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Vaccination, symptomatic infection and negative conversion of viral RNA by body mass index, diabetes, and age: An observational study

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ABSTRACT

Background: The associations of doses of vaccine received with symptomatic infection with SARS-CoV-2 and negative conversion rate of viral RNA by BMI, diabetes, and age are unclear.
Methods: Included were adult cases of SARS-CoV-2 infection hospitalized at a makeshift hospital in Shanghai (N = 38,592). Each case received a real-time reverse transcriptase–polymerase chain reaction (RT-PCR) test every day until discharge. Symptomatic cases had ≥1 pre-specified symptoms. Negative conversion time (NCT) was the duration between the specimen collection date associated with the first positive RT-PCR test and the first test date of the two consecutive negative tests at least 24 h apart. BMI-, diabetes- and age-stratified multivariable logistic and Poisson regressions were applied.
Findings: Coexistence of overweight/obesity and diabetes was associated with a higher risk of symptomatic infection and a longer NCT compared with coexistence of normal weight and without diabetes, but this association was primarily attributed to underlying comorbidities. Compared with absence of vaccination, booster vaccination, but not full vaccination, was consistently associated with a 42 %–56 % lower odds of symptomatic infection and ~1.6–1.8 days of shorter NCT across different strata separately for weight and diabetes. Age-stratified analyses found that the effectiveness of booster vaccination did not attenuate with age, except for preventing symptomatic infection among adults with diabetes.
Interpretation: BMI and diabetes co-determined their associations with symptomatic infection and NCT. Booster vaccination but not full vaccination was associated a lower risk of symptomatic infection, a shorter NCT or both regardless of BMI, diabetes status and age.

1. Introduction

Obesity and diabetes are the two fastest growing cardiometabolic diseases in recent decades [1,2]. Since the first reported case in early December 2019, coronavirus disease 2019 (COVID-19) has spread widely and quickly all over the world and caused unprecedented burden to health, society and the economy. The coexistence of and interactions among the three global pandemics (i.e., obesity, diabetes and COVID-19) likely re-shape the future landscape of disease burden and transform public health and clinical practice for disease prevention and management [3].

Obesity and diabetes have been associated with increased susceptibility to and severity of COVID-19, although the association can be bidirectional [4]. Coexistence of obesity and diabetes may predispose people to a higher risk for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and more severe health consequences [5]. Obesity and diabetes are associated with prolonged viral shedding and thus chances of spreading SARS-CoV-2 increase [6]. The associations of obesity and diabetes with severity of SARS-CoV-2 infection and viral shedding seem stronger in older than younger people [5,6].

Vaccination is highly effective in protecting people from getting infected and developing symptoms and in preventing severe

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illness, hospitalization, and death [7]. Whether the effectiveness of vaccination varies by people with different body mass index (BMI) and different diabetes status has not been well investigated. Addressing this literature map is of paramount public health importance because globally approximately half of the population are overweight, obese or diabetic and the number continues to accumulate [8,9]. Furthermore, the impact of BMI and diabetes on the risk of infection and prognosis after infection differs by SARS-CoV-2 variants because of different characteristics in transmissibility, immunity and severity of infection [10,11]. However, real-world evidence from a large sample is scarce during the Omicron predominance.

Using a large sample of adults infected with the Omicron variant in Shanghai [12], this study aimed to determine the collective associations of weight and diabetes status with symptomatic infection and negative conversion rate of SARS-CoV-2 infection as well as the associations of vaccination with symptomatic infection and negative conversion rate by weight status, diabetes status and age.

2. Methods

2.1. Study population

Since late February 2022, an outbreak of Omicron infection has occurred in Shanghai. People with SARS-CoV-2 infection was diagnosed with a positive result of real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay using nasopharyngeal and oropharyngeal swabs. This analysis included adults with confirmed infection who were admitted to the Shanghai New International Expo Center, a largest makeshift hospital in Shanghai, between April 1 and May 2, 2022. The Shanghai New International Expo Center provided a maximum of 15,000 beds and accepted infected cases from all districts in Shanghai. Due to limited health services provided within the makeshift hospital, infected cases who developed severe illness requiring advanced care were transferred to designated hospitals. This study was approved by the Institutional Review Board of the Makeshift Hospital at the Shanghai New International Expo Center. Informed consent was exempt due to the secondary use of the de-identified data.

