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Novel coronavirus 2019-nCoV: early estimation of epidemiological parameters and epidemic predictions

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Key findings

- We estimate the basic reproduction number of the infection (R_0) to be significantly greater than one. We estimate it to be between 3.6 and 4.0, indicating that 72-75% of transmissions must be prevented by control measures for infections to stop increasing.
- We estimate that only 5.1% (95%CI, 4.8–5.5) of infections in Wuhan are identified, indicating a large number of infections in the community, and also reflecting the difficulty in detecting cases of this new disease. Surveillance for this novel pathogen has been launched very quickly by public health authorities in China, allowing for rapid assessment of the speed of increase of cases in Wuhan and other areas.
- If no change in control or transmission happens, then we expect further outbreaks to occur in other Chinese cities, and that infections will continue to be exported to international destinations at an increasing rate. In 14 days' time (4 February 2020), our model predicts the number of infected people in Wuhan to be greater than 190 thousand (prediction interval, 132,751 to 273,649). We predict the cities with the largest outbreaks elsewhere in China to be Shanghai, Beijing, Guangzhou, Chongqing and Chengdu. We also predict that by 4 Feb 2020, the countries or special administrative regions at greatest risk of importing infections through air travel are Thailand, Japan, Taiwan, Hong Kong, and South Korea.
- Our model suggests that travel restrictions from and to Wuhan city are unlikely to be effective in halting transmission across China; with a 99% effective reduction in travel, the size of the epidemic outside of Wuhan may only be reduced by 24.9% on 4 February.
- There are important caveats to the reliability of our model predictions, based on the assumptions underpinning the model as well as the data used to fit the model. These should be considered when interpreting our findings.

Abstract

In December 2019, a novel coronavirus (2019-nCoV) is thought to have emerged into the human population in Wuhan, China. The number of identified cases in Wuhan has increased

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rapidly since, and cases have been identified in other Chinese cities and other countries (as of 23 January 2020).

We fitted a transmission model to reported case information up to 21 January to estimate key epidemiological measures, and to predict the possible course of the epidemic, as the potential impact of travel restrictions into and from Wuhan.

We estimate the basic reproduction number of the infection (R_0) to be 3.8 (95% confidence interval, 3.6 and 4.0), indicating that 72-75% of transmissions must be prevented by control measures for infections to stop increasing. We estimate that only 5.1% (95%CI, 4.8–5.5) of infections in Wuhan are identified, and by 21 January a total of 11,341 people (prediction interval, 9,217–14,245) had been infected in Wuhan since the start of the year. Should the epidemic continue unabated in Wuhan, we predict the epidemic in Wuhan will be substantially larger by 4 February (191,529 infections; prediction interval, 132,751–273,649), infection will be established in other Chinese cities, and importations to other countries will be more frequent. Our model suggests that travel restrictions from and to Wuhan city are unlikely to be effective in halting transmission across China; with a 99% effective reduction in travel, the size of the epidemic outside of Wuhan may only be reduced by 24.9% on 4 February.

Our findings are critically dependent on the assumptions underpinning our model, and the timing and reporting of confirmed cases, and there is considerable uncertainty associated with the outbreak at this early stage. With these caveats in mind, our work suggests that a basic reproductive number for this 2019-nCoV outbreak is higher compared to other emergent coronaviruses, suggesting that containment or control of this pathogen may be substantially more difficult.

Background and current epidemic situation

On 31 December 2019, Chinese authorities alerted the World Health Organization (WHO) to an outbreak of pneumonia of unknown aetiology in Wuhan City, Hubei Province, China. A novel strain of coronavirus (2019-nCoV) was subsequently isolated from a patient on 7 January 2020 (Tan *et al.* 2020). Most cases from the initial cluster had epidemiological links with a live animal market (Huanan South China Seafood Market), suggesting a possible zoonotic origin (World Health Organization 2020a). However, the definitive source of the virus is unknown. Infections in family clusters as well as in healthcare workers confirm the occurrence of human-to-human transmission, though the extent of this mode of transmission is unclear. On 21 January 2020, the WHO suggested there was possible sustained human-to-human transmission (World Health Organization 2020b).

