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MECHANISTIC AND STATISTICAL MODELS OF SKIN DISEASE TRANSMISSION

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At any one time, more than 160 million children worldwide are infected with skin sores. In remote Aboriginal Australian communities, prevalence is as high as 40%. Skin sores infected with Group A *Streptococcus* (GAS) can lead to a number of acute and chronic health conditions. One of the primary risk factors for GAS infection is scabies, a small mite which causes a break in the skin layer, potentially allowing skin sore infection to take hold. This biological connection is reaffirmed by the observation that mass treatment for scabies in these remote communities has been associated with a reduction in the prevalence of skin sore infection, despite skin sores not being directly targeted. In the most extreme case, it has been hypothesised that the eradication of scabies in remote communities may lead to an eradication of skin sore related infection. Mass drug administration (MDA) is the go-to solution for tackling the high prevalence of disease in these rural settings, but, despite more than 20 years of implementation, sustained reductions in prevalence have not been achieved.

My aim in this thesis is to develop and analyse both mechanistic and statistical models of skin sores and scabies, considering the dynamics of each disease in isolation and coupled together. These models build a framework on which control strategies can be tested, with the aim to develop strategies that will lead to sustained prevalence reductions.

Following a biological introduction and technical information (Chapters 1 and 2), a mechanistic model for scabies infection is introduced. This model includes the dynamics of the life-cycle of the scabies mite, incorporating two methods of treatment for the infection. Mass drug administration strategies are also modelled. The optimal interval between successive MDA doses is calculated to be approximately two weeks.

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The analysis shows that an optimally timed two-dose, 100% effective, 100% coverage MDA is highly unlikely to lead to the eradication of scabies. In fact, four optimally timed successive doses are required for a probability of eradication greater than 1/1000. Next, an annually recurring MDA program is considered, in which some number of optimally timed doses is administered and repeated annually. It is shown that increasing the number of administered doses always increases the probability of eradication. Importantly, moving from a two-dose to a three-dose annual strategy significantly increases the probability of eradication of scabies infection [3].

In order to parameterise a dynamic transmission model for skin sores, at least two key quantities must be estimated: the force of infection and the infectious period. The study in Chapter 4 estimates the age of first infection, which is the inverse of the force of infection, using clinic presentation data of children from birth up to five years. Three survival models are considered: the Kaplan–Meier estimator, the Cox proportional hazards model and the parametric exponential mixture model. The mean age of first infection is estimated to be approximately 10 months for skin sores and nine months for scabies [1]. The work in Chapter 5 estimates both the force of infection and the infectious period by utilising a linearised infectious disease model. The data considered in this chapter consists of longitudinal observations of individuals across three studies. The methodology is verified using simulation estimation and each dataset tested to ensure that it carries sufficient information for use with the estimation method. The estimates for the force of infection vary by an order of magnitude between settings. Estimates of the infectious period are relatively constant at 12–20 days [2].

Chapter 6 consists of a dynamic model for skin sores transmission coupled with models for scabies transmission. Three different scabies models are considered. The first assumes that the dynamics of scabies are at equilibrium. In this case, analytical expressions for key epidemiological quantities can be derived and values for the scabies prevalence below which skin sores will be eradicated can be calculated. Next, two dynamic models of scabies are considered. The first of these is the scabies model introduced in Chapter 3, which includes the full life-cycle of the scabies mite and treatment mechanisms. The second model consists of just three compartments, which is termed the SITS model. The SITS model approximates the complex life-cycle of the scabies mite into two compartments, with the third model compartment being susceptible individuals. The differences in dynamics between these two scabies models are analysed and the impact on the prevalence of skin sores of an MDA which directly targets only scabies is considered. The comparison shows that, relative to the full model, the SITS model overestimates the impact on skin sores prevalence due to the MDA in the time period immediately following the MDA, but also predicts an earlier time of return to pre-MDA endemic infection prevalence. The SITS model also estimates a higher probability of eradication of skin sores compared to the full model. These two results demonstrate that caution should be taken when approximating the life-cycle of the scabies mite to consider the potential impact of MDA, which targets only scabies.

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Finally, Chapter 7 summarises the work presented in my thesis, discusses the limitations of the work and explores potential future directions for this research problem.

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