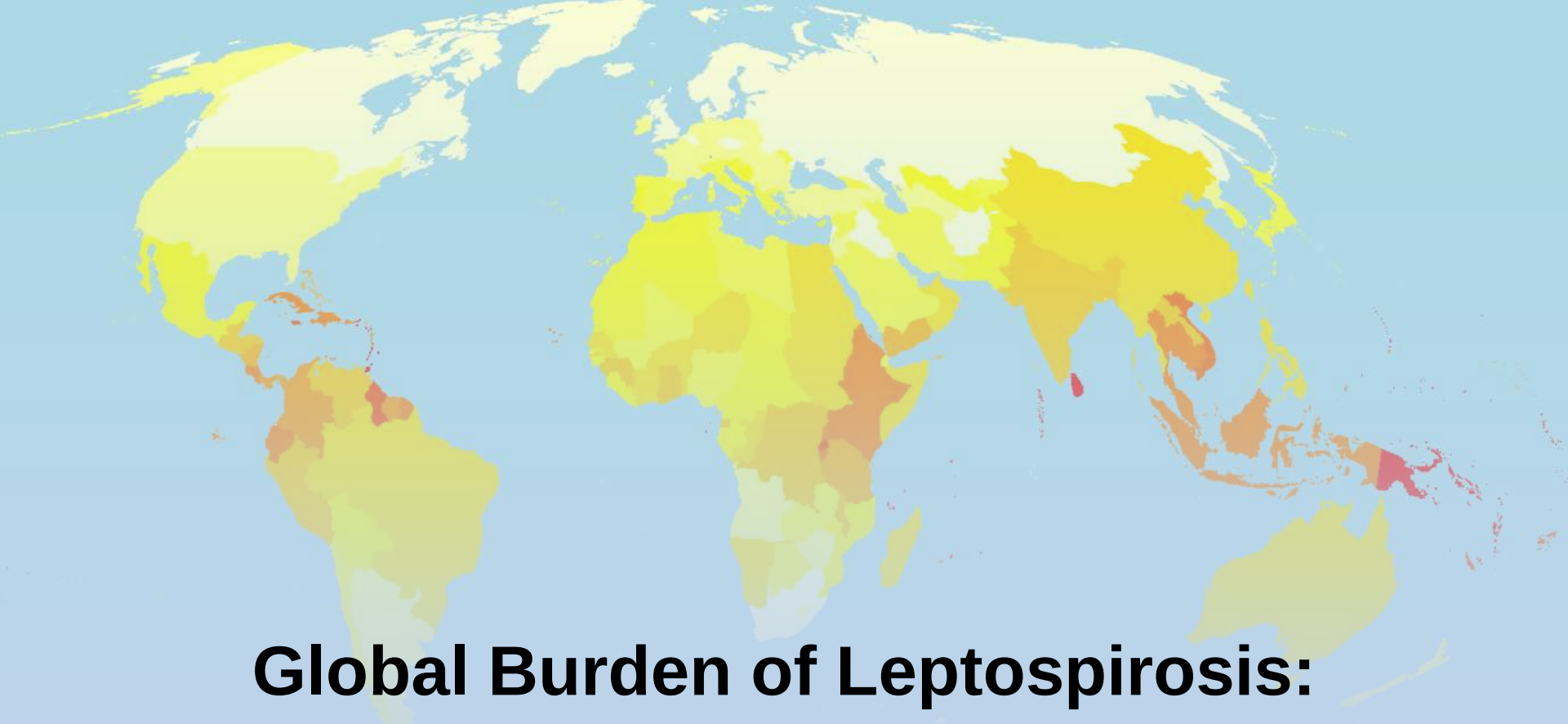

Global Burden of Leptospirosis: Morbidity, Mortality and DALYs

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Global Burden of Disease Study for Leptospirosis: Rationale

- The problem: Leptospirosis is a major, yet under recognized public health problem.
- The solution: Leptospirosis is preventable and treatable
- The plan: Establish accurate estimates of disease burden to compare with other zooonosis and better direct adequate intervention, control and prevention efforts.

