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Controlling infectious disease through the targeted manipulation of contact network structure

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ABSTRACT

Individuals in human and animal populations are linked through dynamic contact networks with characteristic structural features that drive the epidemiology of directly transmissible infectious diseases. Using animal movement data from the British cattle industry as an example, this analysis explores whether disease dynamics can be altered by placing targeted restrictions on contact formation to reconfigure network topology. This was accomplished using a simple network generation algorithm that combined configuration wiring with stochastic block modelling techniques to preserve the weighted in- and out-degree of individual nodes (farms) as well as key demographic characteristics of the individual network connections (movement date, livestock market, and animal production type). We then tested a control strategy based on introducing additional constraints into the network generation algorithm to prevent farms with a high in-degree from selling cattle to farms with a high out-degree as these particular network connections are predicted to have a disproportionately strong role in spreading disease. Results from simple dynamic disease simulation models predicted significantly lower endemic disease prevalences on the trade restricted networks compared to the baseline generated networks. As expected, the relative magnitude of the predicted changes in endemic prevalence was greater for diseases with short infectious periods and low transmission probabilities. Overall, our study findings demonstrate that there is significant potential for controlling multiple infectious diseases simultaneously by manipulating networks to have more epidemiologically favourable topological configurations. Further research is needed to determine whether the economic and social benefits of controlling disease can justify the costs of restricting contact formation.

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1. Introduction

Human and animal populations are susceptible to a wide range of infectious diseases that spread between individuals through everyday social interactions. Until recently, it was common practice to model these contact patterns using mass-action mixing approaches, which assume that individuals in a population all make the same number of contacts and mix homogeneously such that the probability of any two individuals forming a connection is always equal. However, it has now been well-established that the contact distribution is highly right skewed, meaning that a small number of individuals make a disproportionately large number of contacts, and that the contacts themselves organize into complex networks with particular structural features that determine how far and how fast disease can spread within the population (Keeling, 2005; Shirley and Rushton, 2005), For example, the highly right skewed contact distribution leads to the emergence of scale-free behaviour characterized by epidemic thresholds that converge to zero (Barabasi, 2009), higher basic reproduction numbers (R_0) than expected for networks with uniform degree distributions(Woolhouse et al., 2005), and greater tolerance to disease control measures that are applied at random (Albert et al., 2000). Many biological networks also display small-world properties characterized by the local clustering of contacts with the occasional long distance jumps that are responsible for spreading disease to more distant network communities (Watts and Strogatz, 1998).

From an epidemiological perspective, it has consistently been reported that removing the small number of highly connected individuals or highly central network connections is the most cost-effective means of controlling disease at the population level (Christley et al., 2005; Kiss et al., 2006; Munro and Gregory, 2009;

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Pautasso et al., 2009; Rautureau et al., 2012). There are, however, several practical limitations to this approach. First, any intervention that involves physically removing high risk individuals or contacts from the network, such as the use of school closures to mitigate influenza pandemics (Cauchemez et al., 2009), can have significant economic and social costs. It can also be difficult to identify these individuals or contacts without full knowledge of the contact network structure (Kitsak et al., 2010). Second, interventions that involve effectively removing high risk individuals or contacts from the network require there to be an effective vaccination, treatment, or quarantine protocol for the disease of interest. Many infectious diseases of cattle, for example, have a subclinical carrier state for which there are few reliable ante-mortem diagnostic tests or preventive vaccinations and for which quarantine or treatment are unlikely to prevent disease introductions (Lindberg and Alenius, 1999; de la Rua-Domenech et al., 2006; Nielsen and Toft, 2008). Furthermore, these measures are often costly and highly pathogen specific, which leads to necessary trade-offs in resource allocation. As highlighted in a recent review (Carslake et al., 2011), it is important to develop control strategies that are effective against multiple infectious diseases simultaneously.