2.2. Data collection

All the information was collected through medical records and a questionnaire at admission. Telephone interviews were conducted to acquire missing data. Demographic data (age and sex), height, weight, doses of vaccine received ranging from 0 to 3 doses, disease history, and symptoms were self-reported. The following disease history was asked: hypertension, diabetes, cardiovascular disease, asthma, chronic obstructive pulmonary disease, chronic kidney disease and other diseases including hyperthyroidism, gallstones, kidney stones, psoriasis, nasopharyngeal carcinoma, lung cancer, thyroid cancer, kidney transplantation, lumbar disc herniation, Hepatitis B, fatty liver, gout, gastric ulcer, and reflux esophagitis. Twenty-one symptoms were collected including 6 respiratory, 9 systemic, 4 gastrointestinal and 2 sensory symptoms. Respiratory symptoms included cough/expectoration, runny/stuffy nose, sore throat, itchy/dry throat, sneezing, and tachypnea. Systemic symptoms included fever, headache, dizziness, fatigue, muscular soreness, chest pain, chest tightness, sweat, and palpitation. Gastrointestinal symptoms included nausea, vomiting, abdominal pain, and diarrhea. Sensory symptoms were allotriosmia and parageusia.

Of note, the manufacturer and type of vaccine were not collected, but inactivated vaccines from Sinovac and Sinopharm were dominant in China.

2.3. BMI and diabetes

Height, weight and history of diabetes (yes/no) were self-reported at admission. Underweight, normal weight, overweight and obesity had a BMI range of <18.5, 18.5 to <24, 24 to <27.5 and 27.5 kg/m^2 or higher, respectively [13]. The cutoff for obesity of the Chinese standards is 28 kg/m^2. However, due to the stratification analysis by three age groups and four groups of vaccine doses and that prevalence of obesity in China is not high [14], a slightly lower cutoff of 27.5 kg/m^2 was used to obtain more robust estimates. The World Health Organization Asian-specific BMI cutoff for obesity is 27.5 kg/m^2 [15].

2.4. Outcomes

Primary outcomes were symptomatic infection defined as having any 1 of the 21 symptoms and negative conversion time (NCT). Admitted cases were tested for SARS-CoV-2 infection every day until discharge. NCT was calculated as the duration between the specimen collection date associated with the first positive RT-PCR test prior to admission and the first test of the two consecutive negative tests at least 24 h apart which was also the criterion for discharge. A cycle threshold value from an RT-PCR test greater than or equal to 35 was considered negative. People developing severe illness requiring advanced care were transferred out and thus accurate NCT was not available. These individuals were not included for the NCT analysis. Secondary outcomes were respiratory, systemic, gastrointestinal and sensory symptoms.

2.5. Statistical analysis

Infected cases with underweight were a very small sample (n = 27) and thus were excluded from the stratified analysis involving BMI. The distribution of the 21 symptoms by weight status (normal weight, overweight and obesity) and diabetes status (yes/no) was displayed. Characteristics according to weight and diabetes status were described and differences were tested using a chi-square test for categorical variables and ANOVA test or *t* test for continuous variables.

The associations between doses of vaccine received (0 dose as the reference, 1, 2, and 3) and symptomatic vs asymptomatic infection along with each of the 4 symptom types were estimated using logistic regressions, adjusting for age, sex, BMI, and number of comorbidities when appropriate. The association between doses of vaccine received and NCT in days were estimated using Poisson regressions with an identity link, adjusting for age, sex, BMI, number of comorbidities, and symptomatic infection when appropriate. These analyses were stratified by weight status (normal weight, overweight, and obesity), diabetes (yes/no) and age (18–44, 45–64, and ≥65 years).

To assess collective associations of weight and diabetes with symptomatic infection and NCT, all adults were categorized into 6 groups: normal weight and no diabetes, overweight and no diabetes, obesity and no diabetes, normal weight and diabetes, overweight and diabetes, and obesity and diabetes. Two analyses were performed. First, risk of symptomatic infection and difference in NCT for the other 5 groups were compared with the reference group: normal weight and no diabetes. Age, sex, doses of vaccine, number of comorbidities and symptomatic infection (for NCT only) were adjusted. Second, for each of the 6 groups, the associations between doses of vaccine received and symptomatic infection as well as NCT were estimated, adjusting for age, sex, number of comorbidities and symptomatic infection (for NCT only).