Leptospirosis Epidemiology Reference Group

http://www.who.int/zoonoses/diseases/lerg/en

Challenges in Estimating the Burden of Leptospirosis

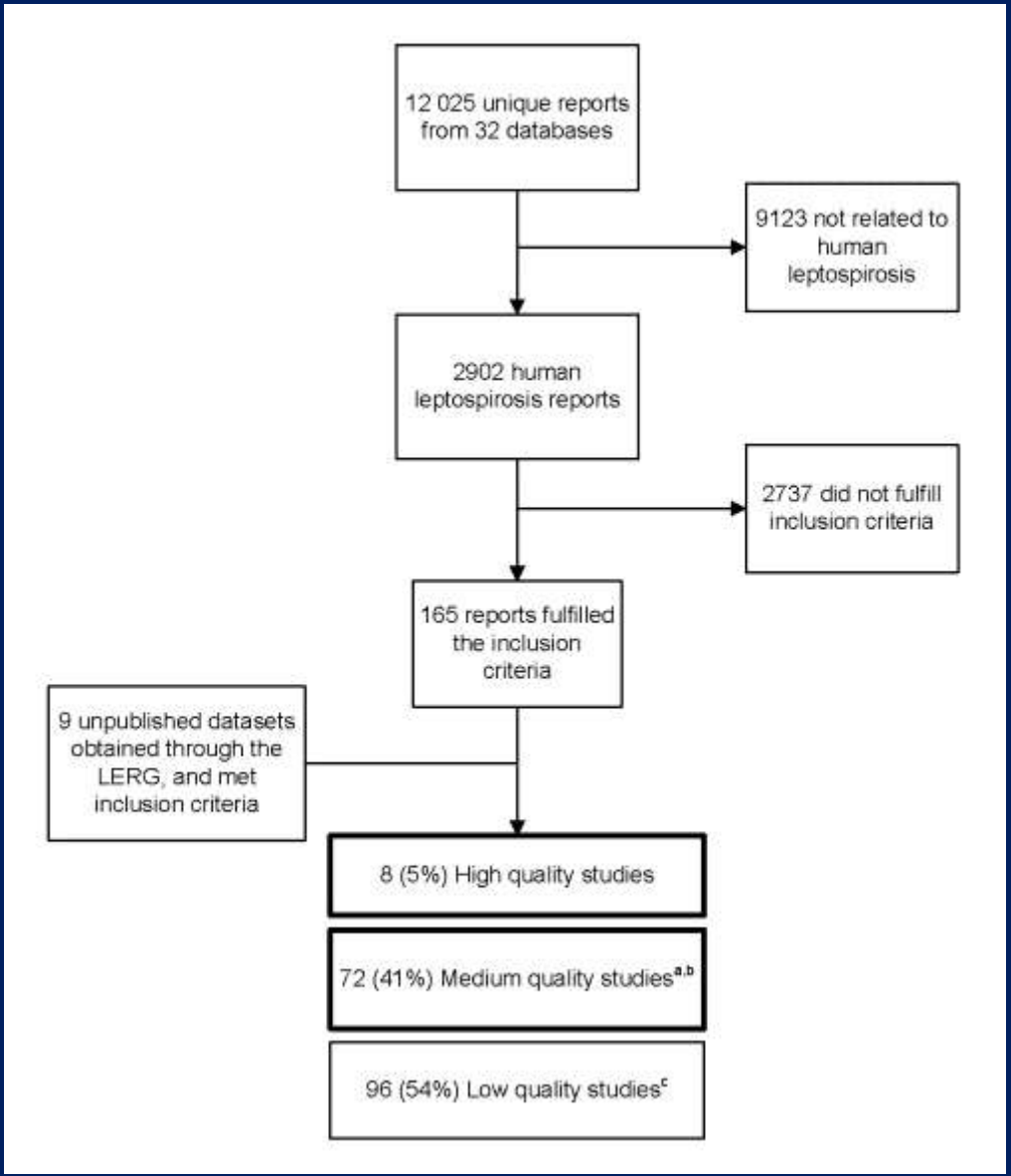
- Epidemiology is highly variable
  - Transmission patterns
  - Agent
  - Geographical region
  - Risk groups and exposures
- Sparse data and lack of prospective population-based studies
- Under-reporting and bias
  - Barriers to laboratory confirmation
  - Few studies in geographical regions and poorest countries

Overview of Approach

1. Perform systematic review, quality assessment and data extraction
2. Explore sources of heterogeneity, risk stratified by age/gender, potential under-reporting
3. Model incidence and mortality at country level
   - Adjust estimates for age/gender distribution
   - Address under-reporting due to incomplete laboratory confirmation
4. Obtain global and regional estimates of mortality and morbidity
5. We estimated country, regional and global DALYs (Disability Adjusted Life Years)

1. Systematic Review and Quality assessment

- Systematic review
  - Morbidity, mortality, case fatality, different morbidity conditions from 1970-2008
- Data sources
  - 32 electronic databases of published literature
  - 9 databases from unreported population-based studies
- Applied inclusion and quality assessment criteria
- Approach approved by LERG



