Supplymentary Material

Appendix A: Concerns on the SAPHIRE model proposed by Hao et al. (2020) (*1*)

The SAPHIRE model included 7 compartments susceptible (S), exposed (E), presymptomatic infectious (P), ascertained infectious (I), unascertained infectious (A), isolation in hospital (H), and removed (R). For ease of understanding, R was suggested understanding as the loss of transmissibility pathologically to be distinguished from H. An individual in S would be infected by individuals in P, I, or A with different transmissibility to get into E and then P after a latent period. At the time point of symptoms onset, an individual transitioning from P to I or A depending on whether they would be lab-confirmed in the future, and the ascertainment rate (r) is the ratio that a patient would be lab-confirmed. For a case to be lab-confirmed, the patient must be both symptomatic and testing positive, which means individuals in I must be symptomatic, while those who were in A could be asymptomatic and their symptoms onset stage was just a hypothetical one which was included in the model for simplicity. The individuals in A would then lose their transmissibility pathologically and transitioned into R. Meanwhile, individuals in I would either lose their transmissibility pathologically (R) before they got confirmed and isolated in hospital, which implies that a patient can be no longer infectious but still test positive or become isolated in hospital (H, lost their transmissibility physically) and eventually then lost their transmissibility pathologically (R). The parameters r and transmission rate (b) vary across five time periods based on key events (e.g., *Chunyun*, the period of intense travel preceding the Spring Festival) and containment interventions. Different from most of other dynamic models fitting number of confirmed diagnosis at time t, the numbers of individuals in all compartment in this model were not directly observable except in I where $I(t)$ is the number of lab-confirmed cases who reported their date of symptoms onset was on time t.

In consideration of the SAPHIRE model described as above, the following four aspects can be potentially improved:

1) The initial ascertainment rate r was estimated based on the assumption of perfect ascertainments in Singapore ignoring asymptomatic individuals which certainly gave an over-conservative estimate of r under the current model as mentioned in Hao et al. (2020). In addition, r should be a continuous function rather than a step function over the five time periods, see the justification in Appendix D.

2) The individuals in A could be very different including asymptomatic, mild cases, and severe cases as evidence by deaths of clinically confirmed cases reported in (*2*), it is hence not optimal to assign a same transmission rate to all individuals in A (note that the proposed transmission rate in A was identical to that of the presymptomatic infectious period P and was $\alpha = 55\%$ of that in I). At the beginning of the pandemic, the medical resources were overburdened. It was likely to have a larger fraction of patients with severe symptoms in A and thus the transmission rate would be close to that of I. When medical resources were replenished and strong screening and public awareness campaign were implemented, the remaining unascertained cases should mostly be asymptomatic or mildly symptomatic, and the transmission rate would be closer to that of P. See why this issue can not be easily resolved in Appendix D.

3) Though only the data of lab-confirmed cases were used in the SAPHIRE model, the isolation due to clinical diagnosis cannot be simply ignored in the model. As mentioned in Hao et al. (2020) the clinically diagnosed cases were excluded in the model. However, there were a significant number of cases in A of the SAPHIRE model who were not lab-confirmed but clinically confirmed and isolated in *fangcang* (square-cabin) hospitals in Wuhan during February 2020 and thus lost their transmissibility before they actually got into R, which implies that clinically-confirmed cases in A would have a faster rate to get into R than other cases in A (*3*).

4) The pre-determined symptomatic infectious period of $D_i = 2.9$ Days is questionable. The symptomatic infectious period D_i was the mean time from symptom onset to loss of transmissibility pathologically, and the value was calculated based on the claim that 44% of secondary cases were infected during the index cases' pre-symptomatic stage by He et al. (2020) (*4*). Regardless of whether such claim is correct (a matter arising paper to He et al. (2020) was published), this 44% of pre-symptomatic spread was estimated based on the confirmed cases with isolation measures outside Wuhan, which is certainly not appropriate to be used to estimate mean time from

symptom onset to loss of transmissibility pathologically. Furthermore, another defect in the calculation of D_i is the inconsistency in the study of Hao et al. (2020), where a constant infectiousness was assumed across the presymptomatic and symptomatic phases of ascertained cases in estimating D_i while in the meantime $\alpha = 0.55$ was used as the ratio of transmission rate of cases in P (presymptomatic) to that of in I (symptomatic). It is important to note that unlike other pre-determined parameters in the model, the value of D_i is quite crucial to the model estimates of interest, see Supplementary Table S1 in Appendix D for detail. Hence a more accurate choice of D_i is essential. It is worth to note that the clearance of all active infections in Hao et al. (2020) was predicted to occur on April 21 (April 8 to May 12), which was not consistent with the active cases detected in Wuhan in mid-May.