All analyses were conducted with R 3.6.1. Statistical significance was determined by 2-sided p values <0.05.

3. Results

Included were 16,826 adults with normal weight, 19,978 with overweight, 1761 with obesity, 34,057 without diabetes and 4535 with diabetes (Table 1). Adults with greater BMI or diabetes were older, were more likely to be men, had a higher prevalence of comorbidities including hypertension, diabetes, cardiovascular disease, chronic kidney disease, and chronic obstructive pulmonary disease, and had a longer NCT, but were less likely to receive booster vaccination. Fig. 1 presents the distribution of the 21 symptoms according to weight and diabetes status. Prevalence of respiratory and systemic symptoms was higher than gastrointestinal and sensory symptoms. Adults with greater BMI or diabetes had a higher prevalence of most symptoms.

Compared with unvaccinated adults, adults receiving three but not two doses had a significantly lower risk of symptomatic infection and shorter NCT regardless of weight status (Table 2). The adjusted odds ratio (OR) (95 % CI) was 0.44 (0.36, 0.53) for normal weight, 0.45 (0.38, 0.53) for overweight and 0.58 (0.36, 0.91) for obesity. The adjusted difference (95 % CI) in NCT was −1.57 (−1.84, −1.30) for normal weight, −1.78 (−2.01, −1.55) for overweight, and −1.66 (−2.34, −1.00) for obesity. Regarding the four specific types of symptoms, the three-dose regimen was consistently associated with a significantly lower risk among adults with

Table 1
Characteristics of COVID-19 cases by weight and diabetes status.

	Weight category*				Diabetes status		
	Normal weight	Overweight	Obesity	*P*	No	Yes	*P*
Sample size	16,826	19,978	1761		34,057	4535	
Age, years, %				<0.001			<0.001
18–44	59.8	40.0	23.9		51.3	22.7	
45–64	33.5	50.2	63.8		41.1	61.6	
65–101	6.6	9.8	12.3		7.5	15.7	
Sex, %				0.001			<0.001
Female	42.9	44.8	44.8		43.6	46.7	
Male	57.1	55.2	55.2		56.4	53.3	
Doses of vaccine, %				<0.001			<0.001
0	3.3	4.3	6.0		3.6	6.2	
1	2.2	1.5	1.0		1.9	1.3	
2	31.2	32.3	33.3		30.8	39.4	
3	63.3	61.9	59.7		63.6	53.1	
BMI, kg/m^2, mean (SD)	22.6 (1.1)	25.4 (0.9)	28.2 (0.7)	<0.001	24.1 (1.8)	25.9 (1.6)	<0.001
Hypertension, %	8.1	33.7	73.1	<0.001	17.3	77.2	<0.001
Diabetes, %	3.3	16.4	40.4	<0.001			
Cardiovascular disease, %	3.1	13.3	29.1	<0.001	6.6	31.4	<0.001
Chronic kidney disease, %	4.9	11.1	20.6	<0.001	5.0	37.9	<0.001
COPD, %	1.1	2.6	4.3	<0.001	1.6	5.3	<0.001
Asthma, %	1.9	2.0	1.6	0.56	1.9	2.2	0.30
Other diseases, %	4.2	4.6	4.1	0.17	4.3	5.3	0.001
No. of comorbidities, %				<0.001			<0.001
0	82.6	56.2	17.5		74.7	8.6	
1	11.0	17.7	25.0		16.0	40.9	
2	4.4	15.5	31.5		7.4	35.4	
≥3	2.1	10.7	26.0		1.9	15.1	
NCT, days, mean (SD)	7.0 (2.6)	7.2 (2.7)	7.4 (2.6)	<0.001	7.1 (2.6)	7.4 (2.6)	<0.001
Having symptoms, %	53.4	56.9	61.3	<0.001	54.3	65.2	<0.001
Systemic, %	50.7	54.1	58.6	<0.001	51.7	61.1	<0.001
Fever	20.6	22.2	23.4	<0.001	21.1	24.9	<0.001
Fatigue	24.6	26.1	28.6	<0.001	25.1	29.2	<0.001
Muscular soreness	26.1	27.7	31.1	<0.001	26.4	33.3	<0.001
Headache	24.8	26.5	28.9	<0.001	25.3	29.6	<0.001
Dizziness	15.9	17.2	18.7	<0.001	16.3	19.6	<0.001
Chest pain	5.4	5.7	7.0	0.02	5.5	6.7	<0.001
Chest tightness	3.5	3.6	3.1	0.54	3.4	4.4	<0.001
Sweat	4.4	4.4	4.9	0.65	4.4	4.5	0.74
Palpitation	2.5	2.7	3.4	0.06	2.7	2.7	0.81
Respiratory, %	51.5	54.7	59.4	<0.001	52.3	62.6	<0.001
Cough/expectoration	36.5	38.5	41.2	<0.001	37.0	43.5	<0.001
Runny/stuffy nose	32.6	34.6	37.9	<0.001	33.3	37.8	<0.001
Sneezing	23.1	24.3	25.2	0.009	23.3	27.7	<0.001
Sore throat	27.1	29.0	31.7	<0.001	27.5	34.4	<0.001
Itchy/dry throat	5.3	5.5	6.8	0.04	5.4	6.2	0.02
Tachypnea	3.6	3.8	4.0	0.59	3.5	5.8	<0.001
Gastrointestinal, %	25.4	26.4	29.8	<0.001	25.5	31.0	<0.001
Nausea	10.1	10.7	11.3	0.13	10.1	13.0	<0.001
Vomiting	7.8	8.3	9.1	0.06	7.9	9.6	<0.001
Abdominal pain	7.8	8.5	10.4	<0.001	7.9	10.8	<0.001
Diarrhea	5.4	5.6	7.2	0.009	5.5	6.5	0.003
Sensory, %	1.3	1.7	1.7	0.03	1.4	2.6	<0.001
Parageusia	0.5	0.6	0.5	0.32	0.5	0.8	0.006
Allotriosmia	0.9	1.1	1.2	0.08	0.9	1.8	<0.001