As of 22 January 2020, over 600 cases have been confirmed, of which 444 are from Hubei province (New York Times 2020a). Cases with travel history to Wuhan have also been reported in other Chinese provinces, including large cities such as Beijing, Shanghai and Shenzhen, as well as other countries, including Thailand (n=4), Japan (n=1), South Korea (n=1), Taiwan (n=1), Hong Kong (n=2), Macau (n=2) and the United States (n=1). Presenting symptoms of cases reported include fever, cough, and shortness of breath (World Health Organization 2020c). Pneumonia, severe acute respiratory syndrome and

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kidney failure have been reported in severe cases. Seventeen deaths have been reported from Wuhan, the majority were elderly or had underlying health conditions (Hong Kong Centre for Health Protection 2020).

Current clinical and epidemiological data are insufficient to understand the full extent of the transmission potential of the epidemic. This comes at a time when there is a substantial increase in travel volume within as well as in and out of China around the Lunar New Year on 25 January 2019. Over 3 billion passenger journeys were predicted for the period between 10 January and 18 February (CGTN 2020), which could significantly increase the spread of the virus.

Domestic and international connectivity of Wuhan

Wuhan is a city of more than 11 million residents and is connected to other cities in China via high-speed railway and frequent commercial airline flights. There were 670,417 passenger bookings departing Wuhan made during January 2017, the top destinations being Shanghai (53,214 bookings), Beijing (51,066 bookings) and Kunming (40,120 bookings) (OAG 2015); Figure 1. While the majority of air travel departing Wuhan is domestic (87.2% of bookings, Jan 2017), Wuhan is connected internationally through both direct and indirect flights (Bogoch *et al.* 2020).

Transmission model

We fitted a deterministic SEIR metapopulation transmission model of infection within and between major Chinese cities to confirmed cases of 2019-nCoV in Chinese cities and cases reported in other countries (see Methods Supplement). We modelled the period from 1 January 2020 when local authorities closed the wet market implicated as the zoonotic source of human infection (World Health Organization 2020a). We only considered human-to-human transmission in our model, and made the assumption that following the closure of the market, no further zoonotic infection contributed to the epidemic dynamics. Coupling between cities followed daily-adjusted rates of travel estimated from monthly-aggregated full itinerary passenger booking data for January 2017, accessed from OAG Traffic Analyser database (OAG 2015), assuming that travellers are drawn randomly from the origin population. We estimated the transmission rate and the recovery rate (the inverse of the infectious period). We assumed that the incubation period was 4 days, based on an estimate for SARS, a related coronavirus (Lessler *et al*. 2009). We also estimated the ascertainment rate within Wuhan, and the initial number of human infections present in Wuhan when the market was closed. Cases in Chinese cities and other countries reported as of 21 January 2020 were used for fitting. Fitting was achieved by predicting the number of infections in all Chinese cities and other countries having onset between 1 and 21 January 2020, and maximizing the likelihood using the *optim* function in the R statistical language (R Core Team 2019).

Epidemiological parameter estimates

We estimated the transmission rate within Wuhan, β, to be 1.07 d^{-1} (95%CI, 1.06–1.09), while we found the infectious period to be 3.6 days (95%CI, 3.6–3.6). We calculated the basic reproduction number, R_0, of the infection to be 3.8 (95%CI, 3.6–4.0), higher than the

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average of SARS estimated from outbreaks during the 2003 epidemic (World Health Organization 2003; Lipsitch *et al.* 2003). This estimate of $R_0$is significantly greater than 1, the epidemic threshold, providing evidence that sustained human-to-human transmission is occurring in China, and further suggests that a concerted effort will be required to control the outbreak.

We estimated that the ascertainment rate in Wuhan is 5.1% (95%CI, 4.8–5.5), reflecting the difficulty in identifying cases of a novel pathogen. Given the generally good accessibility to healthcare in China, this suggests that the majority of infections may be mild and insufficiently serious for individuals to seek treatment. However, it is worth noting that a number of identified cases have died (Centre for Disease Control and Prevention 2020) and that the true case fatality rate has yet to be estimated accurately. We also estimated the size of the epidemic in Wuhan at the time of the market closure to be 24 individuals (95%CI, 22–25). Our estimates of epidemiological parameters are sensitive to our assumption regarding the length of the incubation period; see Figure 2.

