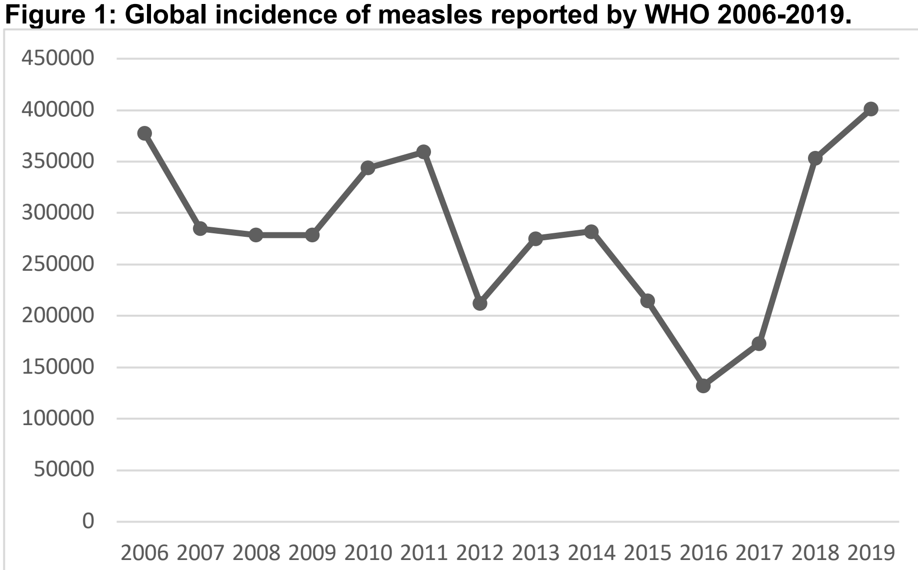
*Feedback from operational stakeholders who manage or respond to outbreaks is that they are often too busy to review literature or obtain relevant background information to assist them with acute response. Unlike a traditional analytical outbreak investigation report, **Watching Briefs** are intended as a rapid resource for public health or other first responders in the field on topical, serious or current outbreaks, and provide a digest of relevant information including key features of an outbreak, comparison with past outbreaks and a literature review. They can be completed by responders to an outbreak, or by anyone interested in or following an outbreak using public or open source data, including news reports.*

Watching brief	
Title	Global re-emergence of measles – 2019 update
Authors	Calin Fraser-Bell
Date of first report of the outbreak	Measles has been resurgent in all continents, with loss of elimination status in Albania, Czechia, Greece and the United Kingdom on August 29th 2019 (1). The United States narrowly escaped losing elimination status in October 2019 (2).
Disease or outbreak	Measles
Origin (*country, city, region*)	Measles is endemic in many low-income countries where low vaccine coverage and resulting low herd immunity leads to ongoing outbreak cycles (3). During outbreaks, international travellers may become infected and import measles to their country of origin on return (4). For example, an outbreak of over 600 cases in New York, USA in 2018-2019, which originated in Israel and the Ukraine, was imported by a traveller (5). Other countries with large measles epidemics include Romania, the Philippines, New Zealand, Madagascar, India and Brazil, though resurgence is global. In New Zealand, 3 clusters were genetically linked to the Philippines outbreak with two cases being recently returned from the Philippines, with 1414 total cases reported to date for 2019 (6, 7).
Suspected Source (specify food source, zoonotic or human origin or other)	Human origin, person to person transmission
Date of outbreak beginning	The outbreaks are ongoing.
Date outbreak declared over	Outbreaks are escalating. The WHO European region is currently in a measles emergency.
Affected countries & regions	*Countries which lost elimination status*: Albania, Czechia, Greece and the United Kingdom in August 2019 (8).

