Contagion: a worthy entrant in the outbreak film genre

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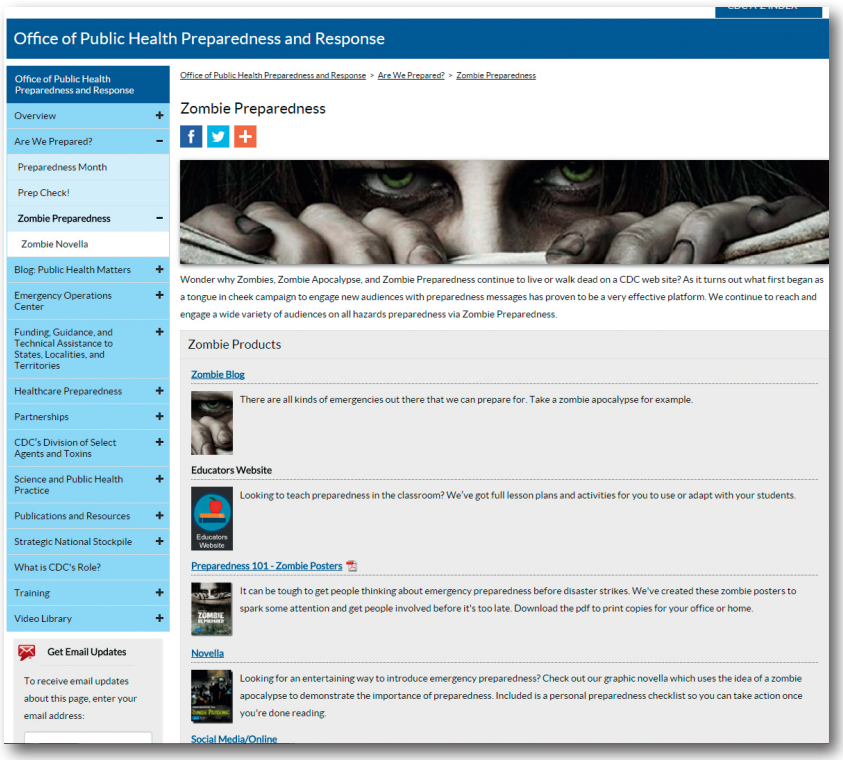
As researchers working in the fields of genomics, infection and epidemiology, we chose to write about *Contagion* for this issue. It wasn't much of a choice, a quick bit of Internet research confirmed that there aren't many films about infectious diseases, outbreaks and epidemiology, with the exception of the fairly terrible *Outbreak* (1995), and the 1970s-tastic sci-fi thriller *The Andromeda Strain*. What we do have plenty of are zombie flicks, and the parallels to outbreaks have been well recognized. Often starting with a virus or uncharacterized pathogen, zombie films exploit the nature of contagion as ever greater numbers of the population are infected, usually with the film's heroic (*World War Z*) or hapless (*Shaun of the Dead*) protagonist tasked with rescuing humanity, or at least staying alive.

Using zombies as a teaching tool

Films like *28 Days Later*, *World War Z* and *Resident Evil* – while enjoyable action tales – don't give any more than a passing glance at the pathogen, either in the form of an expository look at how the zombie apocalypse started, or in the hero's attempt to locate a cure or vaccine. Nevertheless, they and other members of the zombie film canon have inspired movie watchers to spend countless evenings sitting around, plotting zombie survival strategies. Load up on food and swim to a remote island? Build a chainsaw-lined fortress? Hole up in a fortified mall and wait it out? Indeed, people's proclivity for zombie outbreak preparedness has, in fact, proved useful in the real world. In 2011, the Centers for Disease Control and Prevention (CDC) realized that zombies' cultural popularity could be leveraged for teaching the practical aspects of emergency preparedness. It began with what the CDC describes as a "tongue-in-cheek" engagement campaign, but grew into an effective platform now in its fourth year, with educational resources, social media campaigns and a graphic novella all aimed at encouraging people to think through their emergency planning – do they have water? A first-aid kid? An escape route? A family communication plan?

