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Review

Epidemics on dynamic networks

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ABSTRACT

In many populations, the patterns of potentially infectious contacts are transients that can be described as a network with dynamic links. The relative timescales of link and contagion dynamics and the characteristics that drive their tempos can lead to important differences to the static case. Here, we propose some essential nomenclature for their analysis, and then review the relevant literature. We describe recent advances in they apply to infection processes, considering all of the methods used to record, measure and analyse them, and their implications for disease transmission. Finally, we outline some key challenges and opportunities in the field.

1. Introduction

Mathematical modelling of infectious disease transmission has seen a steady march toward the use of more powerful and flexible methods. Early models concentrated on understanding the relationship between epidemiological parameters (transmission rates, infectious periods, etc.) and simple measures of epidemic success such as the basic reproduction number of the disease, or the final epidemic size (Hethcote, 2009). Control of disease was often considered in terms of the impact of measures applied to proportions of the population (“how many should be vaccinated?”), or universal reductions of transmission across the entire population (“how protective must a vaccine be?”). While there has long been a recognition that some individuals may be more important than others for the purposes of transmission and therefore control (Hethcote and Yorke, 1984; Rocha et al., 2011; Galvani and May, 2005), a full consideration of the often profound effect of heterogeneous contact structure on infectious disease dynamics has really only become widespread more recently, and especially since the adoption of methods often originally conceived in the context of social network analysis (Wasserman and Faust, 1994).

In “traditional” compartmental models of disease transmission, individuals are assumed to belong to large populations, possibly subdivided into groups with different risk factors such as different towns/cities, species, or age groups, etc.), but are otherwise identical and assumed to be homogeneously mixing within the compartment, and equally connected outwith the compartment. Such models have generated considerable insight into infectious disease dynamics but become less useful as the available data become more extensive, and the questions addressed consequently become more explicit and precise

with respect to the contact process. The use of frequency dependence in compartmental models is one mechanism for modelling the number of contacts per individual, but is limited in its capacity to include heterogeneity, as it is equivalent to assuming infinitely rapid switching of a fixed number of links between connected individuals with equal probabilities of contact between all members of different compartments of the population.

In a setting of increasing computational power, increasingly specific data, and an awareness of the limitations of homogeneous contact models, static networks (i.e. with contacts between individuals that are fixed and permanent) have become very useful in developing insights into the importance of population structure, and have made a significant recent contribution to epidemiological modelling (Stärk et al., 2006; Dubé et al., 2009; Martínez-López et al., 2009). However, static network methods typically lack the ability to model changes to population contacts themselves over time, i.e. the dynamics of the network. There is now an increasing body of literature concerned with the impact of dynamic networks on the spread of infectious disease. Such studies have investigated a wide variety of network features that can broadly be considered in terms of the ability of infected individuals to infect their local neighbourhoods (e.g. the role of highly connected individuals, as in ‘scale-free’ networks), the ability of disease to spread across large segments of a population (e.g. individuals that connect communities, such as in ‘small-world’ networks) and the resultant implications for targeted disease surveillance and control types (Noremark and Widgren, 2014; Valdano et al., 2015). Disease relevant networks, while sharing many characteristics with other examples of dynamic networks, are subject to particular processes and problems that are typically less pronounced in other systems, due to the sometimes

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profound impact that the interactions between the characteristics of the network and the characteristics of the disease can have on transmission (Epstein et al., 2008; Funk et al., 2010). Despite their potential for wide real-world applicability, dynamic networks are still much less popular in disease modelling than static networks, due in part to the dearth of analytic results on dynamic networks, which has recently been identified as a key challenge for the future of network epidemiology (Pellis et al., 2015).

In this review, we outline dynamic network methods available to an infectious disease epidemiologist, highlighting potential opportunities and difficulties in working with disease-relevant networks derived from data, and providing pointers to available software tools. As our intended audience includes quantitative researchers who are not experts on dynamic network methods, we also go to some effort to establish terminologies and nomenclature for this audience. We consider the impact of the dynamic interaction between changing network structure and disease characteristics, considering the problem broadly in three parts: (i) what is a dynamic network, and what is the impact of the dynamics of the network on an epidemic? (ii) how can we describe, characterise, and measure a dynamic network extracted from data? (iii) what computations can be performed on a dynamic network, and how? Throughout we shall consider particular disease-relevant examples of such networks, concentrating especially on features gleaned from explicit network data. More strictly mathematical approaches, for example using ordinary differential equations to describe the ‘effective degree model’ (Lindquist et al., 2011) in the context of dynamic networks (Taylor et al., 2012) have been shown to provide good agreement to simulation under simple link switching models; however these are outside the scope of this review.

2. Dynamic networks and epidemic processes

The use of networks and graphs has become common in epidemiology, especially in the contexts of transport, sexual, and livestock trading networks (Martínez-López et al., 2009; Dubé et al., 2009). Basic network notation may therefore be familiar, and an extension of that notation to dynamic settings is becoming more common (Braunstein and Ingrosso, 2016; Valdano et al., 2015); here, we outline a particular extension of standard graph theoretic notation (Bondy and Murty, 2007).

A dynamic network is simply a network structure that changes in time: the nature of the change and the notation used for the timing will vary widely and will depend on the nature of the data and application (Holme and Saramäki, 2012; Vernon and Keeling, 2009; Valdano et al., 2015). We therefore extend the standard notation to include a function from edges to the times that they happen. We call $G = (V, E, F)$ a dynamic graph where V and E are vertex and edge sets as usual, and F is a function from E to a set of pairs of natural numbers that will indicate the times at which each edge is active (Fig. 1). Holme and Saramäki

(2012), in common with many others, use notation for temporally changing networks that can express both contacts that occur instantaneously, and one for contacts that exist over a period of time.

A common way of describing a path in a temporal network is as a *time-respecting* or *time-admitting* path (Holme and Saramäki, 2013): informally, a time-respecting path is a sequence of contacts that connect the starting and ending nodes with each contact in the path coming after the one before it in time. A path of this sort could transmit disease from the starting to the ending node, whereas a path that is not time-respecting could not. We say a vertex v_b is *reachable* from v_a if there is a time-respecting path from v_a to v_b . The *reachable set* (sometimes called the *influence set*) of v_a is the set of all vertices reachable from v_a . The reachable set of a node is the set of other nodes that could be infected in an epidemic started at that node.