	Countries at risk of losing elimination status : New Zealand, USA (9). The USA narrowly escaped losing elimination status. *Nations with large epidemics, which never achieved elimination status*: Romania, Ukraine, Philippines, Democratic Republic of the Congo, Madagascar, India, Pakistan, Nigeria, Kazakhstan, Myanmar, Sudan, Angola (1, 9).
Number of cases (specify at what date if ongoing)	401,024 documented cases globally from 1 Jan-09 Sept 2019 (9). Approximately 1 in 10 cases is estimated to be recorded in WHO data.
Clinical features	Fever (>38C), conjunctivitis, cough, coryza, Koplik's spots, leucopoenia, eruptive rash. The incubation period is 7-18 days, with transmission being possible 24 hours before symptoms onset to four days after appearance of the rash.
Mode of transmission (dominant mode and other documented modes)	Measles is a respiratory-transmissible disease. Human to human transmission occurs through inhalation of infected aerosols (originating from an infected human) which is the primary method of transmission; contaminated ambient air can remain infectious for 2 hours. Direct contact with a contaminated surface or infected person can also result in transmission.
Demographics of cases	In nations which have achieved elimination status, infants too young to be vaccinated as well as migrants and adults who are under-vaccinated or unvaccinated are most at risk (10). For nations with ongoing endemic transmission, childhood infection is usual and results in immunity; 52% of cases in the Philippines (January -Jun 2019) were <5 YO (1). Similarly 8111 of Kazakhstan's 9441 cases from Jan-Sept 9 2019 occurred in children <1 YO (1).
Case fatality rate	Case fatality is higher in low income countries, where malnutrition and other illness may predispose to severe outcomes. Vitamin A deficiency is a risk factor for severe measles. A notably high fatality rate of 13.7 per 1000 cases has been recorded for January- 11th May 2019 in the Philippines (11). In the USA fatality rates are approximately 1-2 per 1000 cases (2).
Complications	Complications are more common in children <5 years and adults >20 years, they include pneumonia, bronchitis, croup laryngitis, otitis media, diarrhoea and vomiting. Less common complications include hepatitis, meningitis, encephalitis, miscarriage and stillbirth. Subacute sclerosing panencephalitis is a rare and fatal complication that develops 7-10 years after the initial infection. Measles also results in impaired B-cell immunity and an "immune paresis" even after recovery from measles, which puts people at risk of other infections (11).
Available prevention	An effective and safe vaccine is available to prevent measles, using a live attenuated strain of the virus. The vaccine has high efficacy (93%) after one dose, and 2 doses are recommended to ensure 97% protection (12). The vaccine can also be given as post-exposure prophylaxis in outbreaks. In high income countries, a two-dose schedule at 12 months and 18 months is usual (13). In countries with endemic measles and risk of infection in babies <12 months, the first dose may be given at 9 months (14). The vaccine is less

	effective given at 9 months but can be justified if the risk of disease is high in infants <12 months. Given the high R_0 of measles, herd immunity of at least 93-95% is required to prevent transmission. Good surveillance and monitoring are also required. Predictive models can identify areas at risk of measles outbreaks (15). Normal human immunoglobulin G (IgG) contains high levels of measles antibodies and can also be used for people exposed to measles.
Available treatment	No specific treatment is available, symptoms may be treated with paracetamol and fluid replacement. Vaccines and immunoglobulin can be administered during an outbreak to prevent further cases. Vitamin A should be given to children with measles in countries where vitamin A deficiency is common.
Comparison with past outbreaks	Globally, 2006 was the first year where <500 000 cases were reported since WHO monitoring was established (16). Since 2006 the 2017-2019 period has featured the highest upwards fluctuation of measles incidence recorded (Figure 1) (16). **Figure 1: Global incidence of measles reported by WHO 2006-2019.**  ***Data sourced from WHO measles reports, 2019 data based on monthly data reported to WHO as of August 2019 (16).** **Total measles cases reported by WHO were: 2006 – 377 576, 2007 – 285 031, 2008 – 278 751, 2009 – 278 637, 2010 – 343 806, 2011 – 359 332, 2012 – 212 376, 2013 – 275 307, 2014 – 282 078, 2015 – 214 816, 2016 – 132 413, 2017 – 173 457, 2018 – 353 236, 2019 (reported as of Aug 9th) – 401 024.** The global reductions in incidence commencing in 2006 were due to the concerted effort to establish 2-dose vaccination programs in nations with

	adequate resources. Single-dose vaccination programs were pursued and funded in developing nations through the EPI program. The global incidence of measles is at its highest level since 2006. Throughout 2006 the Ukraine was traced to be the source of 17 imported cases in other countries, with Thailand being the source of 13 (n=126) cases throughout Europe (17). 4% of total European cases were shown to have been imported for 2006 (17). During January-June 2018, 24% of European cases had their importation status known (n= 11 171), 72% of which were reported by the United Kingdom and primarily imported from Romania and the Ukraine (18). The increase in tracing source countries is largely representative of the efforts afforded to achieve measles elimination in the UK since 2006, which was achieved in 2017, and lost in 2019. In 2006 three measles genotypes were associated with epidemics and prolonged outbreaks: D4, D6 and B3. D4 and B3 were both imported from endemic Asian and African nations. Nine total measles genotypes were identified in the European region: D4, D6, B3, B2, D5, D8, D9, G2 and H1 (19). Identical B3 genotypes were recorded in the USA, Canada and Mexico, shown to be originating from Kenya (20). The primary strains responsible for the current resurgence of measles are D8 and B3. From August 2018 to July 2019 Genotype D8 was found to be the cause of most measles cases in USA and Europe; cases in Canada were shown to originate in Pakistan, Thailand and Cambodia (1, 21). B3 and D8 were the imported strains that resulted in endemic transmission (21). B3 and D8 were both present in SEA and were recorded throughout the region (1). D8 spread endemically throughout India, Bangladesh, Nepal, Morocco and Oman, and was the main genotype along with B3 responsible for the Romanian outbreaks since 2016. Japan and most of Africa only featured B3 type measles for the period (1). B3 is currently the predominant measles genotype globally, and has been shown to be more transmissible then other strains in previous outbreaks and exhibit some vaccine resistance (22).
Unusual features	- The concurrent resurgence of measles in multiple regions of the world is unprecedented since a global reduction of incidence beginning in 1996 (23). - Multiple European nations including the UK have lost measles elimination status in 2019. - Differing genotype compositions of measles incidence are occurring in impacted regions, such as in Romania where imported strains were responsible for a large proportion of 2019 cases, despite ongoing endemic transmission (24) - lower protection from 2 doses of vaccine is observed for some measles genotypes, such as B3(25). B3 has also been shown to have higher pathogenicity than other genotypes in animal models (26).