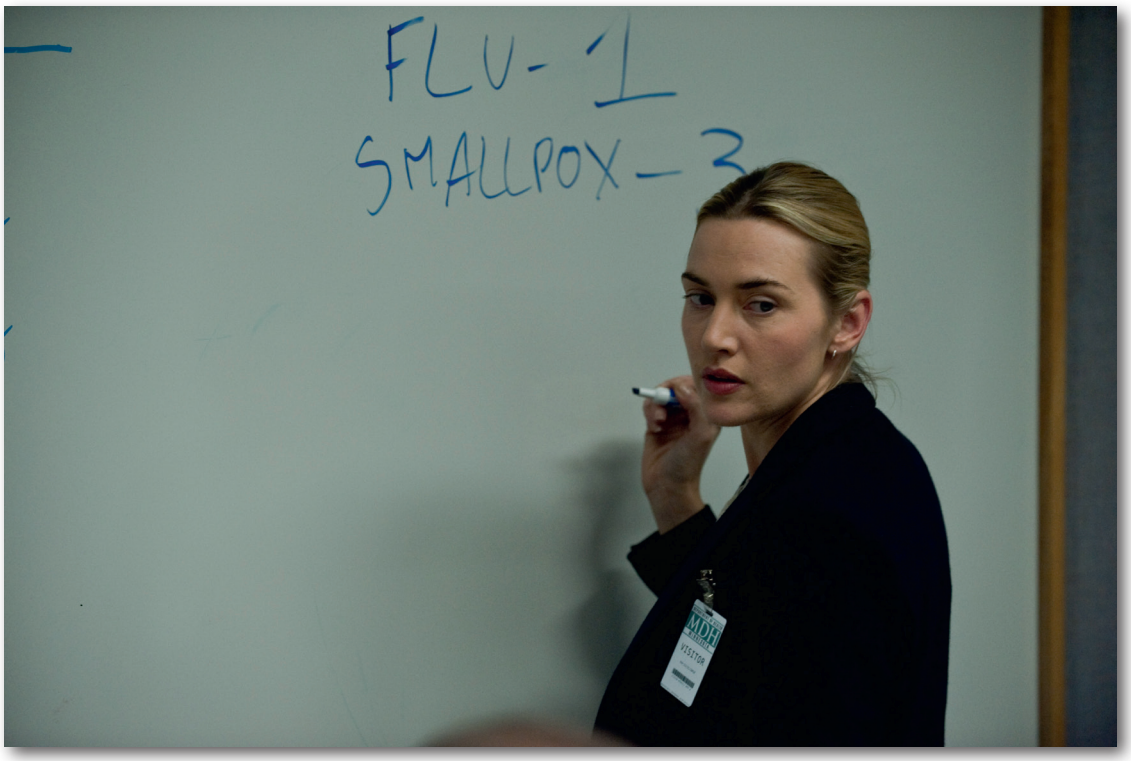
The success of CDC's zombie preparedness campaign raises an intriguing possibility – could pop culture, such as cinema, be used as a teaching tool to raise public awareness of more realistic threats? Could a good *Outbreak* film inspire society to pay more attention to pandemic planning activities, help them understand how an outbreak response unfolds around the world, and demonstrate the realities of developing and trialling new vaccines and therapeutics?



CDC Zombie preparedness website (www.cdc.gov/phpr/zombies.htm)

Mirroring recent outbreaks

Enter Steven Soderbergh's Contagion (2011), where a fictional infectious outbreak is treated solemnly and scientifically. The film mirrored recent scares such as severe acute respiratory syndrome (SARS), but perhaps in 2015 where the world is currently evaluating the aftermath of an Ebola pandemic and battling to control Middle East respiratory syndrome (MERS), it is more



Dr Erin Mears (Kate Winslet) in *Contagion* © Warner Bros. and other respective production studios and distributors

relevant than ever. The 2014–2015 West African Ebola outbreak made it clear that the public – and even many public health employees – had a limited understanding of the Ebola virus (and indeed all viruses), its transmission, and the nature of how various health agencies work – not always together – in an emergency situation. Reporters floated theories that a single mutation would aerosolize the virus (derided by experts as like an elephant suddenly growing wings).