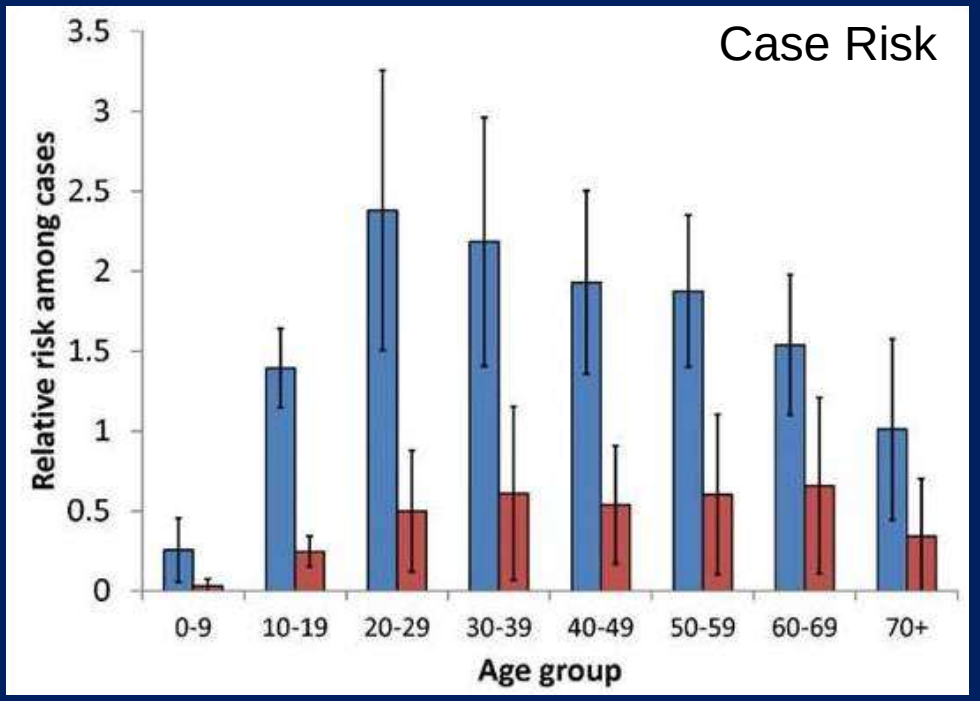
2. Sources of Heterogeneity

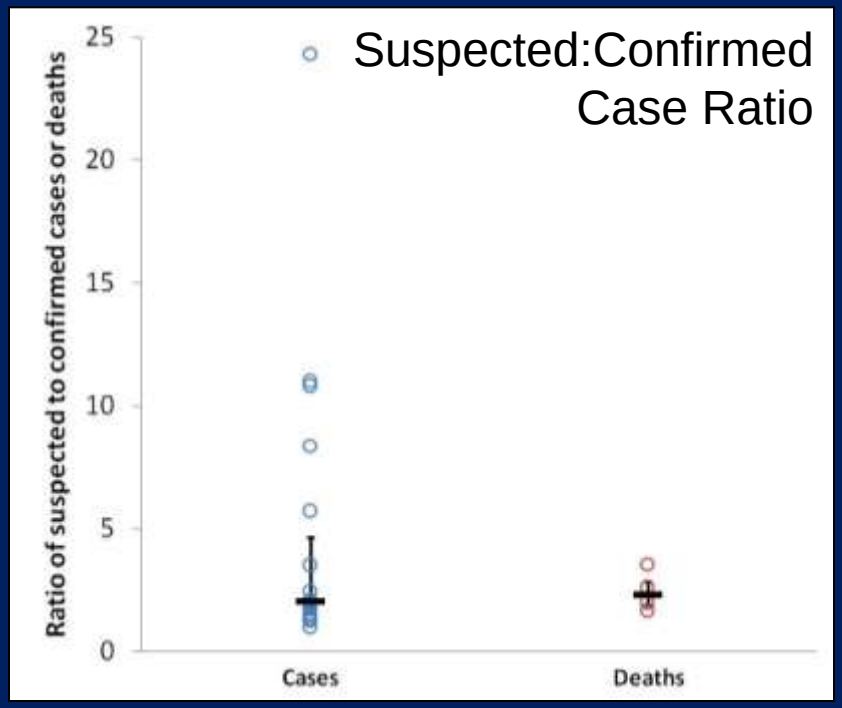
Reported Crude Incidence and Mortality

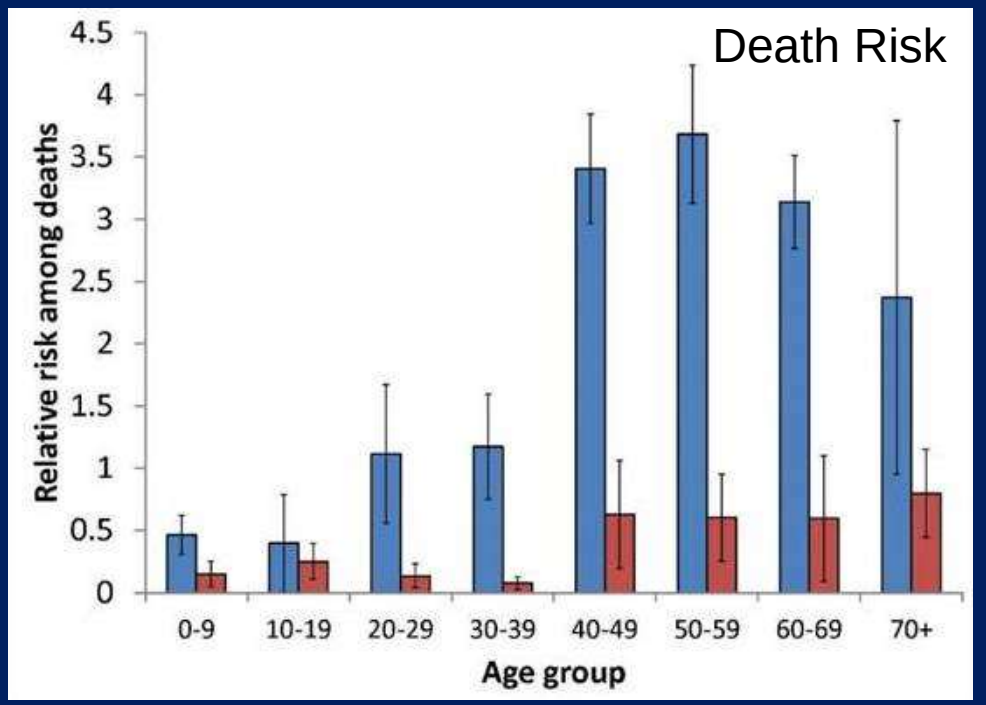
Characteristic	Incidence (N=80)		Mortality (N=35)		Case fatality (N=35)	
	N (%)	Median (IQR)	N (%)	Median (IQR)	N (%)	Median (IQR)
Decade						
1970-1979	9 (11)	6.25 (1.80 – 11.75)	4 (11)	1.34 (0.38 – 2.75)	4 (11)	7.31 (5.62 – 10.17)
1980-1989	19 (24)	12.41 (0.84 – 47.69)	8 (23)	1.27 (0.15 – 2.07)	8 (25)	5.81 (3.68 – 9.60)
1990-1999	26 (33)	3.11 (1.03 – 10.18)	13 (37)	0.15 (0.09 – 0.40)	13 (36)	8.00 (4.80 – 14.29)
2000-2009	26 (33)	4.95 (0.90 – 32.56)	10 (29)	0.15 (0 – 1.07)	10 (28)	0.64 (0.09 – 5.87)
Surveillance						
Active	28 (35)	**12.09 (4.66 – 57.91)**	16 (45)	**0.77 (0.31 – 1.79)**	16 (45)	4.99 (1.37 – 8.01)
Passive	52 (65)	2.13 (0.60 – 12.71)	19 (55)	0.15 (0.06 – 0.49)	19 (55)	6.59 (1.96 – 13.10)
Climate						
Tropical	50 (63)	**12.91 (6.26 – 52.15)**	26 (74)	**0.66 (0.02 – 1.71)**	26 (74)	4.99 (0.99 – 8.03)
Temperate	30 (38)	0.65 (0.37 – 1.88)	9(26)	0.06 (0.23 – 0.09)	9(26)	10.70 (6.59 – 11.90)
Setting						
Rural	7 (9)	**39.85 (20.27 – 287.99)**	4 (11)	0.18 (0 – 0.68)	4 (11)	0.24 (0 – 1.56)
Urban	14 (18)	9.59 (3.00 – 28.20)	4 (11)	0.66 (0.51 – 0.73)	4 (11)	3.58 (1.88 – 5.71)
Mixed	59 (74)	3.02 (0.60 – 12.91)	27 (78)	0.34 (0.09 – 1.69)	27 (78)	8.00 (3.26 – 11.77)