Appendix B: The modified SAPHIRE model

Inspired the SAPHIRE model in Hao et al. (2020), an improved dynamic model was proposed. The proposed model included 6 compartments: susceptible (S), exposed (E), presymptomatic infectious (P), infectious with significant symptoms (I), infectious without significant symptom (A), and removed (R). Note that patients in A could only transit to R by losing transmissibility pathologically while patients in I may reach R by either losing their transmissibility pathologically, isolating upon lab-confirmation, or isolating upon clinical diagnosis. Therefore, the transition rate from I to R is given by $D_i^{-1} + D_q^{-1} + D_c^{-1}$, where D_i and D_q are the period of the symptomatic infectious period and duration from illness onset to lab-confirmation; and D_c is the duration from illness onset to clinical diagnosis which varies at different time period (here let D_c equals to infinity and 10 days before and after February 2 in Wuhan).

Furthermore, it has been found that the transmissibility decays towards the end of infectious period, hence the assumption of a constant transmission rate b throughout compartment I and A might potentially lead to an overestimate of the effective reproduction number R_e in the early stages. A preliminary solution to this problem is to split I into IE (early stage of symptomatic infectious period with a higher transmissibility) and IL (late stage of symptomatic infectious period with a low transmissibility) and split A into AE (early stage of asymptomatic/mild infectious period with a higher transmissibility) and AL (late stage of asymptomatic/mild infectious period with a low transmissibility). The transition dynamics of these states are as follows:

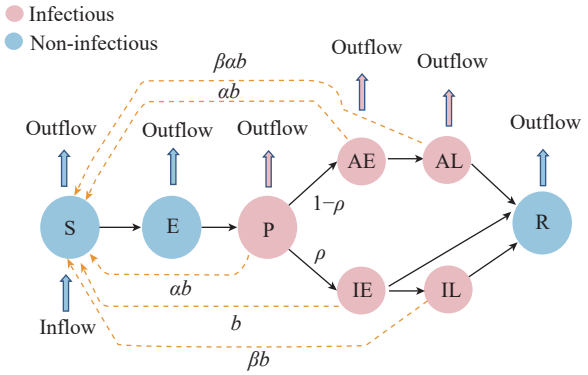
(1) Let $IE \to IL$ and $AE \to AL$ with a rate of $1/D_i^e = 1/3$ which corresponds to the setting in the SAPHIRE model, while $IL \to R$ and $AL \to R$ with a rate of $1/D_i^l = 1/7$. Thus, the expectation of the symptomatic infectious period would be $3 + 7 = 10$ days which is consistent with the choice of $D_i = 10$ days.

(2) Individuals in IE have a transmission rate of b and individuals in AE have a transmission rate of αb.

(3) Individuals in IL have a transmission rate of $\beta_i b$ and individuals in AL have a transmission rate of $\alpha\beta_i b$, where $\beta_i, \beta_a \in [0, 1]$ are the reduction factors of transmissibility in late stage and are unknown parameters to be inferred in the model.

Such modifications would grant us even better compartment homogeneity. See Supplementary Figure S1 for model illustration.

The ODE system of the above model is as follow:



SUPPLEMENTARY FIGURE S1. Transmission dynamics of COVID-19 in Wuhan for modified SAPHIRE model .

$$\frac{dS}{dt} = n - \frac{bS(\alpha P + \alpha A_e + \alpha\beta_a A_l + I_e + \beta_i I_l)}{N} - \frac{nS}{N}$$
$$\frac{dE}{dt} = \frac{bS(\alpha P + \alpha A_e + \alpha\beta_a A_l + I_e + \beta_i I_l)}{N} - \frac{E}{D_e} - \frac{nE}{N}$$
$$\frac{dP}{dt} = \frac{E}{D_e} - \frac{P}{D_p} - \frac{nP}{N}$$
$$\frac{dA_e}{dt} = \frac{(1-\rho)P}{D_p} - \frac{A_e}{D_i^e} - \frac{nA_e}{N}$$
$$\frac{dA_l}{dt} = \frac{A_e}{D_i^e} - \frac{A_l}{D_i^l} - \frac{nA_l}{N}$$
$$\frac{dI_e}{dt} = \frac{\rho P}{D_p} - \frac{I_e}{D_i^e} - \frac{I_e}{D_q} - \frac{I_e}{D_c}$$
$$\frac{dI_l}{dt} = \frac{I_e}{D_i^e} - \frac{I_l}{D_i^l} - \frac{I_l}{D_q} - \frac{I_l}{D_c}$$