Commentators wondered aloud where the World Health Organization (WHO) was and what role they were playing, and conspiracy theories abounded around stockpiles of experimental treatments and backroom decisions about who would receive treatments and who wouldn't. All of these themes were present in *Contagion*. This film traces the origin and rapid global spread of MEV-1, a fictional paramyxovirus that emerges from the Asian palm forests, infects Gwyneth Paltrow, and from there unleashes panic on the world. Thanks to the involvement of several virologists in the production, including famed virus hunters Ian Lipkin and Nathan Wolfe, and emerging threat surveillance gurus Larry Brilliant and Mark Smolinski, *Contagion* succeeds where *Outbreak* did not – in providing a somewhat sanitized but largely realistic overview of the emergence and spread of a deadly virus and public health's race against the clock to contain the threat and develop a vaccine. While *Contagion* doesn't have *Outbreak*'s frantic monkey chase scene and airborne helicopter battles, neither does these authors' careers in infectious disease research and public health (much to the disappointment of J.G., who will admit to being inspired to work in epidemiology having seen *Outbreak* as an impressionable teenager).

Reflecting real life research

Instead, *Contagion* captures the more routine aspects of epidemiology work – the paper notebooks and whiteboard sketches trying to link cases to each other, the frustration that comes with trying to keep a case count going across hundreds, if not thousands, of jurisdictions, and the constant querying around precisely whose budget things are to come out of.

Contagion gets a great deal right. The fictional virus, MEV-1, is borrowed from the Nipah virus (a newly emerged zoonosis that causes severe disease in both animals and humans) including the bat-to-pig-to-human 'spillover' event that launches the outbreak, and the SARS coronavirus, which, like its celluloid cousin, used Hong Kong and its crowded apartment complexes and hotels as a stepping stone to global spread. The uncertainty in the early days of the outbreak is also clear, from the medical doctor who can't offer a diagnosis to the epidemiologist trying to calculate R_0, the virus' reproductive ratio to estimate the potential scale of the problem. Anyone working in public health