Epidemic forecasts

Using our parameterised transmission model, we simulated the impact of an ongoing outbreak in Wuhan to seed infections and outbreaks in other cities of China, and to generate infection in travellers to other countries, through airline travel originating in China. We stress that these projections make strong assumptions: that no control interventions are instigated; that the key epidemiological variables driving epidemic dynamics remain constant; that travel behaviour within China and to the rest of the world continues as per our mobility estimates; finally, we only consider travel by air, and do not include land transportation, particularly via trains.

We estimate that on 21 January 2020, in Wuhan there were 3,493 currently infected individuals (prediction interval, 3,050–4,017), and that a total of 11,341 people (prediction interval, 9,217–14,245) had been infected since the start of the year. We also estimate that there had been 115 infections (prediction interval, 102–131) in other locations of China since the start of the year. For comparative purposes, we estimate the number of people infected in Wuhan from 1 January to 18 January was 4,764 (prediction interval, 3,969–5,817); this is similar to other published estimates (Imai *et al*. 2020) and highlights the estimated rapid growth of the epidemic.

Should the epidemic continue unabated in Wuhan, our model predicts that in 14 days' time (4 Feb 2020) the epidemic in Wuhan will be substantially larger (191,529 infections; prediction interval, 132,751–273,649); see Figure 3A and Table 1. Infected travellers to other Chinese cities will initiate outbreaks in those cities, and that outbreaks will be ongoing in a number of cities, the largest of which will be in Shanghai, Beijing, Guangzhou, Chongqing and Chengdu (Figure 3B and Table 1). By 4 February, there will be an elevated risk of importations into other countries, most notably to Thailand (average of 15.0 imports d^{-1}), Japan (7.8), Taiwan (6.3), Hong Kong (5.8); South Korea (5.5), USA (4.5), Malaysia (4.1), Singapore (3.2), Australia (2.9) and Vietnam (2.7); see Figure 3C.

Effectiveness of travel restrictions from/to Wuhan

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From 23 January 2020, Chinese authorities will restrict travel into and from Wuhan by restricting air, rail and road access (New York Times 2020b), a public health measure unprecedented in scale. We explored the potential impact of a reduction in travel from and to Wuhan, by reducing the appropriate airline traffic by 50%, 80%, 90%, 95% and 99%. Our model predicts that these reductions in travel results in 12.6%, 20.1%, 22.6%, 23.9% and 24.9% reduction in infections, respectively, elsewhere in China by 4 February. Our prediction is In line with other modelling studies of travel restrictions: reducing travel only serves to delay the epidemic reaching other locations, rather than suppressing the spread entirely (Figure 4). It is important to note that as our model only considered air travel, we do not consider the potential impact of travel restrictions relating to land transportation.

Comparison of transmissibility with SARS and MERS

Our estimates of the reproductive number for this novel coronavirus are higher than most estimates reported for SARS and MERS-CoV, but similar to some estimates from subsets of data in the early period of SARS. For the SARS coronavirus, estimates ranged from 1.1 to 4.2 with most estimates between 2 and 3 (Bauch *et al*. 2005). These estimates represent a range of methods and settings. Some estimates come from data that mixes time periods before and after control. Estimates of R_0 also varied based on assumed serial intervals (e.g. Lipsitch *et al*. (2003) estimated R_0 ranging from 2.2 to 3.6 for serial intervals of 8 to 12 days (9). Bauch *et al.* reviewed sources of variation in basic reproductive numbers of SARS and noted that those locations in which outbreaks occurred, R_0 was approximately 3. Estimates from MERS-CoV were uniformly lower, with estimates from Saudi Arabia having a mean less than 1 (~0.5) but exhibited large temporal variability with increases in some periods of time particularly in healthcare settings (Cauchemez *et al*. 2016).