Notions of connectedness, which have been very important in the study of static networks, must be defined with respect to some time bound: we can define dynamic connectedness notions with respect to either an overall time period, or a time period specific to each node, and can include or ignore specific disease dynamics. The overall time period approach without respect to a specific disease approach is the simplest.

Within a given time period, we might say that a network is *temporally strongly connected* if every node is reachable from every other within the time period, *temporally connected* if in every pair of nodes at least one is reachable from the other within the time period, or *temporal contagion connected* if there exists some node such that all other nodes are reachable from it within the time period (with the intuition that a perfectly-spreading contagion starting at that node could infect the entire network within the time period).

Similar to their static network counterparts, these definitions have no reference to any specific contagion, and consider only an overall, potentially long, time frame, accepting all node activity at all nodes within that time frame. In a sense, they are defined for an SI infection that transmits with 100% probability along every potentially infectious contact: in a real-life situation this may be inappropriate. For example, if the disease has a latency period or a limited infectious period, then it may not be possible for all nodes in a node’s reachability set to be infected in an epidemic started by a single disease incursion at that node. Consider a disease incursion that starts at a node that has long periods of time between burst of contacts; if the infectious period of the disease is shorter than the quiet time periods, then the disease may not be transmitted any further, and therefore a network that the above definition would classify as temporal contagion connected may not be temporal contagion connected with respect to this more complex disease. For practical purposes, it is also worth considering that most diseases of any severity likely result in changes in behaviour, and therefore changes in the underlying properties of network dynamics itself; examples of these are discussed further on.

In a more disease-focussed setting, we may have a specified set of time periods of activity for each node v (call all these sets \mathcal{T}), with respect to a specific contagion d , and define the dynamic network $G = (V, E, F)$ as *temporal contagion connected with respect to d, \mathcal{T}* if there exists some vertex that can infect all vertices with d using only contacts within each node’s active time period recorded in \mathcal{T} . In this setting the largest temporal contagion connected set with respect to d, \mathcal{T} in a network is akin to the largest component in a static system from a disease perspective: it represents the largest possible epidemic seeded at a single source.

We include in SI 2 code that computes temporal connectivity and reachability sets on small example networks, which allows us to compute that in the network in part (A) of Fig. 2, over time period 1 to 5, the reachability set of vertex 1 at time 2 is all of the vertices in the network (and therefore this network is at least temporal contagion connected), but the reachability set of vertex 5 at time 1 is only the vertex 4.

Two static networks are *isomorphic* if they have the same adjacency structure up to a relabelling of the vertices: we can adapt this notion to

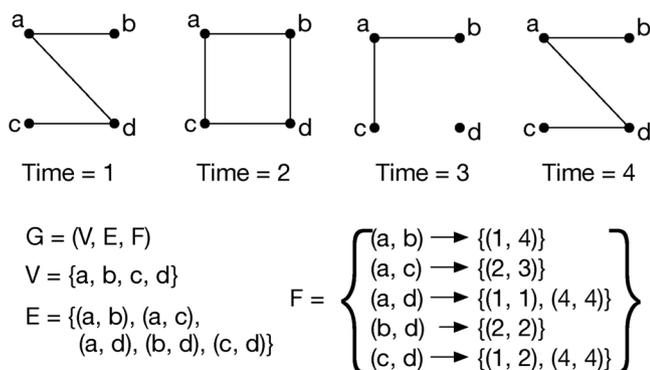


Fig. 1. A dynamically changing graph shown over four time steps, with the $G = (V, E, F)$ notation below.

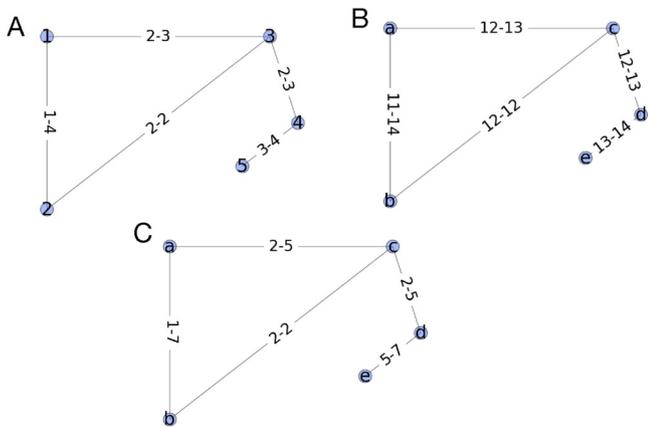


Fig. 2. Examples of temporal isomorphism definitions (produced by code available in SI 2). The mappings between nodes in the three networks are indicated by the geometric embedding (that is, the top left node in A is mapped to the top left node in B, etc). The times spans of the edges are written on the edges. A is temporally isomorphic to B (because the times on the edges in B can be produced by shifting the times on A), and only temporal order isomorphic to C.

the dynamic setting as needed for our application.

In an extremely strict sense, we might say that two dynamic networks are *strictly isomorphic* if they have the same contacts at exactly the same times up to a relabelling of the vertices: this approach may be useful when comparing datasets to check for duplication, but is too strict to be useful when comparing legitimately different datasets. Strict temporal isomorphism is useful when the absolute timing of events is important; for example, when we are looking for common network structures in the forensic examination of epidemics, where transmission is often a result of a single time-specific external event, such as a change in market due to a news event, or a explicitly-timed change in policy; for example, in detecting cattle trading changes due to changes in cattle testing requirements in Scotland (Gates et al., 2013), or immediately after the 2001 foot-and-mouth epidemic in the UK in 2001.

If we are interested in measuring or detecting identical sequences of contacts of the same duration shifted in time, we might call two dynamic networks *temporally isomorphic* if they are isomorphic, but with one of the sequences of contacts shifted by a constant amount in time. For example, this notion might detect a common sequence of contacts that occurs in different places in a network each week throughout a year. This could also apply to many social and market interactions, for example: common daily patterns of activity or trades or social activity that prompts or is prompted by further activity; for example, an international traveller visiting a medical clinic just before travelling, or a sheep farmer who might always sell on his current animals just before buying additional animals in. This pattern will occur at many different points in time, and it is the relative temporal distance between those two events that is relevant for disease control. Depending on the question being addressed, it will often be appropriate, given the noisy nature of contact processes and data capturing them, to allow some time-shifting tolerance in proportion to the variability in the contact and epidemiological processes, even though a more flexible approach might have computational consequences.