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; NCT, negative conversion time; SD, standard deviation.

* People whose weight category belonged to underweight were excluded due to small sample size (n = 27). BMI of 18.5 to < 24 kg/m^2 defined normal weight, 24 to < 27.5 kg/m^2 defined overweight and ≥ 27.5 kg/m^2 defined obesity. The Chinese standard for defining obesity is 28 kg/m^2. This study had multiple stratification analyses and 27.5 kg/m^2 was used to improve the robustness of results. In fact, the World Health Organization Asian-specific BMI cutoff for obesity is 27.5 kg/m^2.

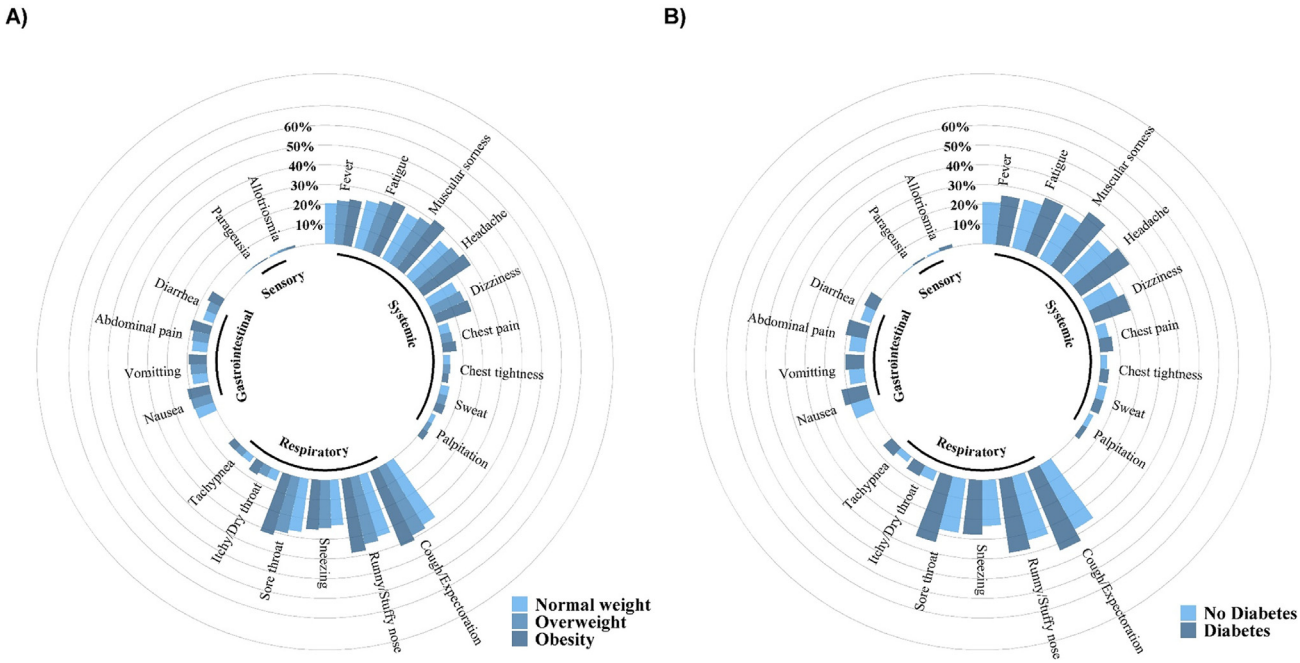

Fig. 1. Distribution of symptoms according to weight status (A) and diabetes status (B) among adults with confirmed SARS-CoV-2 infection.

normal weight or overweight (except gastrointestinal symptoms). Among adults with obesity, the three-dose regimen was associated with a significantly lower risk of sensory symptoms, but not the three other types of symptoms. When stratified by age, the three-dose regimen was consistently associated with a significantly lower risk of symptomatic infection among adults with normal weight or overweight regardless of age. However, age-stratified association for symptomatic infection was not significant among adults with obesity. When specific types of symptoms were examined, booster vaccination was more consistently associated with a lower risk of sensory symptoms. Age-stratified results were generally consistent for NCT except among young adults with obesity. Booster vaccination was associated with a significantly shorter NCT and the magnitude of shortening was greater with older age generally.

The adjusted OR (95 % CI) for symptomatic infection comparing three doses with zero dose of vaccine was 0.46 (0.33, 0.62) among all adults with diabetes, 0.47 (0.32, 0.70) among middle-aged adults with diabetes, 0.65 (0.36, 1.13) among older adults with diabetes, 0.45 (0.39, 0.51) among all adults without diabetes, 0.38 (0.30, 0.47) among young adults without diabetes, 0.58 (0.48, 0.70) among middle-aged adults without diabetes, and 0.52 (0.36, 0.73) among older adults without diabetes (Table 3). Booster vaccination was consistently associated with a significantly lower risk of sensory symptoms regardless of age and diabetes status, but not for the other three types of symptoms. The adjusted difference (95 % CI) in the NCT comparing three doses with zero dose of vaccine received was −1.55 (−1.96, −1.14) for adults with diabetes and −1.71 (−1.89, −1.52) for adults without diabetes. Results were consistent across different age groups.