Critical analysis	Since the advent of measles vaccine in 1971, measles incidence has declined globally and elimination has been achieved in several countries. The resurgence in countries which have elimination status is due to travel-related importation, pockets of under-vaccination, lack of adult catch-up vaccination and accumulation of non-immune people being exposed to infected individuals who have returned from or had contact with someone returning from international travel (27). Identifying at-risk and under-vaccinated populations is critical (28, 29). The reasons for under-vaccination vary internationally, but can be broadly linked to conflict, migration and lack of catch up vaccination and anti-vaccination. Groups who decline vaccination may have religious/spiritual or pseudointellectual motivations (30). The reasons for measles resurgence are complex. In the Ukraine and the Philippines, it is related to conflict. In the Philippines, additionally, there was loss of public confidence in vaccines following withdrawal of a failed dengue vaccine program (31). In the US, anti-vaccination groups and unvaccinated religious communities contribute to measles outbreaks. In a study of Australian measles cases, less than 20% of notified measles was in children of anti-vaccination parents.(32) There are also multiple examples of delayed diagnosis of measles in hospitals, often resulting in exposure of other patients in waiting rooms and resulting outbreaks. Having guidelines for triage of relevant clinical syndromes and asking travel history are relevant strategies in countries with elimination status. It is important that health workers at the front line are educated and made aware of triage protocols or missed diagnoses will occur. Although vaccination provides lasting immunity, the extent that vaccination wanes is largely unknown (33, 34). Changing vaccination policies can leave age cohorts that do not receive catch-up vaccination nonimmune (35). A complete vaccination strategy needs catch-up vaccination programs targeted to under-vaccinated groups (34). There is also a reduction of wild-type measles virus exposures associated with growing cohorts of vaccinated individuals in populations (3). Infants of parents who have vaccine-induced immunity may be at higher risk compared to those born to naturally immune mothers (36). Measles eradication will be much more difficult than smallpox eradication because of the high infectivity of measles due to the much higher R0 of measles. We live in a globalized, interconnected world, and the resurgence of measles in Europe, Asia and New Zealand is globally concerning. The size of the current outbreak in NZ, given the small population of NZ, is a major concern. In Australia, the most frequent travel route is to and from New Zealand (32). In Australia, a vaccination rate of >93% for measles is drawn from the childhood immunization register and does not capture unvaccinated or under-vaccinated older children or adults (34). It is deeply concerning that the UK and three other European countries lost WHO measles elimination status in August this year, with the US looking like it just escaped losing elimination status. This highlights the importance of

	maintaining high vaccination coverage globally and locally. In a study of measles cases in Australia, almost 60% had travelled overseas (mainly for holidays), a large proportion were adults (50%) and adolescents, and <20% were young children of vaccine-refusers (32). To regain control of measles, high vaccination rates are required nationally and globally. Travel vaccination and pre-travel health advice are also important, as travel is the main route of importation of measles. Importation and transmission of measles in high income settings cannot be prevented without a global eradication focus (3).
Key questions	1. The complete phylogeographical analysis of the current global resurgence of measles in Europe is not available but would be informative and may help predict areas of risk. 2. More research is needed into whether some strains of B3 currently circulating have vaccine resistance. 3. The role of potentially long-term waning of vaccine-induced immunity needs to be further studied. 4. Research is required to understand the nature of herd immunity gained with an increased ratio of vaccine induced immunity to naturally acquired immunity in populations. 5. Better surveillance and data collection need to be explored with a current 1 in 10 measles cases estimated to be captured by disease surveillance, with high regional fluctuations in data quality. 6. Some countries such as India and Indonesia have large cohorts of unregistered births,(37, 38) resulting in unvaccinated infants and overestimation of vaccination coverage. Addressing vaccination coverage in areas with low birth registration and access to vaccines is another major concern for eradication of measles.

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