A more permissive notion of temporal isomorphism requires only equivalent order in the contacts, with no regard for the length of times between the contacts. This *temporal order isomorphism* may be used to detect an arrow of time (Bajardi et al., 2011) in contact data, or find repeated patterns in a noisy system where considering the exact temporal spacing of contacts would not be appropriate. This more permissive measure has the advantage that it is independent of subjective choice (“how much tolerance should be allowed”) even though this very permissiveness means that it retains no disease specific context

(e.g. “such as allowing tolerances based on the mean and distribution of disease incubation periods to determine what sequences of contacts are similar”).

We show examples of these temporal isomorphism definitions in Fig. 2, and for illustrative purposes, we include in SI 2 code that computes temporal isomorphisms on these small example networks.

Just as isomorphism concepts must be adjusted to the dynamic nature of a network, connectivity and reachability must take network changes and timing into account. These ideas can also be extended to include a *multilayer* network, in which there are multiple layers of different types of edges. Multilayer networks are common in epidemiology where different types of contact present different disease threats but for the same disease; these are a quickly growing research area (Kivela et al., 2014). When different timeslices at which the network exists are viewed as layers of the network, multilayer networks can also provide a formalism for temporal networks (as in Valdano et al., 2015; Kim and Anderson, 2012): we describe this sort of representation in Section 3.1.

2.1. The impact of temporal dynamics of a network on an epidemic

2.1.1. Interaction of contagion and network timescales

Because our interest is typically in the contagion, there are only some circumstances in which the dynamic process of the network is worth including. Roughly speaking, this is when the two dynamic processes are on similar timescales. If the network changes so slowly that it is likely to remain the same throughout an outbreak, then a static approximation is appropriate. If the network changes much faster than the timescale of the epidemic, then it is either similar to a weighted static network if each node has very restricted partners (i.e. the network is sparse), or it approaches a homogeneously mixing population if the contacts are unrestricted (i.e. the network is dense). However if the network changes over a similar timescale to the node-to-node progression rate of the infection, then the changing network can change the course of the contagion, and it is important to include those changes in analysis. In this section we give examples of when and how this interaction between timescales has an impact on disease spread, prevalence, and persistence.

Perhaps the simplest example of the interaction between network and contagion occurs when the overall structure of the network is retained, but the connectivity of individual nodes changes: here the network and contagion are operating on similar timescales. One example, originally considered by Saramäki and Kaski (2005), considers a small world network where all local links are fixed (for all nodes, $k_{local} = n$, where n is an even constant) but randomly placed links detach and reattach to random nodes at a fixed rate σ , with all random links assumed to reduce the pathlength between nodes compared to the network restricted to only local links. The conditions for criticality of this system has previously been considered under conditions of ergodicity (e.g. as generated by a Markov chain), where an appropriate static representation of the network will have the same characteristics as the original, dynamic network (Kao, 2010). In this approach, a static network is generated by assigning an infectious period to reach node, drawn from an exponential distribution with mean period τ_{inc} . Then a number ν_{rand} random links are generated and placed on the small-world network with the restriction that the distance between the two connected nodes is greater than $n/2$.

While infected links are few, link switching is more likely to create a connection from an infected to an uninfected, “free” node, whereas the opposite would become true as more nodes are infected. In the early period the switching rate therefore defines an effective infectious period over a given link, with a concomitant increase in the number of connected links, and the ratio of infection rate to switching rate being the critical scaling.

Analogue to an approach showing the relationship between static networks and mean-field models (Keeling and Grenfell 2000), it is

relatively straightforward to identify a correction that results in final epidemics that have the same distribution under stochastic simulation for different switching rates, and both for static and dynamic representations (Kao, 2010). Further mathematical details can be found in SI 3.

The “ergodic assumption” of random link switching is of course extremely restrictive, and unlikely to be satisfied by most real systems; thus a snapshot of a temporal information that includes all edges over a fixed time scale can lose a large amount of information: a possible measure of this loss can be found in a comparison of paths in a snapshot and time-respecting paths in the temporal network. In a snapshot, because of the loss of temporal information, we may see paths that are temporally impossible routes of contagion flow, giving us a false idea of the potential infection flow between pairs of nodes. The fraction of snapshot paths that are not time-respecting (and therefore could not transmit infection from the starting to ending nodes) is a rough measure of how important it is to use a temporal network rather than a static snapshot when determining potential infection flow between nodes.

For example, in the cattle trading network in Great Britain, only about half of the paths of two contacts are time-respecting for timeframes over a week, with a substantially smaller fraction being time-respecting for longer paths. The fraction of paths that are temporally possible decreases slightly as longer timeframes are used for the snapshot. When measuring properties of individual nodes, distance in a snapshot therefore may be a poor proxy for disease flow by animal trade between two farms in the Great Britain cattle trading network, and therefore in this case the loss of the temporal information in the static approximation could result in substantially incorrect predictions of disease spread, though it may still give qualitatively useful insight (Kao et al., 2006).

2.1.2. Non-Markov temporal patterns

A variety of non-Markov temporal patterns are important for the spread of contagion, including burstiness of human behaviour, repeated cycles of behaviour due to circadian or seasonal changes, and other divergence of waiting times from a memoryless Poisson process.

Barabasi (2005) observes that the timing of human behaviour often does not follow a Poisson distribution, but instead better follows a heavy-tailed distribution: events happen in concentrated bursts, interspersed by long waiting periods [17]. This property is called “burstiness”, and has been observed and investigated in many areas of human activity – most commonly electronic communication, though also in written communication and other activities (Oliveira and Barabasi, 2005). While the contagion itself may cause bursty behaviour, burstiness is most frequently studied as a property of the underlying network rather than as caused by the contagion.

Min et al. (2011) use an analytical approach combined with experiments on an artificial tree-like network to show that bursty activity can slow an epidemic, compared to uniformly randomly distributed activity. Iribarren and Moro (2009) find a similar slowing effect in an experimental setting on an email contact network. In a disease setting, Nickbakhsh et al. (2013), showed how the duration of incubation and infectious periods interacts with timings of vehicular movements between farms to either increase or decrease the transmission potential for avian influenza. Additional experiments conducted by removing different levels of temporal structure from a network show that the burstiness of human communication increases the spread of a contagion in some networks (Takaguchi et al., 2013), but slows it in others (Karsai et al., 2011). Karsai et al. (2011) were able to distinguish between different levels of temporal structure; they found that an increase in spreading was due to burstiness and correlation between the topological structure of the network and the frequency of contacts. Why and when burstiness has these differing effects is an area of active research (Holme and Saramäki, 2013).