2. Descriptive Analyses

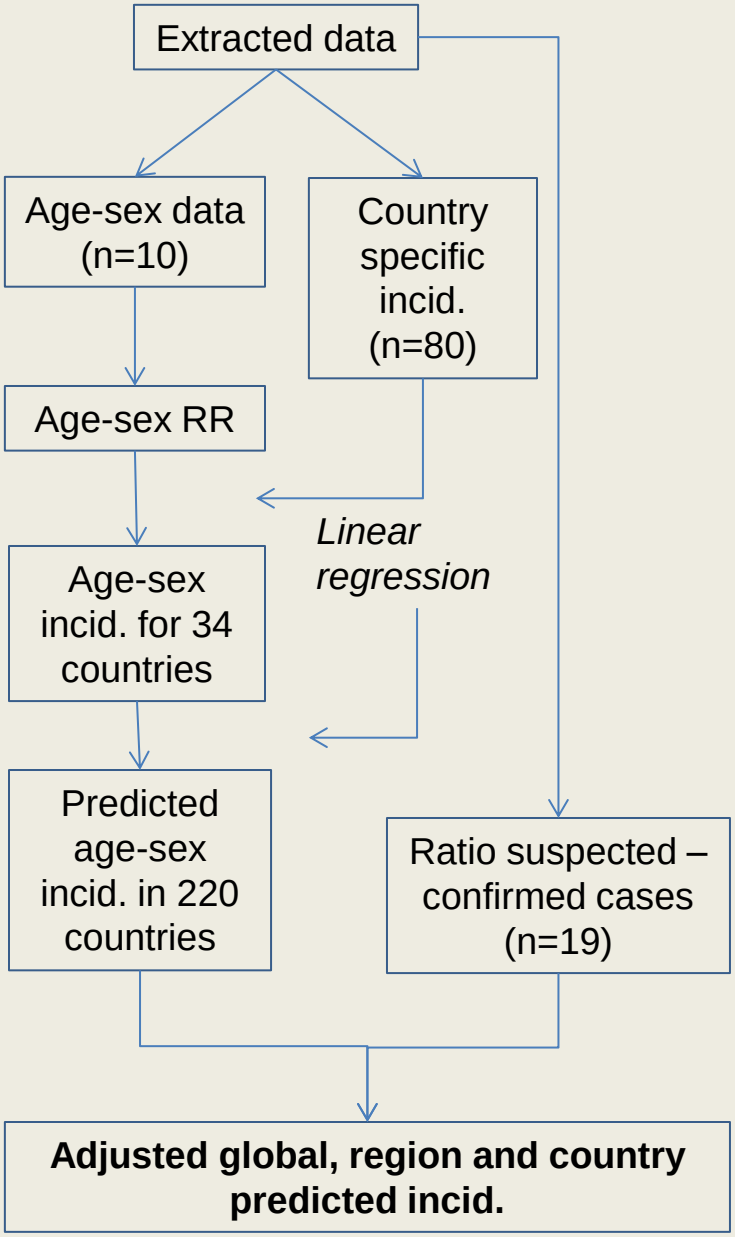
- Age/gender-specific risk
  - 10 studies with morbidity data
  - 3 studies with case fatality data
- Under-reporting
  - Suspected vs confirmed cases
  - 19 morbidity studies
  - 4 mortality studies