A comparison of the efficiency of transmission in this outbreak and in SARS outbreaks can be seen as well in simple comparisons of doubling times in each outbreak. In SARS, doubling times varied from 4.6 days to 14.2 days depending on setting (doubling time, Td=6.0 (1358 over 63 days, Singapore), Td=4.6 (425 over 41 days, Hong Kong), Td=14.2 (7919 over 185 days, overall)) (Lipsitch *et al.* 2003). Using the counts of confirmed cases as of 22 January (444) and assuming the outbreak began on 15 December 2019, we find a doubling time of 4.1. However, using our estimates of the size of the outbreak on 1 and 21 January (24 and 11,257 people respectively) we estimate a doubling time of 2.3. We note this is similar to estimates from the SARS outbreak in Hong Kong (Lipsitch *et al.* 2003).

Limitations

Our model necessarily makes a number of assumptions. Our estimates of the reproductive number of this novel coronavirus are tied to the specific time period and data analysed here, and this measure may change substantially over the course of this outbreak and as additional data arrives. Additionally, the spatial component of our model is dependent upon only airline travel; the model does not include rail and road transportation, so we may underestimate local connectivity. Our modelling of Wuhan travel restrictions does not account for stochastic effects, and so may underestimate the potential effect of travel restrictions as a consequence. We also do not attempt to account for any dynamic changes in control or other factors than may influence transmission, nor changes in surveillance and reporting effort.

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Earlier novel coronavirus (SARS and MERS-CoV) outbreaks found evidence for substantial heterogeneity in reproductive numbers between individuals (Cauchemez *et al.* 2016; Bauch *et al.* 2005; Chowell *et al.* 2004). In our analysis, we assume that there is little heterogeneity in reproductive numbers and this assumption may change our estimated reproductive number. Additionally, R_0 estimates tend to be reduced as case information accumulates, though control measures may also be introduced during these periods. Our estimate of R_0 may also reflect the dynamics of surveillance effort and reporting rather than just the dynamics of the epidemic.

A key uncertainty of this outbreak is when it started. We have chosen to model transmission from 1 January onwards. Surveillance in China and elsewhere only started once the outbreak was identified in Wuhan. Had the outbreak started much earlier, and both domestic and international infections occurred before January and in early January (while surveillance was ramping up), our estimates of the reproductive number would mostly decrease.

A threat to the accuracy of these projections is if a substantial proportion of infection has been due to multiple exposures to animals that has been curtailed in some way. These data may also represent a period of high transmission (due to favourable seasonal conditions, stochastic variation or selection bias in detecting large clusters of transmission) that will not be sustained over long periods of time.

Summary

We are still in the early days of this outbreak and there is much uncertainty in both the scale of the outbreak, as well as key epidemiological information regarding transmission. However, the rapidity of the growth of cases since the recognition of the outbreak is much greater than that observed in outbreaks of either SARS or MERS-CoV. This is consistent with our higher estimates of the reproductive number for this outbreak compared to these other emergent coronaviruses, suggesting that containment or control of this pathogen may be substantially more difficult.

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Figures

Figure 1. Connectivity of Wuhan to other cities and provinces in mainland China, based on total commercial airline traffic from Wuhan in January 2017. Traffic is based on the number of departing bookings.