Livestock movement networks are one example where strong seasonal effects are coupled with weekly trading patterns that are likely to

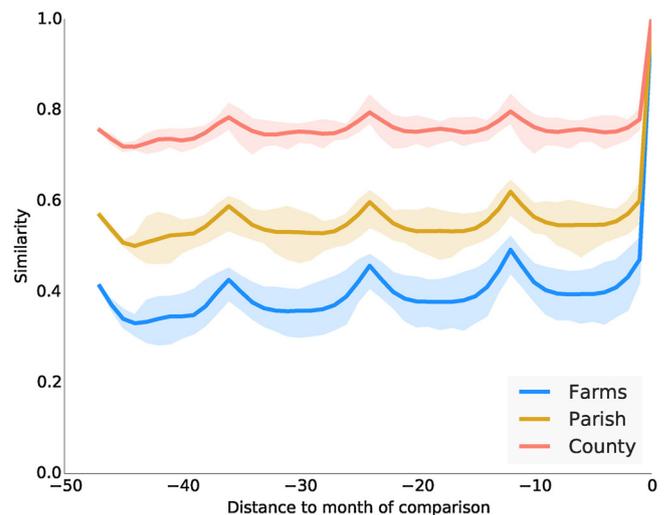


Fig. 3. A plot of the mean similarity (calculated using a method of set similarity counting) of cattle movements in Great Britain between each month of 2011 and months up to four years previous. The blue line (bottom) shows similarity of unaggregated movements, the yellow (middle) movements to parishes, and the pink (top) movements to counties. The background shaded envelopes are between the maximum and minimum values over all 12 months of 2011. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

be important to varying degrees, depending on the timescale and infectiousness of transmission. Measuring the fraction of movements that are repeated between months of varying temporal distances via aggregation of destinations at three levels: un-aggregated (that is, movements from farms to farms), movements from farms to parishes, and movements from farms to counties illustrates the impact of these patterns. If the network is very consistent, then disease models run on the past will be good predictors of the future; if the network changes a lot over time, then we cannot rely on the past to predict the future.

The scallop-edges pattern visible in Fig. 3 with peaks at 12-month distances from the month being examined shows us that there is a strong seasonality in the cattle trading network in Great Britain. A month is most similar to that same month in previous years, and least similar to months six months away from it in previous years. If a single month is being used for livestock disease simulation in Great Britain, it is important to use the appropriate month: we should not use the previous October to simulate a disease outbreak this April. These effects are also seen elsewhere, with many practical examples of the magnitude and direction of effect that temporal information can have on modelling a contagion, including the fraction of paths in a network that are time-respecting, and the importance of burstiness (Noremark and Widgren, 2014; Bajardi et al., 2011; Takaguchi et al., 2013).

2.1.3. Infection events driving network dynamics

A more complex situation occurs when the temporal processes of the network and disease interact not only in timescale, but also more directly: when the infection events themselves can change the network structure, which then impacts further disease spread.

The contagion may drive changes in the network: consider a rumour (i.e. a non-disease contagion) spreading over human mobile phone contacts. A node being infected (hearing the rumour) could prompt that node to make more contacts, because it now has interesting information to share. Similarly rumors of disease spread may causes changes in behavior, for example individuals fleeing from the Black Death (Epstein et al., 2008; Funk et al., 2010; Kao et al., 2007), or on a smaller scale, a farm that is infected with a disease may be influenced to sell on animals due to them doing poorly, or may be prevented from selling on animals due to a detection of the infection, as in the case of bovine tuberculosis

(Green et al., 2008; Reynolds, 2006). Modelling of the recent Ebola outbreak in West Africa has incorporated changes in the contact process over the course of the epidemic (Drake et al., 2015) and has highlighted the need for detailed datasets on human contact patterns and their changes in response to an outbreak (Chowell and Nishiura, 2015). Gallos and Fefferman (2015) show that, in epidemic models on several classes of networks, the removal of nodes due to death or immunity can quickly change the connectedness and overall topology of the underlying network. There is evidence that the AIDS epidemic has resulted in changes to sexual behaviour, and therefore to the sexual contact network, both in response to awareness of the overall epidemic (Gregson et al., 1998; Mah and Shelton, 2011), as well as to personal infection events at each node (Mah and Shelton, 2011). While there is limited real-data evidence that sero-assortative contact rewiring occurs, models indicate that this sort of rewiring would have an impact on the overall shape of the network, and therefore the subsequent epidemic (Volz and Meyers, 2007).

We also note that, as well as changes due to individual response, centrally-mandated interventions (themselves motivated by infection events) made with the intention of changing a contact network can also have a significant effect on the spread of disease e.g. in the case of school closures to slow the spread of pandemic influenza (Hens et al., 2009).

3. Characterising and measuring data-derived dynamic networks

Given the potentially important interaction between network and epidemic dynamics, it is important to understand the dynamics of an underlying network when possible. Here, we outline popular methods for handling dynamic networks that might be useful in epidemiological applications.

3.1. Transformations to static networks

Because there is a significant bank of analytic methods for static networks, it is common to transform a dynamic network to a static one for analysis.

The most common way of processing a temporally changing network into a static one is to produce an ordered series of static graphs, in which each in the series is an aggregation of the edges in the original dynamic network over some specified period of time (for disease relevant problems, this is most likely to be the effective infectious period of the disease at the node level). Within that time, the timing of edges is ignored to produce a snapshot. Depending on the level of aggregation, anywhere from all to none of the temporal information may be lost. As discussed previously, the temporal information in a dynamically changing network can have a significant impact on the estimated disease spread, so snapshots can be deceptive, particularly if inappropriate time periods are used (Holme and Saramäki, 2013; Vernon and Keeling, 2009).

Several groups (Cheng et al., 2003; Whitbeck et al., 2012) use an idea related to the weighted transitive closure of a dynamic network $G = (V, E, F)$ to produce a *reachability graph* with the same vertex set as G in which for $u, v \in V$ there is an edge from u to v if there is a time-respecting path from u to v in G . A weight may be placed on that edge derived from the number of edges in the u -to- v time-respecting path, or its time delay.