Compared with adults with normal weight and without diabetes, adults with overweight and diabetes as well as adults with obesity and diabetes had significantly higher risk of symptomatic infection, but this association became insignificant after adjusting for comorbidities. Similar results were found for NCT (Table 4). Table 5 presents the associations between vaccination and symptomatic infection and NCT stratified by weight and diabetes status. The three-dose regimen was consistently associated with a significantly lower risk of symptomatic infection regardless of weight status among adults without diabetes. However, among adults with diabetes, the three-dose regimen was associated with a significantly lower risk of symptomatic infection only among adults with overweight. The three-dose regimen was associated with a significantly lower risk of sensory symptoms except among adults with obesity but without diabetes. For NCT, the three-dose regimen was consistently associated with a ∼1.3–2.0 days of shorter NCT regardless of weight and diabetes status.

4. Discussion

Among over 38,000 adults with confirmed SARS-CoV-2 infection, coexistence of overweight/obesity and diabetes was associated with a higher risk of symptomatic infection and a longer NCT compared with coexistence of normal weight and without diabetes, but this association was primarily attributed to underlying comorbidities. Booster vaccination but not full vaccination was associated a lower risk of symptomatic infection or a shorter NCT or both regardless of weight, diabetes and age, except among young adults with obesity.

Obesity and diabetes are associated with severity of COVID-19, but diabetes appears to be a stronger risk factor [3,16]. Similarly, this study found that among people without diabetes, overweight or obesity was not associated with symptomatic infection compared with normal weight, although the NCT was slightly longer. Evidence mostly from western countries suggests that severe obesity with BMI $\geq$ 35 kg/m^2 was a more consistent independent risk factor for severe COVID-19 outcomes than obesity with BMI $\geq$ 30 kg/m^2 [3]. There is no criterion to define severe obesity in Chinese and severe obesity in China is not commonly seen [17]. According to this study, people with overweight/obesity and diabetes had a higher risk of symptomatic infection and a prolonged NCT than people with normal weight and without diabetes. However, these associations were primarily driven by the comorbidities that coexisted. For example, over 50 % of adults with dia-

Table 2
Associations of vaccine doses with symptomatic infection and negative conversion of viral RNA by weight and age.