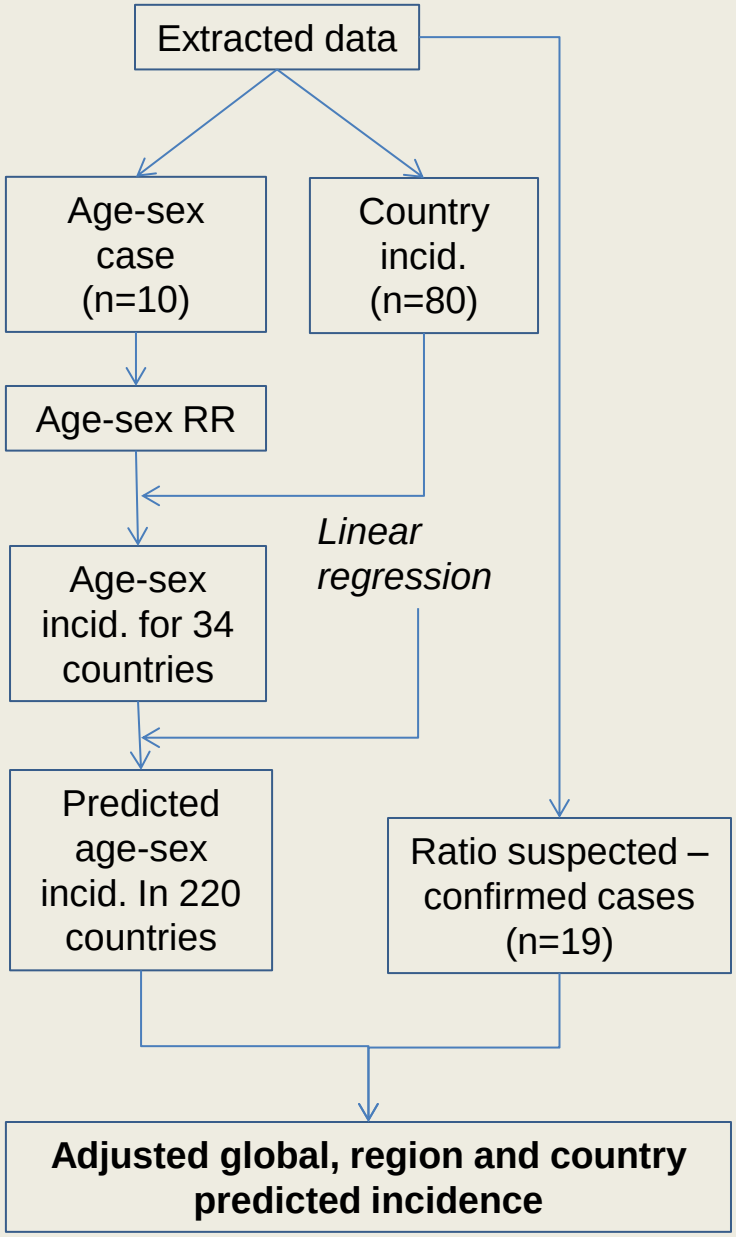
3. Modeling Approach for Estimating Morbidity

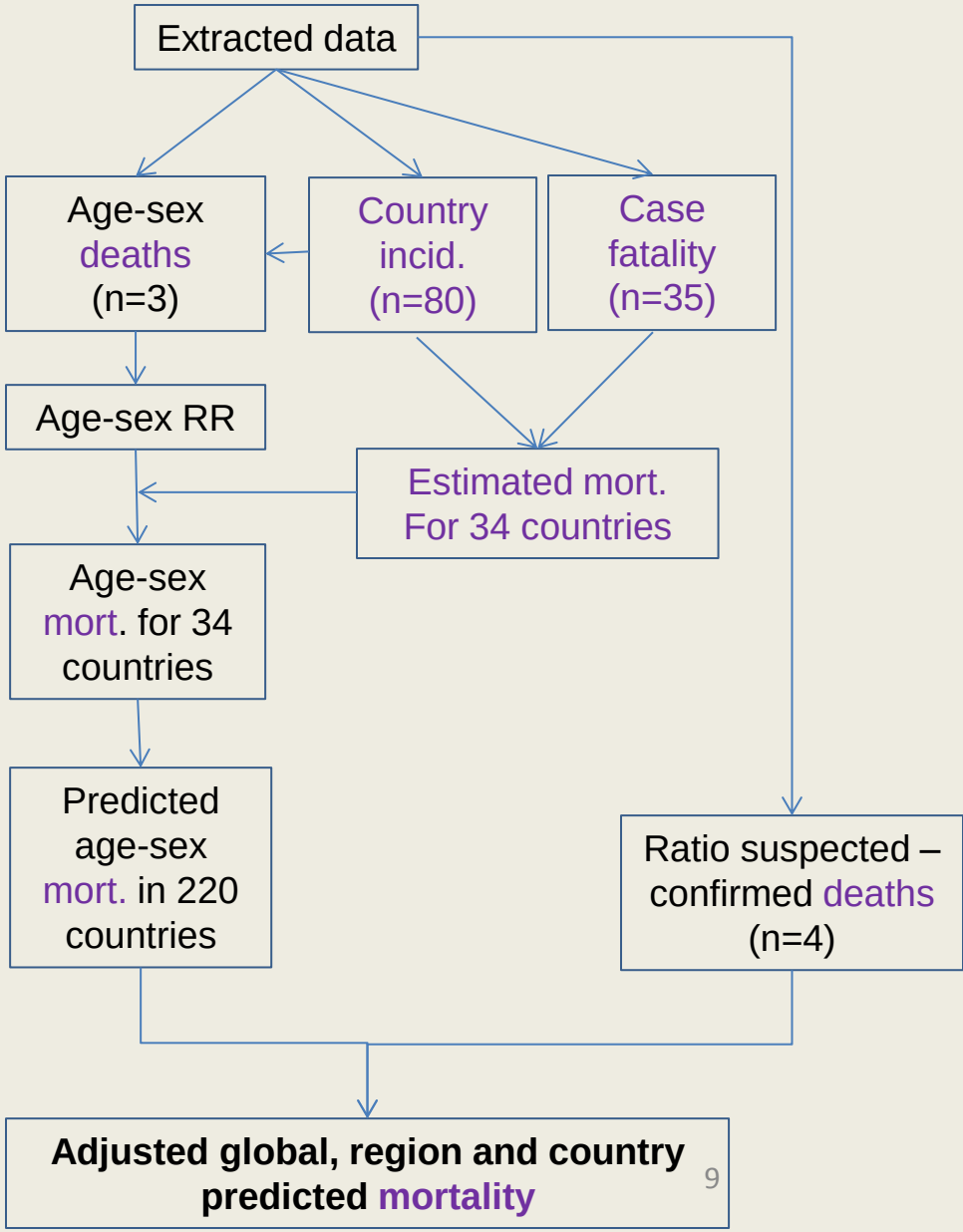


Linear regression model to predict age- and gender-specific incidence and mortality in 220 countries