A reachability graph summarises information valuable for estimating contagion spread on the network: especially useful is that the outward degree of a node will be the maximum size of an outbreak starting at that node over the time frame used to construct the reachability graph. This is closely aligned with the previously-described idea of a reachability set: every node that can be infected in an epidemic started at that node will be directly adjacent to that node. The main disadvantage of computing a reachability graph is that it can be very dense, and therefore difficult to work with if the original network was

large. In addition, considerable information on the timing of contacts can be lost in the summarisation.

The *line graph* of static network $G = (V, E)$ is a network with E as its vertex set, in which two vertices in E are adjacent if they share an endpoint in G . Riolo et al. (2001) use an augmentation of line graphs that accounts for the timing of contacts with a directed edge. Heath et al. (2008) describe a related approach. Using the cattle trading network in Great Britain, they produce a directed line graph as follows: let $G = (V, E, F)$ be the original dynamic network. Then create a static directed network $G' = (E, D)$ where there is an edge $(e \rightarrow f) \in D$ if the contact f in G occurs after or during e , but within some set time period. This time period may be varied by the type of node in the original graph (farm, slaughterhouse, etc) that is involved. They run a simulated contagion on this network, and find that including the temporal information gives differences in epidemic size as compared to an analogous process run on the original network. A line graph approach can be particularly useful when contacts in the original dynamic network are qualitatively different in some way: these can then be considered as different classes of vertices in the resulting line graph.

Miritello et al. (2011) use an approach that combines an explicit SIR disease model and a dynamic network to produce a static network that describes the spread of contagion in that network. Their method gives an estimate of the expected outbreak size, as well as the epidemic threshold on that network. It is similar to static network percolation methods, and is closely coupled to the SIR model; recompilation may be required for every different pathogen under consideration.

The authors Enright and Kao in Epidemics 10, 2016, along with Kim and Anderson (2012) use a method that has likely also been used informally by other researchers, and is based on creating a node in a static directed network for each node at each time necessary in the original dynamic network.

More formally, if $G = (V, E, F)$ is the original dynamic network, then we create a static directed $G_\phi = (V_\phi, E_\phi)$ where:

- V_ϕ contains exactly $\{(v, t)\}$ where $v \in V$ and t occurs in at least one F (e) where $e \in E$ and v is an endpoint of e
- E_ϕ contains exactly $(v_i, t_i) \rightarrow (v_j, t_j)$ where either:
 - $(v_i \rightarrow v_j) \in E$ and $t_i = t_j$ is in at least one member of $F(v_i \rightarrow v_j)$, or
 - $v_i = v_j$ and t_j is the minimum time such that $(v_i, t_j) \in V_\phi$ and $t_i < t_j$

This network then admits analysis by conventional static network tools, and conventional static network disease models. A simulated disease spreading in this network will only move from one node to another along what would be time-admitting paths in the original network.

3.2. Measuring dynamic network structure

Static network measures are very commonly (Easley and Kleinberg, 2010) used to assess the vulnerability of a network and measure how it will respond to contagion. As a simple first step to modelling contagion on temporal networks, it is important to understand the analogous temporal network parameters. First, we discuss measures applied to individual nodes, and then move on to measures related to multi-node patterns. These approaches could allow us to identify agents that are particularly important to disease control on a network, and that could then be targeted for intervention. Second, we describe several means of approximating a dynamic network with a static network, which may render it more amenable to analysis by conventional means.

3.2.1. Node measures

In any but the most homogeneously mixing populations some individuals have a disproportionate impact on the size of an epidemic. This impact may, for example, be due to a high degree of connections (as in the case of “superspreaders” Galvani and May, 2005; Matthews and Woolhouse, 2005; James et al., 2007), or due to having a critical

role in joining-up a network (as in a “bridge” Shu et al., 2012; Lawyer, 2015). Node measures provide an imperfect, but useful, way of capturing some of these types of importance. These considerations of course pre-date the recent explosion of analyses in the network context (e.g. Hethcote and Yorke, 1984; Levins, 1969), however the natural expression of these considerations in a network context has added considerably to our understanding of these processes. Further, and particularly relevant to this review, it has motivated analyses of the role of dynamics of the contact structure itself.

The *degree* of a node in a static contact network is simply a count of the number of potentially infectious contacts it makes; in a directed network, we may consider also the *in-degree* and *out-degree* (Bondy and Murty, 2007). We can adapt these to dynamic networks in a number of ways by counting contacts or neighbours over some time period, and calculating the maximum, minimum, or mean over a variety of these time periods, possibly taking the duration of each contact into account.

Degree measures will identify the nodes with the most contacts or the most neighbours as the most important: this is of use when identifying potential superspreaders. In the case of an STI spreading on a sexual contact network, high degree nodes might, for example, be sex workers, who typically have a large number of contacts with short duration (Galvani and May, 2005; Lloyd and May, 2001). Analogously, in the context of a livestock trading network, the nodes with highest degree are likely to be markets or dealers, who play a critical role in a fast-spreading epidemic, but, because of the short residence time of individuals on them, would be less important for chronic infections.

More complex node measures exist to identify nodes that are important for disease flow in a more subtle way: nodes can have disproportionate importance without directly infecting a large number of other nodes. *Betweenness* is useful for measuring how likely it is that a flow of a disease will have to pass through a node when moving through the shortest paths in a network, and is useful for identifying bridging nodes that provide a connection between otherwise-separate parts of a network.

Adaptations of betweenness to dynamic networks must adapt the crucial notion of a shortest path in the network: some adaptations consider time-admitting paths shortest in time, some shortest in number of edges (Tang et al., 2010; Holme and Saramäki, 2012), and some a combination of the two (Kim and Anderson, 2012). If we are concerned about the speed of spread of a disease that has a relatively low transmission probability with each contact, we may be more concerned with the path shortest in edges, if a disease with a short infectious period or short detection time, perhaps the shortest in time.