Numerous theoretical modelling studies have shown that the transmission dynamics of many infectious diseases can be altered by modifying specific structural properties of the contact network. For example, increasing network clustering almost invariably slows epidemic spread due to the rapid depletion of local susceptible contacts (Holme and Kim, 2002; Newman, 2003; Volz et al., 2011). In assortative networks where highly connected individuals form contacts with other highly connected individuals, disease tends to spread more rapidly (Newman, 2002; Kiss et al., 2008), but the probability of extinction is greater (Nishiura et al., 2011) and fewer individuals become infected over the course of the epidemic (Badham and Stocker, 2010). Other researchers have also explored the effects of homogenizing the degree distribution (May and Lloyd, 2001; Pastor-Satorras and Vespignani, 2002; Ames et al., 2011) or introducing higher order community structures (Liu and Bambi, 2005; Salathé and Jones, 2010). However, it is difficult to determine whether these observations have practical value for disease control since the network generation models often use arbitrary rules and scaling constants to generate the desired structural properties. For example, preferential attachment has been used as a mechanism to explain scale-free degree distributions (Barabasi and Albert, 1999). In this system, the probability of a new connection forming with a node is significantly greater if the node already has other network contacts. Additional rules can be introduced to increase the likelihood that any two neighbours of a node will also form connections, thereby creating networks with specified clustering coefficients (Newman, 2001; Holme and Kim, 2002; Vazquez, 2003). In biological systems, there are inherent constraints to contact formation such as geographical distance, social preferences, and seasonality that limit the potential variation in network topology (Mahmood et al., 2010).

An alternative approach is to generate contact networks from first principles based on a sound understanding of the biological, social, and financial factors driving contact formation (Mahmood et al., 2010). Recent work has demonstrated that it is possible to replicate human mobility patterns from information on job opportunities and the assumption that individuals would seek to maximize income while minimizing commuting distance (Simini et al., 2012). In the cattle industry, high transportation costs also result in most contacts occurring over short distances. Lindström and colleagues used this principle to construct theoretical cattle networks where the probability of contact formation was modelled as a function distance between herds and the demographic characteristics of the farm (Lindström et al., 2009, 2011, 2013). Stochastic block modelling, where farms are assigned into groups and contacts generated based on the probability that any two farms within a group or between groups will form a contact (Karrer and Newman, 2011), was used successfully to generate contact networks with spatial clustering to describe transmission pathways for the 2007 equine influenza outbreak in Australia (Firestone et al., 2011). However, both approaches ignored the timing of movements and the latter study ignored the production characteristics of the farm, which are important constraints to contact formation in livestock populations (Bajardi et al., 2011; Holme and Saramäki, 2012).

In this analysis, we first present a novel framework for generating contact networks from first principles that uses configuration wiring (Serrano and Boguna, 2005) to preserve the number of contacts made by individuals and stochastic block modelling (Karrer and Newman, 2011) to preserve important demographic features of the network connections. Movement data from the British cattle industry is used for illustrative purposes. Cattle farms are highly constrained in the number of animals that must be bought or sold each year to meet production needs and contacts can only form between farms that are trading the same production type of cattle through the same livestock markets at the same time of year. We then show how the basic network generation algorithm can be modified to test control strategies that minimize the probability of forming contacts with a disproportionately strong risk of spreading disease through the network. Our results are used to the highlight the potential for controlling infectious disease in human and animal populations by intentionally engineering contact networks to have more epidemiologically favourable structural features.

2. Materials and methods

2.1. Cattle movement data

Records of the births, deaths, and movements of individual cattle in Great Britain have been stored in the electronic Cattle Tracing System (CTS) database operated by the British Cattle Movement Service (BCMS) since 1998 (Mitchell et al., 2005). This database was created under European Union Council Regulation (EC) No 820/97 as part of larger efforts to restore consumer confidence in the safety of livestock products following the bovine spongiform encephalopathy (BSE) crisis in 1996 and has provided researchers with an unprecedented opportunity to generate detailed network representations of industry contact patterns (Kao et al., 2006; Green et al., 2008; Keeling et al., 2010; Tinsley et al., 2012). Each movement record contains basic information on the animal identification number, the departure location type and identification number, the destination location type and identification number, and the movement date. This may be linked with demographic information for each animal (including the sex, breed, birth date, death date, and any previously or subsequently recorded calvings) to infer its production purpose at the time of movement (Gates, 2014).

An extract of the CTS database containing all known records through April 2010 was provided by the Department for Environment, Food, and Rural Affairs (DEFRA). This analysis focused on the subset of all individual beef and dairy cattle movements between locations classified as agricultural holdings, landless keepers (farmers that raise cattle on rented land), and livestock markets during the 2006 calendar year. The reason for selecting this year was so that sufficient pre- and post-movement data was available to classify animals into production groups at the time of movement. As the primary focus of this analysis was on the spread of disease through livestock trade, we excluded movements to locations classified as abattoirs, showgrounds, and artificial insemination centres. Movements to abattoirs represent a dead end for disease transmission, while small number of movements to showgrounds and artificial insemination centres (less than 0.5% of all individual cattle

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