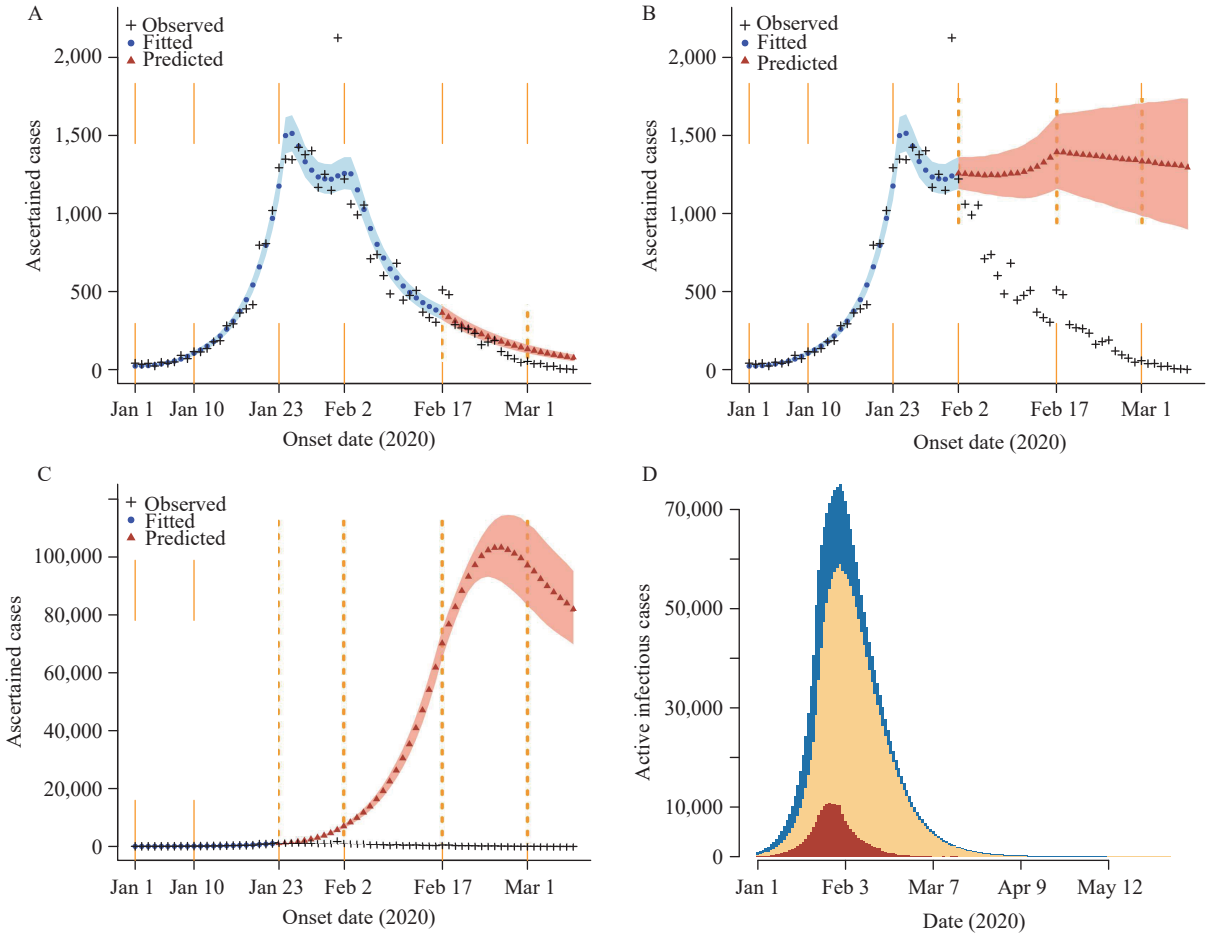
where b is the unknown transmission rate for significantly symptomatic cases in early stages and varies different time periods (set the five time periods as in Hao et al. (2020) for the demonstration in Wuhan); α is the ratio of the transmission rate of presymptomatic/asymptomatic/mild cases to that of significantly symptomatic cases and is prefixed; ρ is the unknown fraction of infections with significant symptoms; β_i and β_a are defined as before, set $\beta_i = \beta_a$ by assuming the trends of viral load are independent to symptoms; D_e, D_p, D_q, and D_c are the latent period, presymptomatic infectious period, duration from illness onset to isolation and duration from illness onset to clinical diagnosis respectively and are all predetermined. Under such setting, the transmission rate for AE is reasonable to be a constant over time and equal to the one for P. In addition, the lab-confirmation rate can be better presented as the function of the ratio between cases with insignificant (no/mild) and significant symptoms, and the time dependent ratio between the isolation/diagnosis and removal speed. Appendix E and F are for estimation method, choices of initial values, parameter settings, and sensitive analysis for the modified model.

