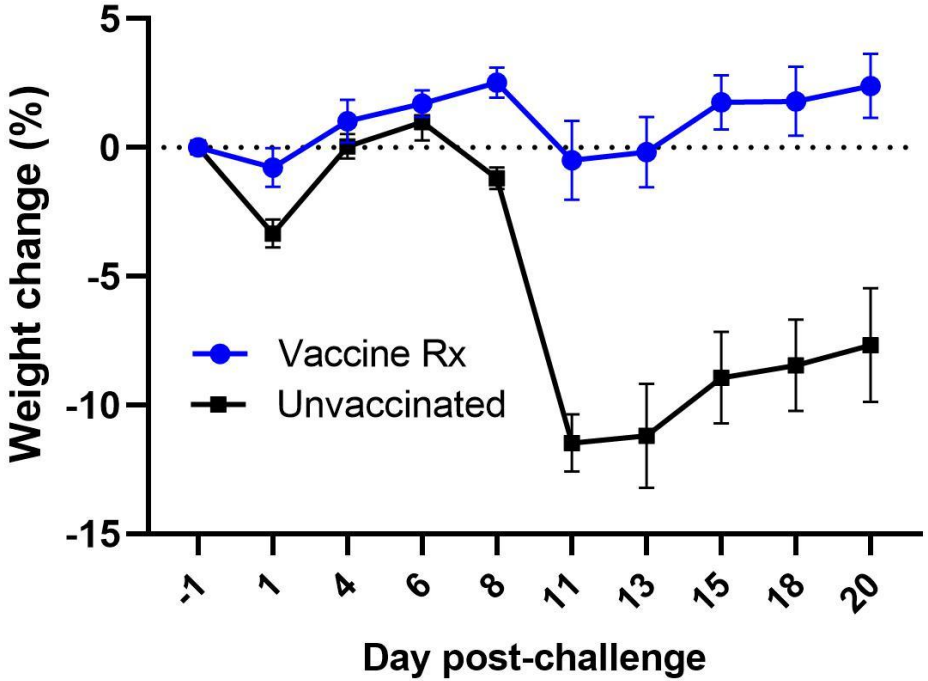
Adverse reactions that may occur in subjects with pre-existing immunity include:

- intensified local reaction at injection site shortly after vaccination. Rarely, an abscess develops and requires drainage.

A new human vaccine against Q fever

New Q fever vaccine tested in guinea pigs





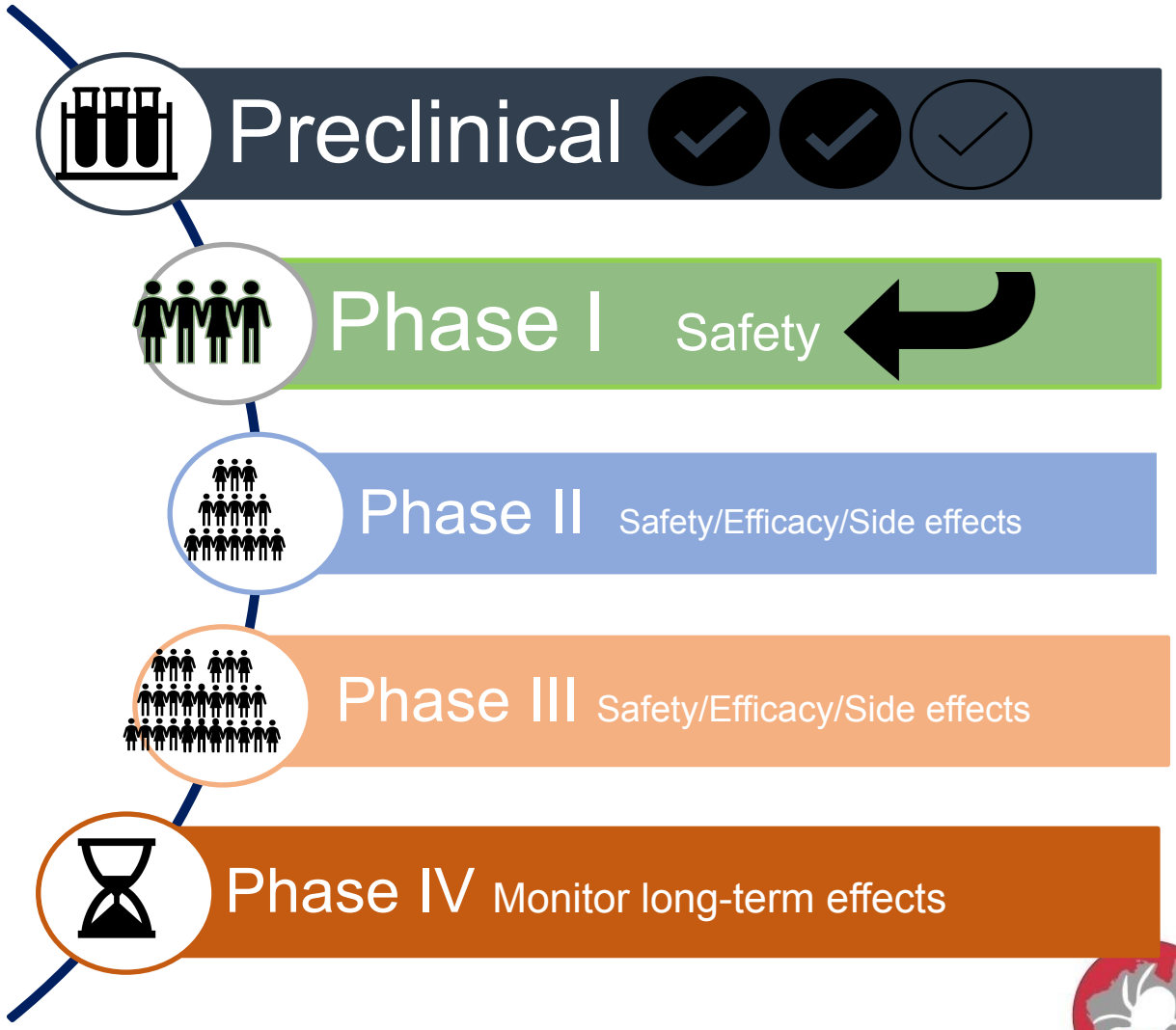
Average 3.9 febrile days (Unvacc.) vs 0.7 febrile days (Vaccine Rx)

Next steps

- Test whether additional doses of vaccine (2 or 3) will improve protection
- Test whether the vaccine is reactogenic in immune guinea pigs

- **Will the vaccine provide protection in humans?**

  → Phase 1 trial needed



Thank you for your attention

Thanks to DMTC for funding towards the development of this vaccine.