Where betweenness measures how important a node is to flow across the network, *closeness* measures how close (on average, in number of edges) a node is to other nodes, and therefore how quickly an epidemic starting at that node might infect a large proportion of the network. Again, the idea of a shortest path is important for this measure, and must be adapted in a dynamic network to use paths shortest in time, edges, or both (Tang et al., 2010; Pan and Saramäki, 2011). Temporal centrality is more correlated with importance in an epidemic than static versions on an aggregation of the network, stressing the importance of using an appropriate dynamic measure when possible (Tang et al., 2010; Huang and Yu, 2017). Spectral centrality measures are based on manipulations of a matrix that records the connectivity of a network and typically recursively include the importance of a node's neighbours in that node's importance: that is, a node adjacent to a very important node will, itself, have enhanced importance. Computing these measures can be very computationally intensive, and (if done by simulation) may require many iterations and restarts. Temporal adaptations of spectral measures make use of an adapted matrix structure (Holme and Saramäki, 2012; Valdano et al., 2015; Grindrod and Higham, 2013; Mantzaris and Higham, 2013), and have been predominantly applied to electronic contact networks to identify important nodes, but they have the potential to provide an indicator of which are likely to be the most commonly infected nodes on a randomly

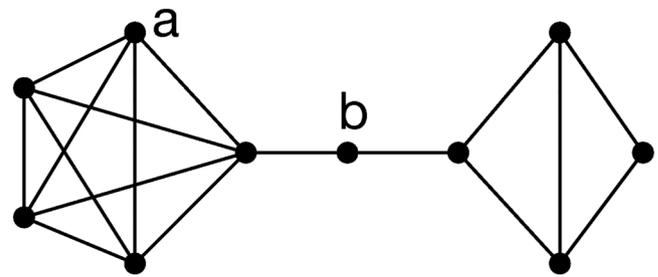


Fig. 4. An example of differences in centrality node measures: node *a* has higher degree than *b*, but much lower betweenness than *b*. In an epidemic, *a* is important because it could infect, or be infected by, a larger number of other nodes, whereas node *b* is important because it is the bridge between the left and right sides of the network.

challenged, disease-relevant network.

All of these measures for nodes will give us slightly different perspectives on node importance: we might apply them jointly in an attempt to find the nodes most important for disease spread on the network.

In many real-world networks these measures will often but not always coincide (cf. Fig. 4). While there are many examples (Lawyer, 2015; Martínez-López et al., 2009; Christley et al., 2005) of the use of static network centrality measures in identifying important nodes for epidemic spread, and there is evidence that dynamic centrality is useful for identifying epidemiologically-important nodes in dynamic networks (Mantzaris and Higham, 2013; Pan and Saramäki, 2011), dynamic centrality measures are not yet widely used in the epidemiology of biological infections. Dynamic betweenness, closeness, and spectral measures can be used to identify nodes that are important for the overall spread of disease on the network: these nodes could be targets for extra biosecurity, vaccination, or surveillance.

3.2.2. Measures of network patterns

Moving beyond the extreme locality of measuring a single node, measures of patterns or groups of nodes in the network also have applications in epidemiological analysis.

In a static network, the *clustering coefficient* gives a measure of how likely a single node's neighbours are to be adjacent. Clustering is often seen in real-life static networks, and has an important impact on the spread of contagion (Easley and Kleinberg, 2010; Serrano and Boguñá, 2006; Badham and Stocker, 2010), sometimes slowing and sometimes speeding spread, depending on the phase of the epidemic. When adapted to the dynamic setting, one may allow contacts at different times to still constitute a cluster, or require simultaneous contacts (Cui et al., 2013). In networks derived from face-to-face contacts and WiFi usage, Cui et al. (2013) find that the transmissibility threshold required for an epidemic is lower in dynamic networks when clustered edges are also clustered together in time, and higher when edges that form clusters in an aggregation of the network are separated by long periods of time. However, when many individuals are infected, clustering can result in a large fraction of potentially infectious contacts being ‘wasted’ on already infected individuals, therefore slowing the epidemic.

Beyond the simplicity of clustering, other work has measured the persistence or repetition of patterns. Repeated shapes between the same nodes are studied by Lahiri and Berger-Wolf (2007) as *persistent subgraphs*, who provide an algorithm to detect them, and give many examples of them in real networks. In contrast, *motifs* are isomorphic subgraphs that appear repeatedly throughout different parts of the network, involving different nodes. Static motifs have been used in static networks, and have been particularly useful in characterising biological control networks (Alon, 2007). A large variety of methods have been used to apply motif-counting to temporal networks, varying from counting static motifs over many snapshots of a temporal network

(Braha and Bar-Yam, 2009), to the counting of temporal motifs in a full temporal network by Kovanen et al. (2011). House et al. (2009) use a motif-based approach with an ODE approximation to network dynamics to approximately simulate epidemics on a network with less computation than would be required for a full simulation.

The use of motifs highlights the importance of a clear idea of isomorphism for temporal networks: Kovanen et al. (2011) consider a subgraph to be one of their motifs if it is temporal order isomorphic to the motif, but only count occurrences that are completely within some pre-assigned time window. That is, if their time window is a week, they count any set of contacts that occur in the right order with the right topology as an occurrence of the motif, but do not, within that week, consider the magnitude of the time delays between contacts in the motif occurrence. This is appropriate only for some disease scenarios: if the disease's infectious period is much shorter than the time window, then the relative temporal delays between contacts may be very important, and therefore temporal isomorphism might be important.

Using a variety of motif approaches, researchers have found evidence for the importance of motifs in networks that might contribute to our understanding of disease spread. Bajardi et al. (2011) counted the frequency of directed time-respecting paths of cattle trades in the Italian cattle trading network, and found that there are far more than found in a time-reversed model. In contrast, we have found minimal differences in a time-reversed version of the British cattle trading network. We find that in a time window of two weeks or more only about half of the paths of two trades, and about one-fifth of the paths of three trades are time-respecting. This difference could be attributable to differences in agricultural regulations in Great Britain and Italy.

Braha and Bar-Yam (2009), using their static aggregation approach, found that highly connected motifs are more common in an email contact dataset than a null-model would predict. Dense clustering is also characteristic of real static networks, and is important for disease control. As we note above, densely clustered networks speed an epidemic in some phases, and then slow it in others when it results in most potentially-infectious contacts being to already infected individuals (Badham and Stocker, 2010).

Kovanen et al. (2011) find significant homophily in the motifs in their contact networks: contact of nodes to other similar nodes is known to be an important factor in disease spread, especially if node categories have implications for disease susceptibility or spreading potential.