Appendix C: Detailed results

The similar estimation method in Hao et al. (2020) is used in this study. Note that all CIs without further specifications are 95% CIs throughout this paper. The estimated cumulative number of infections up until March 8 was 194,302 (170,190–220,691) by fitting data from all 5 periods, this number increased to 198,748 (173,856–226,051) if the trend of the fourth period was assumed, 355,907 (301,525–418,579) if the trend of the third period was assumed or 11,507,840 (10,688,446–12,336,104) if the trend of the second period was assumed, see Supplementary Figure S2A–C for details. These represented a 2.24%, 44.16%, and 96.91% reduction of infections by the measures taken in the fifth period, the fourth and the fifth periods combined, and the last three periods combined, respectively. Note that under the trend of second period the total number of infections exceeded the total population of Wuhan. It was because the population inflow and outflow in Wuhan was about 800,000 per day before lockdown, the estimated number of infections could therefore be regarded as the number of infection in/from Wuhan.

The number of daily active infections (including cases in P, I, and A) peaked at 75,093 (64,342–87,068) on February 1 and dropped to 6 (1–13) on May 14 (Supplementary Figure S2D). If the trend remained unchanged as in the fifth period, the number of significantly symptomatic infections (I) would first become zero on April 12 (April 3 to April 23), and the clearance of all infections (namely $E + P + I + A = 0$) would occur on June 4 (June 15 to July 5). Compared with the estimates in Hao et al. (2020), the estimate on A was much more heavily tailed implying the high covertness of COVID-19. Considering a few cases detected in Wuhan in mid-May, the estimate on the clearance of all active infections was more consistent with the official report in Wuhan than what was predicted in Hao et al. (2020) (*5*–*6*).

Regarding continuous surveillance and interventions, based on the modified model that if control measures were lifted after zero new reported case in a consecutive period of 14 days, the probability of resurgence, defined as the number of active significantly symptomatic cases greater than 100, was still as high as 0.72, and the surge was



SUPPLEMENTARY FIGURE S2. Results of secondary analysis: epidemic trends under hypothetic policies, and estimations of standing active virus carriers. (A) Prediction using parameters estimated from the fourth period (February 2–16). (B) Prediction using parameters estimated from the third period (January 23 to February 1). (C) Prediction using parameters estimated from the second period (January 10 to January 22). The shaded areas are 95% credible intervals, and the colored points are the mean values based on 20,000 MCMC samples. (D) Estimated number of pre-symptomatic infections (P, in blue), infections without significant symptoms (A, in yellow) and infections with significant symptoms (I, in red) in Wuhan.

predicted to occur on Day 41 (31–57) after lifting controls. Compared with the results in Hao et al. (2020), estimates on the probability of resurgence were much higher, which suggests continuous efforts in interventions is essential to contain the spread of the pandemic.