	Symptomatic infection*, odds ratio (95 % CI)					Negative conversion time†, difference (95 % CI), days
	Overall	Systemic	Respiratory	Gastrointestinal	Sensory	
Normal weight						
All adults						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
1 dose	0.88 (0.66, 1.17)	0.83 (0.63, 1.09)	1.02 (0.78, 1.33)	0.82 (0.60, 1.11)	0.75 (0.44, 1.24)	0.06 (−0.35, 0.47)
2 doses	0.69 (0.57, 0.84)	0.89 (0.74, 1.06)	0.99 (0.83, 1.19)	1.13 (0.93, 1.38)	0.11 (0.08, 0.17)	−0.48 (−0.76, −0.21)
3 doses	0.44 (0.36, 0.53)	0.59 (0.49, 0.71)	0.64 (0.53, 0.76)	0.80 (0.66, 0.97)	0.10 (0.07, 0.14)	−1.57 (−1.84, −1.30)
18–44 years						
2 vs 0 doses	0.61 (0.45, 0.81)	0.81 (0.62, 1.07)	1.03 (0.78, 1.35)	1.24 (0.91, 1.70)	0.07 (0.04, 0.13)	−0.27 (−0.68, 0.12)
3 vs 0 doses	0.35 (0.26, 0.46)	0.51 (0.39, 0.66)	0.59 (0.45, 0.77)	0.73 (0.54, 1.00)	0.08 (0.04, 0.13)	−1.39 (−1.79, −0.99)
45–64 years						
2 vs 0 doses	0.83 (0.61, 1.11)	1.08 (0.81, 1.44)	1.07 (0.80, 1.42)	0.99 (0.73, 1.36)	0.12 (0.06, 0.22)	−0.51 (−0.94, −0.08)
3 vs 0 doses	0.61 (0.45, 0.81)	0.81 (0.61, 1.07)	0.81 (0.61, 1.06)	0.99 (0.73, 1.35)	0.08 (0.05, 0.15)	−1.56 (−1.99, −1.15)
≥65 years						
2 vs 0 doses	0.72 (0.40, 1.26)	0.79 (0.46, 1.33)	0.78 (0.45, 1.32)	1.27 (0.80, 2.04)	0.49 (0.13, 1.95)	−0.95 (−1.83, −0.10)
3 vs 0 doses	0.53 (0.30, 0.89)	0.59 (0.36, 0.96)	0.62 (0.37, 1.01)	0.77 (0.50, 1.20)	0.34 (0.11, 1.30)	−1.96 (−2.77, −1.18)
Overweight						
All adults						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
1 dose	0.83 (0.63, 1.12)	0.74 (0.57, 0.97)	0.94 (0.72, 1.24)	0.93 (0.69, 1.25)	0.97 (0.63, 1.48)	−0.34 (−0.76, 0.08)
2 doses	0.69 (0.58, 0.81)	1.05 (0.90, 1.22)	1.10 (0.95, 1.28)	1.12 (0.96, 1.32)	0.11 (0.08, 0.15)	−0.79 (−1.03, −0.56)
3 doses	0.45 (0.38, 0.53)	0.70 (0.60, 0.80)	0.73 (0.63, 0.85)	0.92 (0.79, 1.07)	0.08 (0.06, 0.11)	−1.78 (−2.01, −1.55)
18–44 years						
2 vs 0 doses	0.64 (0.46, 0.89)	1.15 (0.85, 1.57)	1.26 (0.93, 1.71)	1.53 (1.05, 2.27)	0.05 (0.02, 0.09)	−0.85 (−1.34, −0.38)
3 vs 0 doses	0.39 (0.28, 0.53)	0.70 (0.52, 0.95)	0.75 (0.56, 1.02)	1.06 (0.73, 1.57)	0.05 (0.03, 0.08)	−1.76 (−2.24, −1.30)
45–64 years						
2 vs 0 doses	0.77 (0.61, 0.96)	1.07 (0.86, 1.32)	1.23 (1.00, 1.51)	0.98 (0.78, 1.23)	0.10 (0.06, 0.14)	−0.60 (−0.92, −0.29)
3 vs 0 doses	0.53 (0.43, 0.66)	0.75 (0.61, 0.92)	0.86 (0.70, 1.05)	0.93 (0.75, 1.16)	0.06 (0.04, 0.09)	−1.65 (−1.96, −1.35)
≥65 years						
2 vs 0 doses	0.69 (0.44, 1.05)	1.07 (0.74, 1.53)	0.83 (0.56, 1.20)	1.27 (0.94, 1.74)	0.31 (0.16, 0.61)	−0.69 (−1.32, −0.08)
3 vs 0 doses	0.51 (0.34, 0.74)	0.83 (0.59, 1.15)	0.73 (0.51, 1.02)	0.93 (0.69, 1.24)	0.22 (0.12, 0.42)	−1.94 (−2.51, −1.39)
Obesity						
All adults						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