Variable	R Squared
Distance from the equator	0.105
% urbanization of population	0.243
Life expectancy at birth	0.405
Tropical island	0.478
Complete model	0.600

3. Modeling Approach for Estimating Mortality





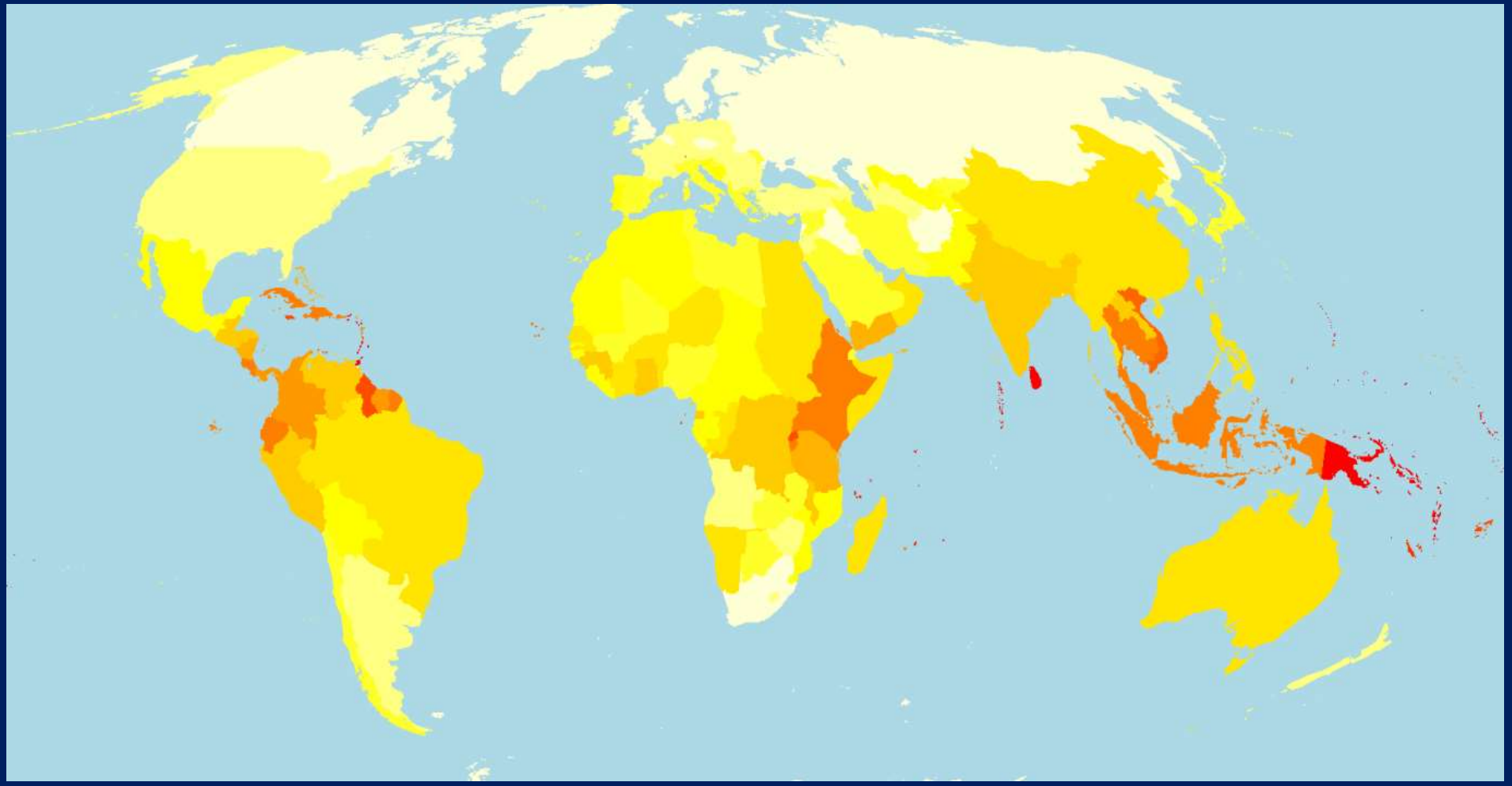
4. Global Estimates of Morbidity and Mortality

Region	Annual Morbidity*	Cases	Deaths
Worldwide	14.77 (4.38-25.03)	1,030,000 (305000-1750000)	58,900 (23800-95800)
Sub S.Africa	22.15 (8.29-37.56)	99,500 (37200-169000)	7600 (3100-12100)
Caribbean	22.33 (7.51-37.87)	18,700 (6300-31700)	900 (300-1500)
SE Asia	56.06 (19.72-99.06)	181,000 (63600-319000)	10 200 (4200-17400)
SE Asia	19.06 (6.53-34.36)	283,000 (97000-510000)	16 100 (5600-27200)
Oceania	14.36 (5.09-24.49)	241,000 (85400-411000)	11 400 (4600-19300)

* Cases per 100,000 population

- Adult males with age 20-49 years of age accounted for 48% (95% CI, 40 – 61%) and 42% (95% CI, 34 – 53%) of the predicted annual cases and deaths worldwide, respectively
- 73% cases occur between Tropic of Cancer and Capricorn