Appendix D: Detailed explanation to issues in Hao et al. (2020)

The mean transmissibility in A defined by Hao et al. (2020) should be a time/configuration dependent function $\alpha(t)$, which were determined by averaging the transmissibility between patient with symptoms and those with no/mild symptom in A. Unfortunately, these two sub-populations of A were unidentifiable in the proposed model structure by Hao et al. (2020). One relatively easy potential fix of the issue was to replace αA with $\alpha_i A$ and allow α_i changing over different time steps in the paper. However, according to the definition of A, patients that did not get diagnosed could only increase through symptom onset and decrease through the loss of infectivity. Thus, the evolution of the sub-population proportion within A must be continuous in time. Meanwhile, the changes in containment measures/lab-confirmed rates in different steps in this model could only lead to changes to the evolution rate but not the proportion itself. This fact made it inappropriate to treat α as a step function. By similar argument, the setting of r in Hao et al. (2020) as a step function is also questionable.

SUPPLEMENTARY TABLE S1. Sensitivity analysis on the choice of D_i the SAPHIRE model. With a longer infectious period, it is expected to obtain a higher reproduction number in the beginning of the epidemic and a longer time needed to clear all infections in the Wuhan.

D_i (days)	Ascertainment rate	R_e in Period 1	R_e in Period 2	R_e in Period 3	R_e in Period 4	R_e in Period 5	Date of the clearance of all infections
2.9	12.7% (10.2%−15.6%)	3.54 (3.41−3.68)	3.32 (3.20−3.45)	1.18 (1.11−1.25)	0.51 (0.47−0.54)	0.28 (0.23−0.32)	April 21 (April 8 to May 12)
5	12.2% (9.8%−15.1%)	4.16 (4.00−4.33)	3.80 (3.65−3.95)	1.37 (1.28−1.45)	0.49 (0.45−0.52)	0.21 (0.18−0.26)	May 7 (April 21 to May 30)
7	12.1% (9.8%−15.1%)	4.68 (4.48−4.88)	4.18 (4.00−4.35)	1.56 (1.45−1.67)	0.49 (0.45−0.53)	0.18 (0.15−0.22)	May 28 (May 9 to June 25)
9	11.9% (9.5%−14.7%)	5.12 (4.89−5.35)	4.48 (4.28−4.68)	1.76 (1.65−1.89)	0.51 (0.47−0.55)	0.16 (0.13−0.20)	June 21 (May 31 to July 19)
13	11.1% (8.9%−13.7%)	5.83 (5.56−6.10)	4.93 (4.71−5.14)	2.18 (2.03−2.34)	0.57 (0.52−0.61)	0.15 (0.12−0.19)	July 19 (July 18 to July 19)

Appendix E: Estimation method

A major obstacle in parameter inference of the modified model is that now no compartment is directly observable. To be precise, $I(d)$ is the inflow of I on day d satisfying a Poisson distribution with $\lambda_d = \rho P_{d-1} D_p^{-1}$, while the observed data only consisted of those who had symptoms onset on day d provided that they would be diagnosed in the future, namely, a sub-population in I. Therefore, the distribution of such sub-population was estimated under this model. Fortunately, by the thinning argument of a Poisson process, the size of the sub-population of interest satisfies Poisson distribution with $\bar{\lambda}_d = rP_{d-1} D_p^{-1} q_d$, where q_d is the probability that a patient with symptom onset on day d would be diagnosed in the future. Moreover given D_n, the duration from symptom onset to the time point that test turns to negative, and D_q are predetermined in Hao el al (2020), the exact value of q_d can be independently calculated using the following stochastic viewpoint of the dynamic model: consider $N_1(t)$ a time-dependent Poisson Process/Poisson Point Measure, with intensity equals to $D_q(d) = 21, 15, 10, 6, 3$ on different stages, and $N_2(t)$ a time homogeneous Poisson Process with intensity D_n independent to N_1. For each d, define stopping times

$$\tau_{d,1} = \inf\{t \geq d, N_1(t) = N_1(t-) + 1\}$$

and

$$\tau_{d,2} = \inf\{t \geq d, N_2(t) = N_1(t-) + 1\}$$

be the first jumps times after d. Then q_d can be calculated can the probability that $\tau_{d,1} < \tau_{d,2}$. The specific values of q_d can either be calculated manually for each d or can be approximated numerically using frequencies obtained from multiple independent stochastic simulations. Since the precision of numerical simulation can be guaranteed by law of large numbers and large deviation theory, it was used here to approximate the values of q_d's with 10^5 stochastic realizations for each d.