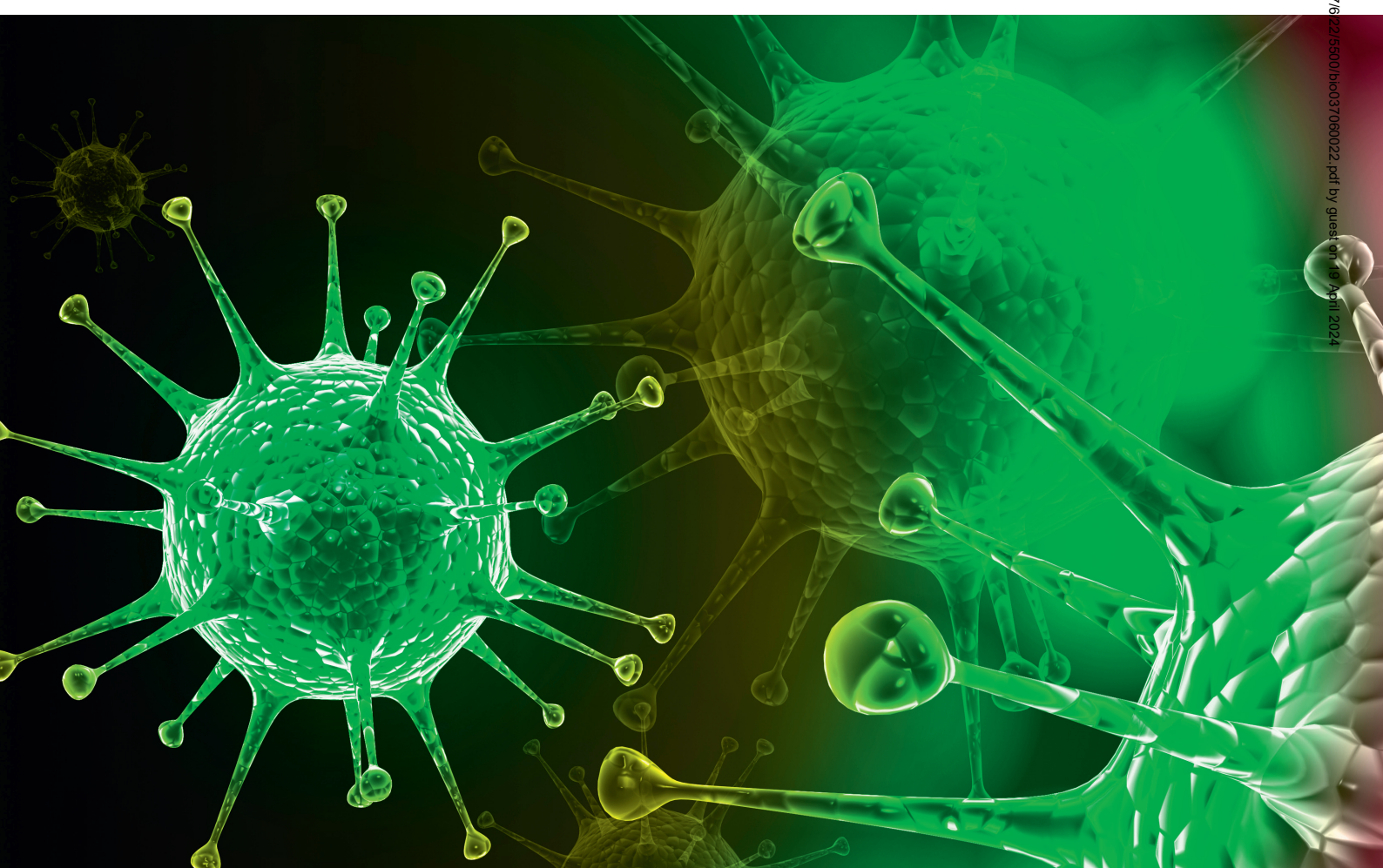
R_0 – the 'reproductive ratio'

R_0 is a tool that epidemiologists use to understand an infectious disease's potential to spread amongst a population. It describes the average number of people that one sick person will ultimately infect during an outbreak – a disease with an R_0 of 2, for example – something like the Ebola virus – is one in which every one sick person will go on to infect two more people. The R_0 of a disease isn't set in stone – it will vary over the course of an outbreak or epidemic and depends on characteristics of the host, pathogen and environment – but the general rule is that when R_0 is less than 1, the outbreak will eventually die out. Which disease has the highest R_0? Measles! One infected measles patient is estimated to give rise to 12–20 more secondary infections!

or government science will chuckle at the administrator who is mostly concerned with "whose budget will this come from?"

As in real life, this uncertainty manifests as fear amongst the public – their suspicions that the CDC is 'in bed' with big pharma, their misplaced belief in a sham remedy peddled over the Internet by an unscrupulous rumour-monger (played by Jude Law, channelling a kind of paranoid Julian Assange character), and the stampede at a pharmacy when a queue of people are told there's only a limited supply of the aforementioned remedy to go around. The current scandal of 'anti-vaxxers' and the misinformation they spread is relevant here.