The time that a pathogen might take to get from one node in a network to another is an important indicator of the speed of an epidemic, and can be expressed with the *latency* of a path dynamic network. The latency of a time-respecting path is the time between the first and last edge in the path; sometimes the term latency is also applied to two vertices, in which case it is the shortest latency of a time-respecting path between those vertices. Of course, the latency between two vertices may vary over time.

Holme and Saramaki, following Pan and Saramäki (2011), show that, for two vertices, latency plotted against time displays a sawtooth pattern, with latency declining linearly toward local minima at the time when a time-respecting path starts from u to v , and then increasing sharply at that time. If contacts have substantial duration, then this pattern may look somewhat different, with local minima becoming local minima plateaus. The picture becomes more complicated when we consider the network as a whole: we may wish to know the latency overall for the network over some time span. This would give a measure of how fast, on average, an epidemic could spread over the network.

4. Collecting data and using dynamic networks

Disease relevant data on network dynamics would ideally include not only identification of the links between individuals, representing the potential for infectious disease contact; but also additional information including the probability that contact would result in transmission, which will be due to a combination of the nature of contact

(e.g. is it skin-to-skin contact, close aerosol contact, etc.), the duration of contact, and the impact of duration on transmission.

Datasets that characterize patterns of human movement (where the distance of movement in terms of transmission chains shortens the chains generated by pathogen movement alone) are both rare and highly sought after. Compared to animals or plants, the challenges of tracking humans are considerable. First, the individual takes considerably more importance in analysis, and therefore approximations that are sensible for tracking livestock or wildlife and have implications for the individual that may not be acceptable for humans (Eames et al., 2015). Second, considerations of individual privacy and civil liberties, while important for livestock diseases, are critical when considering tracking individual human movements, especially at a whole population scale. Third, and considering the detail that is often being demanded, the patterns of human movements that are relevant to disease transmission can be considerably more complex, with individual decision-making playing an important role.

Typically, proxies for human movement are used, such as known patterns of transport (Colizza et al., 2006; Danon et al., 2011; Keeling et al., 2010), however such patterns typically identify only broad characteristics of network dynamics (e.g. seasonal changes) that do not capture the complexities of individual human interactions. Survey data (Eames et al., 2015) can be used to gain more individual level insight, but are subject to the biases of human recall. A more direct approach involves direct tracking via proxy devices, such as mobile phone networks, including both the patterns of phone location (to identify spatial proximity), and also usage (to identify potential close contacts). In all these cases, it remains difficult to relate the identified dynamic networks to the contacts that are most likely to be a risk for disease transmission.

In comparison to human data, the analysis of diseases of livestock has considerable advantages. Because activity is largely commercial, the systems involved are relatively simple, and increasingly well recorded. Data protection issues remain important, but, because the details involved typically less intimate than for human data, are usually easier to accommodate. However, like human data, what is recorded is not necessarily representative, with exemptions to contact reporting on the basis of commercial necessities and practicalities having the potential to introduce meaningful biases into the available data (Orton et al., 2012). Despite these difficulties, the detail of data available in these systems is considerably greater than for either humans or wildlife (Keeling et al., 2010). An interesting recent development is the implementation of schemes to electronically tag individual animals (Umstatter et al., 2012). This both has the potential to eliminate many potential biases (many of the biases introduced are a result of exemptions to recording that will no longer be necessary under an automated electronic system) and provide finer, more immediate detail to network characterisation, allowing for real time management of rapidly spreading infectious diseases, though the potential for this to improve disease control is as yet untested. Nonetheless, the early availability of explicit dynamic data for livestock movements, motivated by the need to solve real problems, has been an important driver for analysis.

Wildlife are considerably less well observed than either humans or livestock. However, tracking of wildlife can be important for conservation purposes, and also because of their role as sources of zoonotic infection. Acquiring data on wildlife movement dynamics is typically labor intensive, with little scope for the type of opportunistic sampling that underpins much of the characterisation for humans and livestock. Traditionally, this might involve survey data, either through field observation studies (Craft, 2015; Reynolds et al., 2015) or via collecting observational data from local inhabitants (Hampson et al., 2009), though the latter requires either wildlife that can easily be observed, or disease that is sufficiently important so that observers will identify it. However, while wildlife movements and transmission dynamics are less well recorded than for either people (by proxy) or livestock (directly), tracking of wildlife has become increasingly sophisticated through the

use of GPS collar technology for understanding inter-specific interactions (e.g. Barasona et al., 2014), use of data-loggers or camera-traps to describe contact networks e.g. Kukiela et al. (2013) and use of unmanned aircraft systems (UAS) or remote sensing to understand spatial patterns of host distribution and abundance (Barasona et al., 2014; Yang et al., 2005).

It is important to distinguish the social network (of potentially infectious contacts) from the transmission network, which represents the realized pattern of transmission arising from the movement of the pathogen population between individuals. Methods for generating the transmission network largely center around obtaining increasingly detailed representations of the genetic substitutions that arise through the replication of the pathogen. Once the expected rate of substitution is high enough that at least one is expected to occur per generation of transmission, then obtaining close to the full genome of the pathogen means that the data are directly useful for identifying who infected whom, though with some difficulties that arise due to sampling density. Understanding population structure in terms of population coalescent models is an active area of research, in particular in cases where the fundamental assumption of coalescent theory (that the population is large and homogeneously mixed) is being strongly rejected, and the additional flexibility of network formulations are most valuable (Frost et al., 2015; Kao et al., 2014).

If dynamic network data is explicitly available or if it could be simulated to sufficient accuracy for a system, any of a number of different software packages can be used to incorporate or analyse it. Though most network packages focus mainly on static networks, several general network analysis tools have temporal network visualizers, including SoNIA and Gephi. *ORA, which is developed at Carnegie Mellon University, can calculate several temporal metrics. Noremark and Widgren (2014) provide a package for the R language that traces contacts, as well as time-respecting inward and outward contact chains.

We expect that as temporal networks become more important in the study of contagion on networks more software will be made available for more platforms.

4.1. Running epidemic models on dynamic networks

Forward microsimulations of epidemic disease that incorporate known dynamic contacts have become a standard approach when such data are available (Eubank et al., 2004; Enright and Kao, 2016; Dawson et al., 2015; Brooks-Pollock et al., 2014), but reusable code for these computations is still relatively rare (though some does exist, e.g.: ComplexNetworkSim Python package, the EpiModel and SimInf R packages Widgren et al., 2016).