Appendix F: Choices of initial values, parameter settings and sensitive analysis

Supplementary Table S2 provides a list of parameter settings in the modified model for all five periods. The initial values of I, A were estimated as follows:

(1) Let $I^c(0)$ the number of symptoms onset cases during December 29 to 31 who would be lab-confirmed in the future; $r_0 = 0.23$ be the initial lab-confirmed rate in Wuhan among symptomatic case which was calculated based on assuming complete diagnosis of early cases among symptomatic cases in Singapore; and $\rho_0 = 0.7$ be the proportion of symptomatic patients (*1*,*7*–*9*).

(2) The initial population of symptoms onset patients in Wuhan namely $A(0) + I(0)$ were hence given by $I^c(0) r_0^{-1} \rho_0^{-1}$.

(3) The ratio between A(0) and I(0), it should be roughly the same as the unknown diagnosable ratio ρ in the ODE system of the modified model. By "fix point iteration" method, ρ was estimated to be 0.26, hence $I(0) = 0.26 I^c(0) r_0^{-1} \rho_0^{-1}$ and $A(0) = 0.74 I^c(0) r_0^{-1} \rho_0^{-1}$.

(4) $AE(0) = A(0) D_i^e / D_i$, $AL(0) = A(0) D_i^l / D_i$, $IE(0) = I(0) D_i^e / D_i$, $IL(0) = I(0) D_i^l / D_i$.

In the original paper, $P_I(0)$ and $E_I(0)$ stood for the numbers of lab-confirmed cases with onset during January 12,

SUPPLEMENTARY TABLE S2. Parameter settings for five periods.

Parameter	Meaning	Jan 1–9	Jan 10–22	Jan 23–Feb 1	Feb 2–16	Feb 17–Mar 8
b	Transmission rate of significant cases	b_{12}	b_{12}	b_3	b_4	b_5
ρ	Fraction of infections with significant symptoms or diagnosable ratio	ρ	ρ	ρ	ρ	ρ
α	Ratio of transmission rate of no/mild symptomatic patients to that of significantly symptomatic patients	0.55	0.55	0.55	0.55	0.55
D_e	Latent period	2.9	2.9	2.9	2.9	2.9
D_p	Presymptomatic infectious period	2.3	2.3	2.3	2.3	2.3
D_q	Duration from illness onset to lab-confirmation/isolation	21	15	10	6	3
D_n	Duration from symptom onset to negative test result	14	14	14	14	14
D_c	Duration from symptom onset to clinical-confirmed diagnosis/isolation	∞	∞	∞	10	10
N	Population size	10,000,000	10,000,000	10,000,000	10,000,000	10,000,000
n	Daily inbound and outbound size	500,000	800,000	0	0	0

2020 and during January 3 to 5, 2020. According to the same reasonings as for $A(0)+I(0)$, there were $E(0) = E_I(0)\, r_0^{-1}\rho_0^{-1}$ and $P(0) = P_I(0)\, r_0^{-1}\rho_0^{-1}$. The estimates of parameters of interest were given in Supplementary Table S3 with a sensitivity analysis on D_n. Note that it was reasonable to believe that the mean duration from symptom onset to negative test result is less than 21 days, $D_n = 14$ was used in the main model (see upper left panel of Supplementary Figure S2 in (*4*) for reference). The estimates are relatively robust to the different choice of D_n.

SUPPLEMENTARY TABLE S3. Estimated transmission rates, overall lab-confirmation rate, and diagnosable ratio from the sensitivity analysis where $D_n = 14$ is used in the main model.

	r	b_{12}	b_3	b_4	b_5	ρ	$\beta i=\beta a$
D_n=10	0.18(0.16, 0.21)	1.01(0.91,1.10)	0.20(0.18, 0.23)	0.10(0.08, 0.13)	0.07(0.05,0.1)	0.32(0.28, 0.37)	0.40(0.17, 0.66)
D_n=14	0.17(0.15, 0.19)	1.03(0.94, 1.13)	0.21(0.18, 0.24)	0.10(0.08, 0.12)	0.07(0.05,0.09)	0.26(0.23, 0.29)	0.46 (0.22, 0.71)
D_n=21	0.15(0.13, 0.17)	1.06(0.97,1.15)	0.22(0.19, 0.24)	0.10(0.08, 0.12)	0.06(0.04,0.09)	0.20(0.18, 0.23)	0.48(0.24, 0.73)

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