On the other hand, there are several aspects of the story that don't ring true, though they largely represent the concessions one has to make in telling a complex scientific story in a concise, lay-friendly and action-packed way. Buzzwords are used – sequencing, receptor entry, case fatality ratio – and there's a tantalizing flash of a phylogenetic tree, but the actual process underlying much of the work in a pandemic, including the pivotal development and rigorous testing of the vaccine, is glossed over – understandable, given that much of it is grunt work like pipetting, waiting for a bioinformatics analysis to finish, or running endless permutations of a model and emailing a PDF full of scenarios around to one's colleagues. Similarly, the work of thousands of people is collapsed into a handful of characters. This is necessary if viewers are to keep who's who straight in their heads, but it is worth noting that were our planet to experience a pandemic affecting one in every 12 people, there would be more than two epidemiologists on the case (and – spoiler alert - if one of those epidemiologists died early in the outbreak and the other were kidnapped, we would certainly send replacements).



Plans for a sequel

In dreaming up the next great outbreak movie, one could imagine something that takes the best elements of *Contagion*, which provided a gentle introduction to key concepts such as R_0, molecular virological analysis and field epidemiology (along with bureaucracy, budgets and conspiracy theories) and updates the storyline to include the latest technological developments, but also the learnings from the recent Ebola outbreak. Instead of a virus that instantly works its way around the world, there'd likely be a slow burn in a part of the world where spillover events are more common. Given that surveillance is largely focused on the Gwyneths of the world and not the Guineans, the next pandemic virus will probably circulate undetected for some time before jumping on a flight to a more populous region. In line with this, our updated film would also show an early response that came from the ground up rather than the top down, with NGOs (non-governmental organizations) and in-community workers raising the alarm bells long before military trucks roll down the streets blaring orders, and focusing their immediate efforts on establishing care centres and not reviewing surveillance footage to determine who coughed on whom.

Our molecular story would also be different. Whereas *Contagion*'s infectious agent was initially a mystery, taking about a week to sequence and characterize in specialized CDC and academic labs, new technologies like the Oxford Nanopore DNA sequencer mean that with a small amount of preparation, clinical samples can be loaded onto a small, USB-powered sequencer that can read all of the nucleic acids – host and pathogen – present in a sample and quickly return a diagnosis. The technology has already been rolled out to analyse the Ebola virus in Guinea (theatlantic.com/science/archive/2015/09/ebola-sequencer-dna-minion/405466/), while other research groups have created software that reports the analysis results in real time, giving an easily readable 'instant diagnosis'.

The same sequencing technologies that allow us to diagnose a novel pathogen from a clinical sample can also be used to survey the organism's genetics in real time. Phylogenetic trees of outbreak samples can assist in identifying epidemiological patterns within the data, from geographical trends that reveal hotspot communities and cross-border spread, to individual person-to-person transmission events, including the role of highly contagious super-spreaders. A novel pathogen – especially a quickly mutating RNA virus – could be genetically monitored for the emergence of key mutations too. Though Contagion's premise of a single mutation suddenly doubling the R_0 of the virus is unlikely (but not entirely out of the realm of possibility for an airborne virus, as recent gain of function studies in highly pathogenic avian influenza have already shown), monitoring mutations might point to drift away from effective treatments and reveal quickly changing epitopes, with their implications for vaccine design and efficacy.

The question when it comes to the next great pandemic is not *if*, but *when*. Many experts predict a novel influenza virus to be the next great threat, but past pandemics have shown that the only thing we can expect is the unexpected. We can prepare, however, and preparation is as much about sensitizing the public to the possibility of a pandemic as it is developing public health emergency management plans. Pop culture is an effective tool for reaching the public, and a few more entries in the *Outbreak* film genre might go a long way to educating the public about what a pandemic might look like and what sort of response they can realistically expect. And it certainly won't involve monkey chases and helicopters. ■

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Dr. Jennifer Gardy is a Senior Scientist at the British Columbia Centre for Disease Control and a Canada Research Chair in Public Health Genomics at the University of British Columbia. Her research involves using genome sequencing to track outbreaks of infectious disease, and she is not ashamed to admit that seeing the film Outbreak as an impressionable teenager directly led to her pursuing microbiology and epidemiology as a career path. When not tracking outbreaks, she occasionally hosts science documentaries for Canadian television, and understands the many concessions filmmakers must make in telling a science story to the public.