This rarity is a major challenge for the use of temporal networks in epidemiology. EpiModel is also capable of modelling a network from network data (using one of several random graph models) and then simulating on the modelled networks, rather than from explicitly specified network contacts.

While we recommend the use of an appropriate package for dynamic network epidemic simulation, for explanatory reasons we include a small amount of code in SI 2 that runs a simple forward epidemic simulation on a dynamic network with specified edge activity times, for demonstration purposes.

Beyond direct simulation and the previously-described node and network measures, recent work by Valdano et al. (2015) gives a method of calculating the epidemic threshold of a dynamic network (with code available at github.com/eugenio-valdano/threshold) directly: in cases where no particular contagion is under investigation, this may be appropriate as a probe on the susceptibility of a dynamic network to disease.

4.2. Modelling random and real temporal networks

When a full, exact, network is not available, or when a number of

'similar' copies of a real network are required for simulation, modelling methods for producing dynamic networks may be of use.

Given a presumed static snapshot of a dynamic networks, several methods have been proposed for capturing some relevant dynamic properties of the network. Volz and Meyers (2007) employ a differential-equation based model as an intermediate approach between the use of a static network and the use of a continuous mass-action model. Given a network that is random with respect to some known degree distribution, they incorporate a neighbour-exchange model on that network into the differential equations needed to model a SIR epidemic, by modelling the change in the number of contacts that span infection compartments through the course of an epidemic on the changing network. Even though their approach gives a deterministic set of equations, they find their results are similar to those obtained using a more conventional discrete simulation method. Barrat et al. (2013) use a trajectory-based approach; they seed a potentially large number of random walks on that network, then use those random walks to create orders of contacts on the edges. Using a real-world example of a farm trading network, they show that by choosing relatively simple distributions for the start points, direction choice, and length of those random walks, they can create temporal networks that mimic real-world network properties, including burstiness and seasonality. It is likely that any temporal pattern can be modelled in this way given sufficiently complex trajectory distributions: we suggest an investigation of the minimum trajectory complexity needed to model any some class of temporal pattern as an area for future study. The modelling of sexual networks is a particularly active area of research because of the importance of sexually transmitted infections, and the availability of sexual contact data. The importance of the dynamic nature of the network is well-supported by research showing that removing temporal information in a network changes a disease model's predictions (Rocha et al., 2011; Schmid and Kretzschmar, 2012). The relative impact of concurrency *versus* switching of contacts has been of particular interest, as concurrency of sexual partnerships is thought to be important in the spread of HIV (Morris and Kretzschmar, 1995; Kretzschmar and Morris, 1996).

Schmid and Kretzschmar (2012) describe an individual-based model in which each individual has an upper-limit capacity on the number of concurrent sexual partnerships, with pair formation and separation simulated as dynamic processes, with each individual having its own probabilities of formation and separation drawn from an appropriate distribution. They fit their model using Dutch and UK data from medical records and surveys, and focus on four summary measures of sexual activity: recent number of sexual partners, the gap in time between sexual partners, the length of a partnership, and the cumulative lifetime number of partners. Some of these measures are affected at the population level by increasing individual heterogeneity, and some are not - this emphasises the importance of understanding both the micro- and macro-level characteristics important for a particular application. Sometimes a simpler approach is successful: Robinson et al. (2012) use an adaptation of the configuration model (Molloy and Reed, 1995) to generate a dynamic sexual contact network. Their model has few parameters, but is successful at fitting known distributions of sexual partnership length and gap time between partnerships.

5. Conclusion

The analysis of temporal information added to disease-relevant network data has been driven by many factors. First, there is a human and veterinary public health interest in the role of the individual agent in the transmission of disease, as the individual is often the unit of interest where disease control is concerned. Second, there is an increased availability of data detailing these temporal variations, making such considerations not just scientifically interesting, but of practical utility as well. Third, the increased activity in integrating models with data, often by directly fitting using Bayesian statistical approaches have

highlighted pitfalls of simple static approximations. These complexities can often be overcome by simple extensions of static network approaches, but will be continually challenged by the drive to make greater use of increasingly detailed data. One area where these interactions have shown success is the study of infectious diseases over livestock movement networks. Here links amongst theoretical development, statistical inference and practical disease epidemiological problems has been particularly strong, most likely because of the combination of the availability of good dynamic network data and observable well recorded epidemics. As the availability of similarly dense data increases, these successes are being replicated in other systems.

Despite these successes in the study of dynamic contagion networks in particular, many challenges still remain, particularly with respect to infectious diseases. We outline some important ones here. First, the often considerable variability in the immune response of individuals exacerbates the importance of variability in network dynamics, and increases the challenge associated with trying to identify the role of the agent, as these factors are not usually captured in the methods used to capture network data. Second, the importance of pathogen sequence data in identifying the transmission network, and the enormous promise of exploiting sequence data for the forensic examination of outbreak patterns, means that linking the transmission network to the contact network appears tantalisingly achievable; however where there has been success, it has been dependent on having a good understanding of permissible contact pathways - approaches that link the explicit transmission networks associated with pathogen sequence with properties of generic dynamic network models are therefore of considerable importance, highlighting the more general need in linking parametric models that capture network dynamics with inference methods to estimate those parameters. In principle, the additional insight gained from a dynamics representation of networks could be used, for example, to refine our understanding of the most vulnerable nodes in a network, and therefore improve targeting of nodes (for example, for vaccination, biosecurity or surveillance). However, we are not aware of such recommendations being made. This may be in part because, while packages to analyse dynamic network data may exist, they may not be well publicised, and so bridging the gap between methods development and practical application remains a challenge. Finally, the increased emphasis on a systems-based approaches to tackling disease problems increases the demand for the development of integrative frameworks that consider multiple biological scales, possibly multiple hosts, and the role of human and/or animal behaviour, across all the relevant temporal scales and temporal drivers discussed here. Such frameworks are likely to lie beyond the capabilities of purely analytical approaches. Overcoming these challenges will require exploiting in combination the technological advances that allow the recording of large dense datasets describing explicit disease-relevant networks over time, the ever greater computational power available at decreasing cost and with increasing accessibility to non-specialist users, and the ongoing development, as reviewed here, of algorithmic approaches to bring data and analytical insight together.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.epidem.2018.04.003>.

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