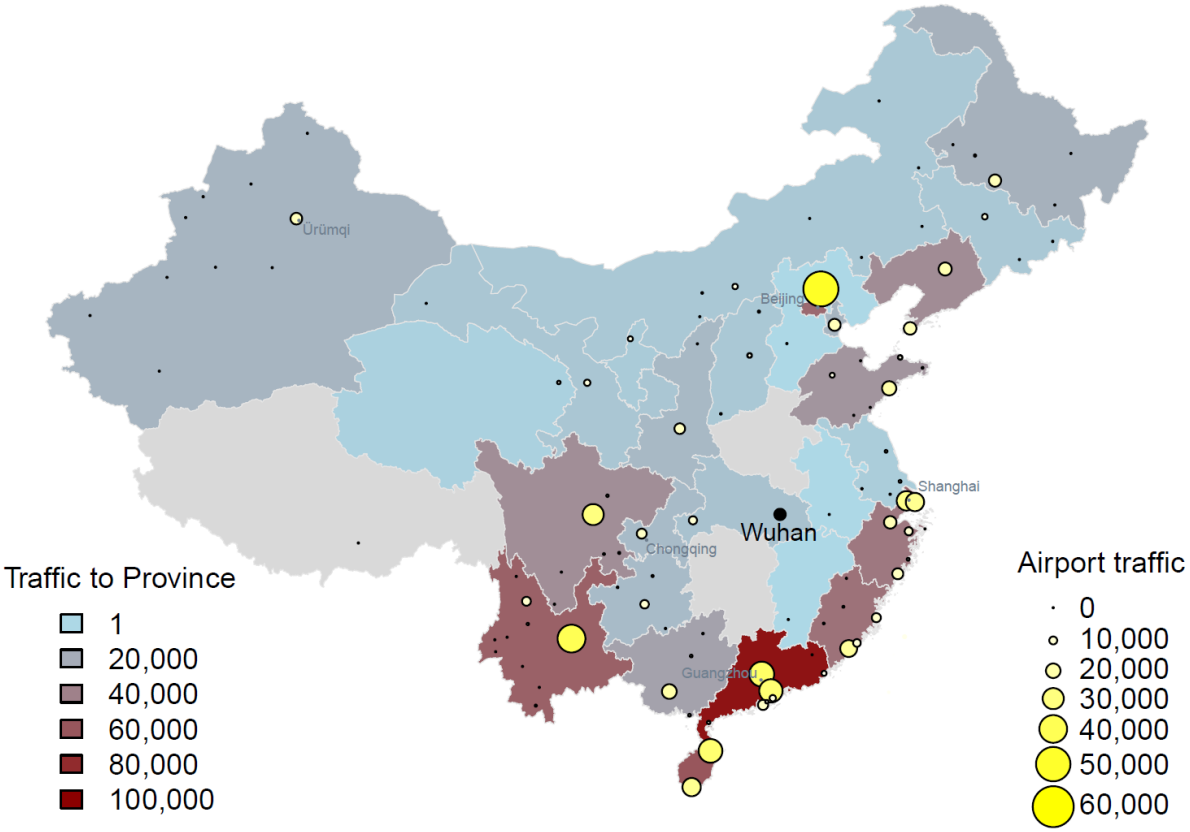
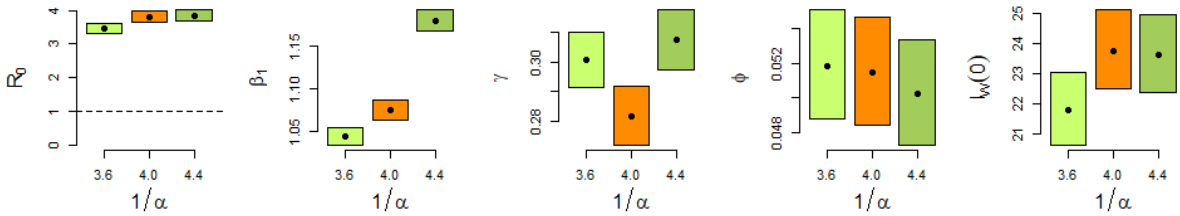


Figure 2. Sensitivity of parameter estimates to assumed incubation period. Boxes represent the 95% confidence intervals around point estimates (black dots), as the incubation period is varied.



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Figure 3. Epidemic predictions for (**A**) Wuhan, (**B**) selected Chinese cities and (**C**) selected countries. Uncertainty in estimated model parameters is reflected by 500 repeated simulations with parameter values drawn randomly from the distribution of fit estimates.