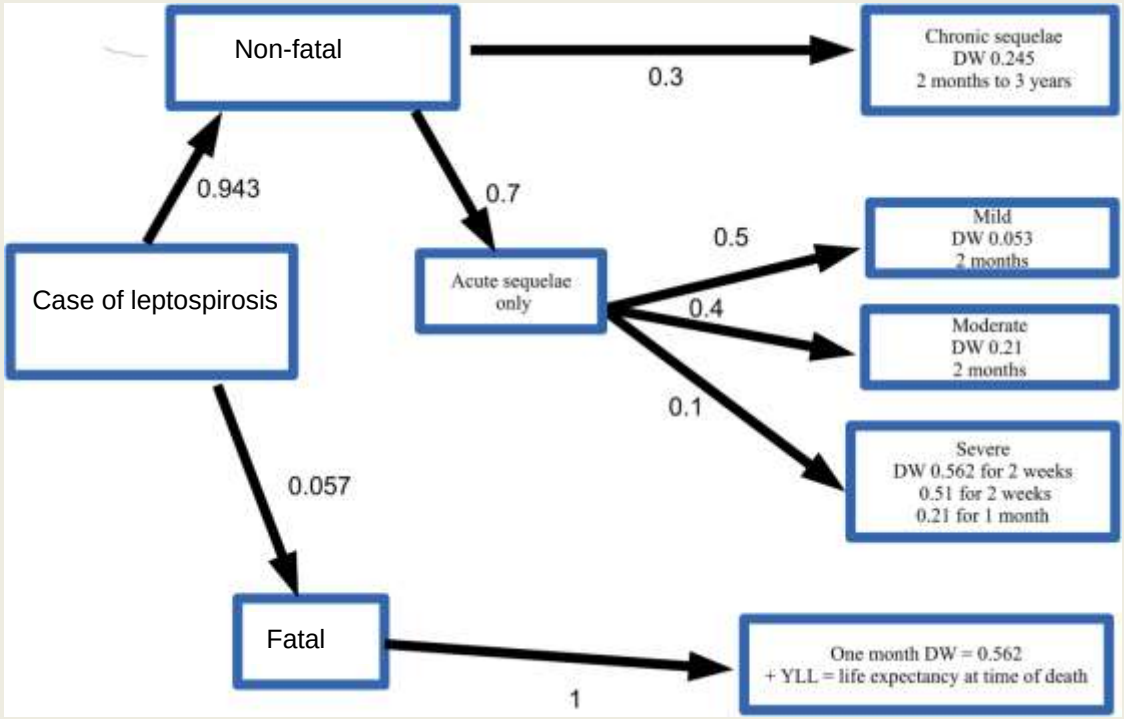
4. Global Estimates of Morbidity and Mortality



Annual disease incidence is represented as an exponential colour gradient from white (0-3), yellow (7-10), orange (20-25) to red (over 100), in cases per 100 000 population.

5. Approach for Estimating DALYs

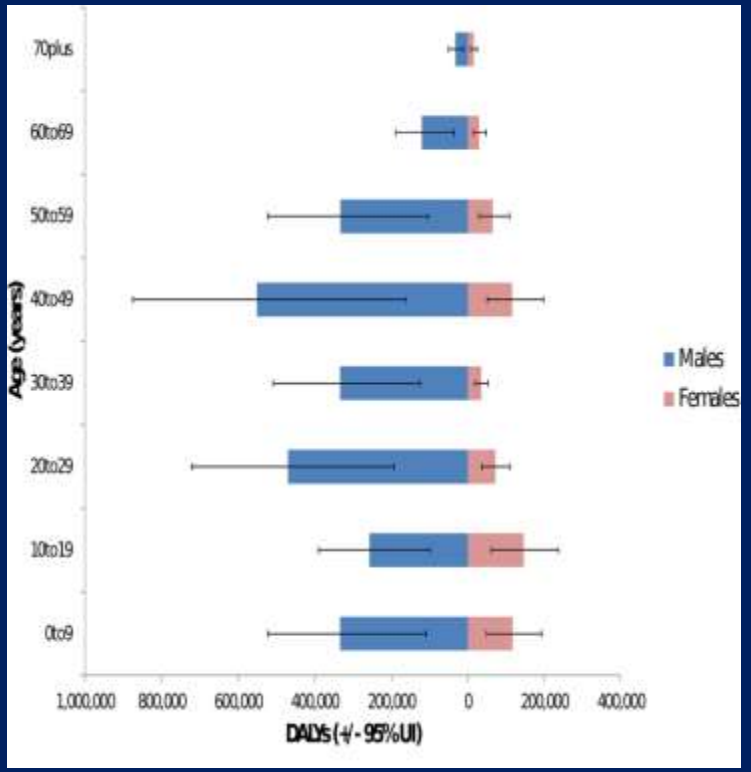
- YLL
  - Mortality from SR
- YLD
  - Incidence from SR
    - Dialysis
    - Infection
    - Uveitis



