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出版情報：MI lecture note series. 60, pp.59-62, 2014-11-28. 九州大学マス・フォア・インダストリ研究所
バージョン：
権利関係：

エボラウイルス病の流行モデルと隔離の効果推定

Modelling Ebola virus disease epidemic and estimation of the effectiveness of case isolation

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概要

2014 年西アフリカ地域を中心にエボラウイルスの流行が生じた．本研究ではリアルタイム研究の一環として，ヒト感染者 1 人あたりが生み出すヒト 2 次感染者数を意味する実効再生産数を時刻および国別で推定した．リベリアとシエラレオネの国別の実効再生産数は 6 月以降に継続的に 1 を上回っていた．全流行が制御できていないことを反映しているものと考えられた．

エボラウイルス病の流行動態研究では，ヒト感染者の隔離の有効性が鍵となる．今回，統計モデルを用いてウイルス感染個体における病期に対する相対的感染性を定量的に明らかにするとともに、感染症の隔離の効果を定量的に推定した．隔離は 2 次感染を部分的に防ぐことに役立つものと推定された．また，観察された発病間隔は隔離のために実際の発病間隔よりも短くなる傾向が明らかにされた．病期に対する相対的二次感染頻度の推定手法を確立することは、多くの新興感染症に関する隔離ガイドライン策定の根拠を与える礎となることが期待される．

Abstract

We estimated the effective reproduction number of Ebola virus disease, i.e. average number of secondary cases produced by a single primary case at calendar time t (Rt), for the ongoing epidemic in West Africa from March to August 2014. Estimates of Rt for the Guinea, Sierra Leone and Liberia, countries that are experiencing sustained community transmission were consistently above 1.0 since June 2014. Country-specific estimates of Rt for Liberia and Sierra Leone lied between 1.0 and 2.0, reflecting continuous growth of cases in these countries. Rt below 2 indicate that control could be attained by preventing over half of the secondary transmissions per primary case (e.g. by means of effective case isolation and contact tracing).

Whereas numerous methods have been proposed for estimating the efficacy and effectiveness of vaccination against infectious diseases, little has been made to assess the protective effect of non-pharmaceutical interventions such as quarantine, case

isolation and contact tracing. The present study focused on case isolation, aiming to offer a novel method to estimate its effectiveness based on epidemiological data. We define the protective effect of isolation as the reduction in the number of secondary transmission events (i.e. the relative reduction in the reproduction number). Two learning points were gained from this statistical exercise. First, the effectiveness of case isolation is quantifiable given that who-acquired-infection-from-whom network is empirically available. Second, observed serial interval estimates in literature are likely underestimated when the effectiveness of isolation is substantial. Other datasets that might permit similar estimation is household transmission data the analytical method of which will be briefly presented.

1. Background

The largest and first regional outbreak of Ebola virus disease (EVD) has been unfolding in West Africa since approximately December 2013. The outbreak was not recognised until March 2014, which facilitated the spread to neighbouring Sierra Leone and Liberia through porous borders as well as Nigeria via a commercial airplane on 20 July. The World Health Organization (WHO) declared this EVD epidemic a Public Health Emergency of International Concern on 8 August 2014. The effective reproduction number, Rt, which measures the average number of secondary cases generated by a typical primary case at a given calendar time, can be helpful to understand the EVD transmission dynamics over time in affected countries as well as gauge the effect of control interventions. Values of $Rt<1$ indicate that the epidemic is in a downward trend. By contrast, an epidemic is in an increasing trend if $Rt>1$. In this study, we estimated Rt, in real time in order to assess the current status of the evolving outbreak across countries affected in 2014.

2. Methods

We analysed the cumulative case counts reported by the WHO as of 26 August 2014. Case counts are classified into three categories, i.e. confirmed, probable and suspected case according to diagnostic criteria of WHO. Two different sets of grouped data were analysed, i.e. (i) confirmed plus probable cases and (ii) the total number of reported cases (i.e. confirmed, probable and suspected cases). To estimate the Rt, we employed a mathematical model together with time- and country-specific incidence data. Using the so-called “next generation matrix”, we estimated the average number of secondary cases produced by a primary case at time t within single country and between two countries. We also computed the Rt for all countries (hereafter referred to as the ‘global’ estimate of the reproduction number) by further analyzing the matrix.

3. Results

Our estimates of the Rt for all countries reached levels below unity in April and May, but has appeared to be continuously above 1 since early June. Estimates of Rt using total case reports from June to July 2014, a period during which exponential growth of cases has been observed in Sierra Leone and Liberia, ranged from 1.4 to 1.7, respectively. Estimates of Rt in Sierra Leone and Liberia appeared to be consistently above 1.0. The estimates of Rt in Liberia reaching values up to 2.0 indicate that the outbreak could only be brought under control if more than half of secondary transmissions per primary case were prevented. The transnational spread per person appears to have been reduced over time, but our most recent model estimates still suggest a non-negligible number of secondary cases arising from transnational spread.

4. Discussion

Our statistical analysis of the reproduction number of EVD in West Africa has demonstrated that the continuous growth of cases from June to August 2014 signalled a major epidemic, which is in line with estimates of the Rt above 1.0. Our estimated reproduction numbers, broadly ranging from 1 to 2, are consistent with published estimates from prior outbreaks in Central Africa (e.g. the reproduction number for EVD has been estimated at 1.83 for an outbreak in Congo in 1995 and 1.34 in Uganda in 2000 prior to the implementation of control intervention). Our estimates of Rt below 2 indicate that the outbreak could be brought under control if more than half of secondary transmissions per primary case are prevented. Uncontrolled cross-border transmission could fuel a major epidemic to take off in new geographical areas (e.g. as seen in Liberia). Close monitoring of this evolving epidemic should continue in order to assess the status of the outbreak in real time and guide control interventions in the region.

4. 参考文献

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6. 用語解説：

実効再生産数…ある時刻 t において 1 人の感染者が生み出す 2 次感染者数の平均値を意味する．1 より低ければ感染者数は次第に減衰していくことを意味するが，R>1 は新規感染者数が次第に増えている（流行が拡大傾向である）ことを意味する．

実効再生産数を R と書き，仮に R>1 であるとする．ここで全ての接触のうち比率 p だけが隔離などによって防がれたとすると，残りの(1-p)の間だけで伝播が起こるので隔離下の再生産数は(1-p)R となる．これが 1 を下回れば感染者数を減少せしめられる．その条件を p について解くと，p>1-1/R となる．例えば R=2 であれば，p>0.5 以上の感染性を持つ接触が防がれれば感染者数を減らしめることが可能である．

謝辞

本研究は，JSPS 科研費 26700028，厚生労働科学研究委託費（H26-新興実用化-一般-016）および公益財団法人住友電工グループ社会貢献基金 2013 年度学術・研究助成の助成を受けて行なわれました．ここに深謝いたします．