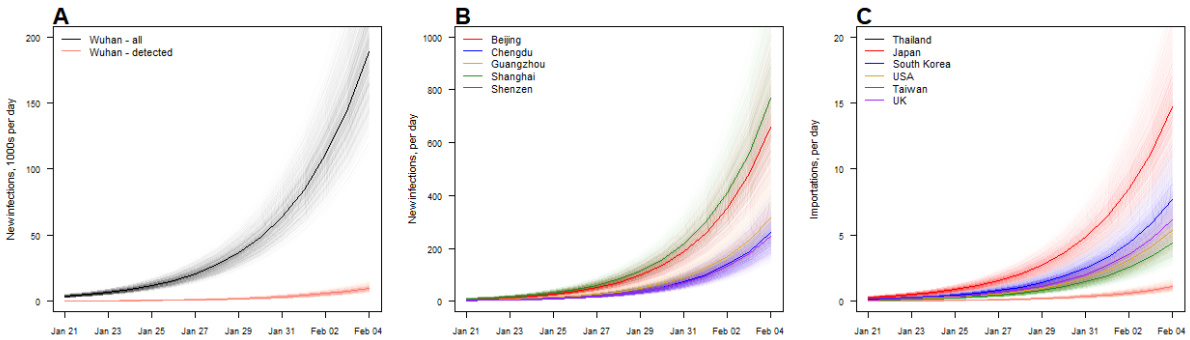
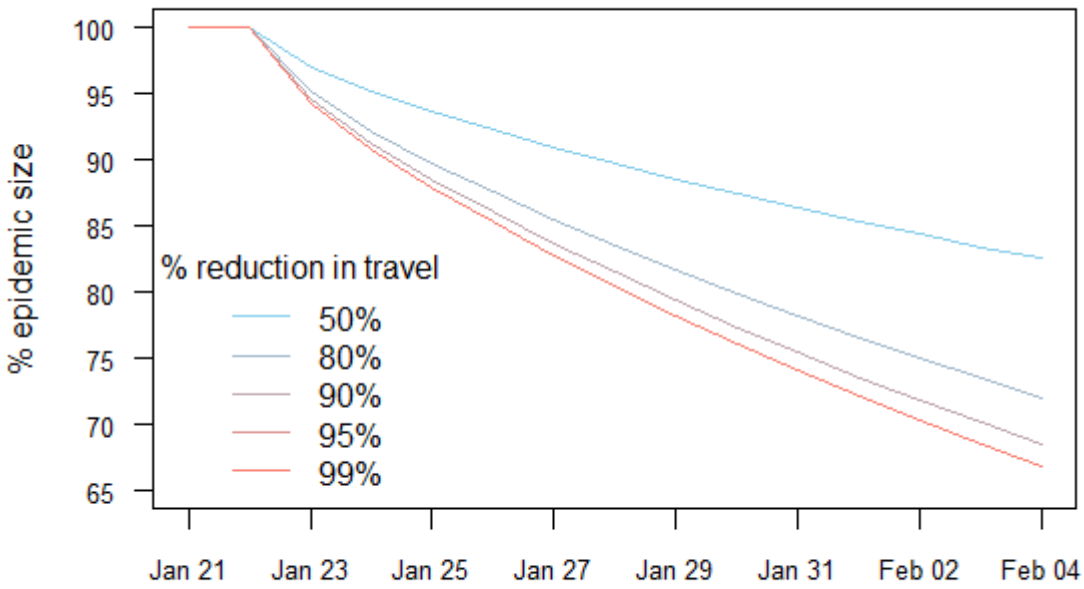


Figure 4. Effect of imposing travel restrictions from/to Wuhan on 23 Jan 2020 onwards. Here, we compare increasing the predicted number of infections across cities of mainland China



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Tables

Table 1. Predicted epidemic sizes in selected cities on 4 February 2020 assuming no change in transmissibility from current time to 4 February.

City	Epidemic size			Detected cases (assuming 5.1% ascertainment rate)		
	mean	2.5% quantile	97.5% quantile	mean	2.5% quantile	97.5% quantile
Wuhan	250,370	164,602	351,396	12,884	8,470	18,082
Shanghai	915	590	1,308	47	30	67
Beijing	786	507	1,124	40	26	58
Guangzhou	377	244	540	19	13	28
Chengdu	308	199	440	16	10	23
Shenzhen	293	189	420	15	10	22
Chongqing	290	187	414	15	10	21
Kunming	186	120	266	10	6	14
Tianjin	179	116	256	9	6	13
Xi'an/Xianyang	175	113	251	9	6	13
Harbin	124	80	177	6	4	9
Qingdao	124	80	177	6	4	9
Hangzhou	119	77	170	6	4	9
Shenyang	104	67	148	5	3	8
Nanning	103	66	147	5	3	8

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