DW: Disability weight

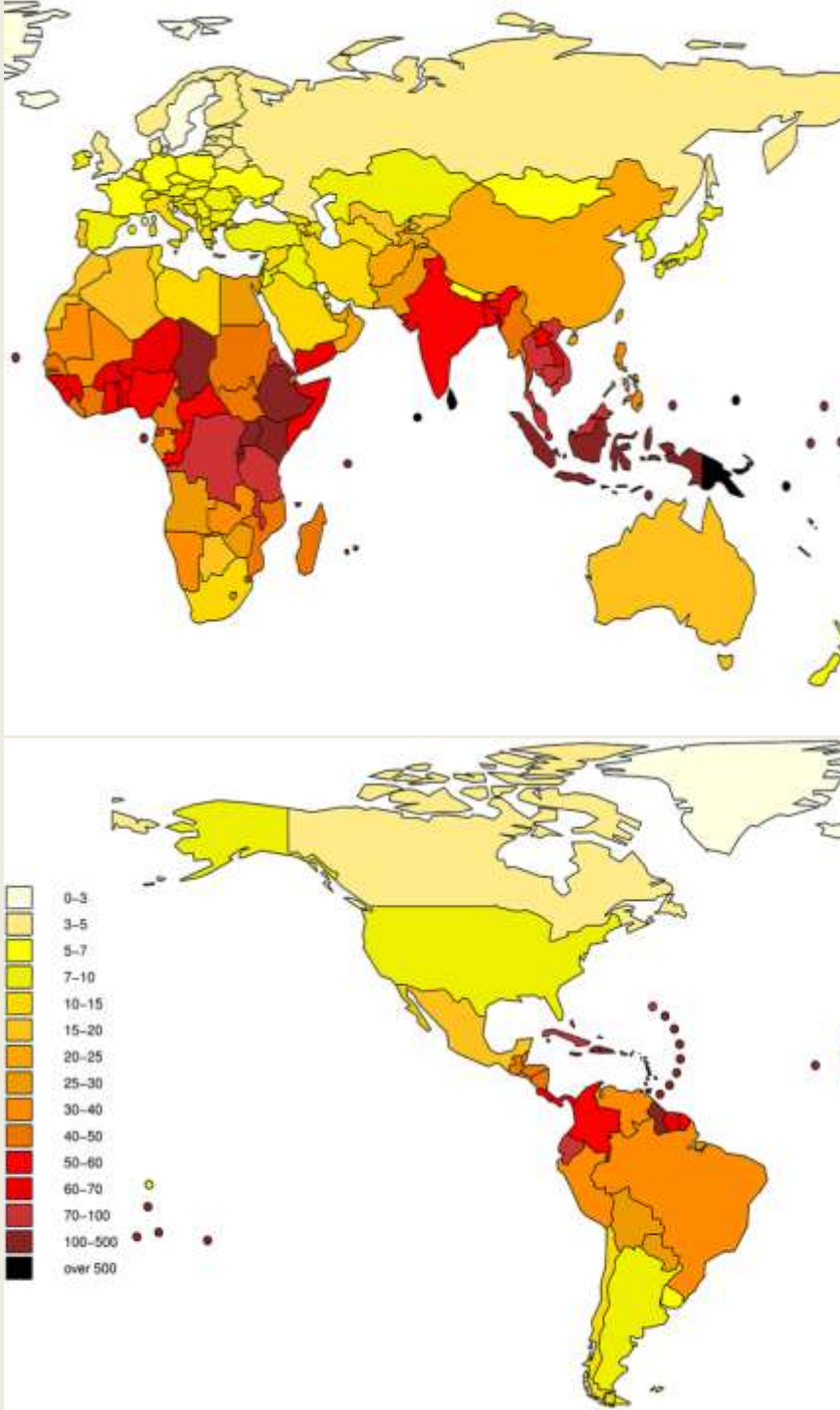
5. Global Estimates of DALYs

- **2.90 million DALYs** are lost per annum (UIs 1.25–4.54 million)
  - 2.80 million YLLs (1.16 – 4.46 million). 96.5% of the DALYs
  - 103,200 YLDs (38,800–188,100).
- **Males** account approximately **80%** of the total burden



5. Annual burden of disease by GBD region.

GBD region	DALYs/100,000
Asia Pacific	12 (5.2-20)
Central Asia	14 (5-22)
East Asia	22 (8.7-38)
South Asia	50 (18-88)
South East Asia	137 (58-224)
Australasia	16 (6.4-28)
Caribbean	127 (52-203)
Andean L. America	46 (18-81)
Central L. America	33 (13-54)
Tropical Latin America	31 (12-54)
North Africa	18 (7.4-28)
Oceania	515 (196-879)
Central Sub-S. Africa	78(30-133)
Eastern Sub-S. Africa	106 (42-168)
Southern Sub-S. Africa	18 (7.4-28)
Western Sub-S.Africa	48 (18-75)



Limitations

- Sparse quality-assured data and poor representative information in some regions
  - ➢ Model captured a significant degree of the variability
- Mortality data was incomplete and was modeled using incidence and case fatality
- Global mean estimates were used for case fatality and age/gender risk
- Data were hospital-based, therefore estimates do not include less severe disease
- Sequela data was incomplete and from developed countries and may introduce uncertainty in the YLD
  - ➢ YLD was less than 5% of the total burden
- With all global BoD studies, country-level estimates associated with uncertainty and should be interpreted with caution

Discussion

- Incidence consistent with prior qualitative estimates
- Morbidity, mortality and DALYs comparable or greater than observed for other diseases
  - Similar number of deaths than canine rabies (59,000)
  - 70% of the global burden of cholera (DALYs)
- Greatest burden in the poorest countries from tropical regions
- Large effect of under-reporting due to incomplete laboratory confirmation
- Highest risk occurs in young adult males
- Predicted high burden regions such as Africa, where surveillance and research have traditionally neglected leptospirosis and there is little data

Future Directions

- Validate findings with regional or national burden of disease studies
- Establish or improve surveillance in regions with high predicted burden of disease
- Urgent need to address under-reporting and barriers to laboratory confirmation.
- Population-based studies to estimate burden at community level

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- Fiocruz
- GLEAN

The global burden of leptospirosis and the top seven listed neglected tropical diseases

Diseases	Number of Cases	Deaths	DALYs (millions)
Intestinal nematodes	1,723 million	2,700	5.19
Leishmaniasis	10 million	51,600	3.32
Schistosomiasis	252 million	11,700	3.31
Leptospirosis*	1 million	**58,900**	2.90
Lymphatic filariasis	36 million	-	2.78
Food-borne trematodiasis	16 million	-	1.88
Rabies	1,100	26,400	1.46
Dengue	179,000**	14,700	0.83