1 dose	1.60 (0.51, 6.12)	1.52 (0.51, 5.15)	2.35 (0.76, 8.91)	1.22 (0.40, 3.47)	NA	−0.11 (−1.70, 1.62)
2 doses	1.00 (0.61, 1.59)	1.10 (0.69, 1.73)	1.35 (0.85, 2.10)	1.09 (0.69, 1.73)	0.26 (0.09, 0.73)	−0.96 (−1.66, −0.28)
3 doses	0.58 (0.36, 0.91)	0.69 (0.44, 1.06)	0.81 (0.52, 1.23)	1.00 (0.65, 1.58)	0.22 (0.09, 0.59)	−1.66 (−2.34, −1.00)
18–44 years						
2 vs 0 doses	1.16 (0.32, 3.86)	0.97 (0.27, 3.23)	1.13 (0.32, 3.76)	1.66 (0.46, 7.78)	NA	−0.63 (−2.51, 1.06)
3 vs 0 doses	0.57 (0.16, 1.84)	0.56 (0.16, 1.81)	0.55 (0.16, 1.79)	0.97 (0.28, 4.53)	NA	−1.16 (−3.02, 0.49)
45–64 years						
2 vs 0 doses	0.94 (0.50, 1.70)	1.13 (0.62, 2.02)	1.34 (0.74, 2.37)	1.01 (0.55, 1.90)	0.11 (0.02, 0.43)	−0.81 (−1.70, 0.04)
3 vs 0 doses	0.61 (0.33, 1.09)	0.76 (0.42, 1.32)	0.92 (0.52, 1.59)	1.02 (0.57, 1.90)	0.11 (0.03, 0.40)	−1.57 (−2.43, −0.75)
≥65 years						
2 vs 0 doses	1.38 (0.40, 4.63)	1.31 (0.44, 3.82)	1.98 (0.67, 5.94)	0.86 (0.35, 2.14)	1.16 (0.21, 7.29)	−1.35 (−3.04, 0.29)
3 vs 0 doses	0.53 (0.18, 1.35)	0.67 (0.26, 1.60)	0.76 (0.31, 1.75)	1.19 (0.55, 2.70)	0.33 (0.05, 2.00)	−2.35 (−3.86, −0.91)

* Estimates were obtained from logistic regressions, adjusting for age, sex, and number of comorbidities.
† Estimates were obtained from Poisson regressions, adjusting for age, sex, number of comorbidities, and symptomatic infection.

betes had two or more comorbidities compared with 8 % among adults without diabetes.

Compared with that obesity and diabetes themselves did not have a substantial independent influence on risk of symptomatic infection and NCT, vaccination status played a more important role. This is the first real-world study to examine the associations between different doses of vaccine and risk of developing symptoms and negative conversion rate of viral RNA by BMI levels and diabetes in combination. The effectiveness of vaccination appeared to be similar in people with and without obesity [18]. Vaccination in diabetes was also recommended [19]. However, many questions remain unresolved including preferred vaccine type, doses of vaccine required, and effectiveness for reducing risk of symptomatic infection and viral shedding. China primarily relies on inactivated vaccines for which data are scarce. This study found that booster vaccination provided more durable and stronger protection than full vaccination and full vaccination was not associated with a lower risk of symptomatic infection among vulnerable groups such as people with diabetes or obesity or old age. Type 1 diabetes and type 2 diabetes are equally at risk of severe illness from COVID-19, but the effectiveness of vaccination for preventing people with different diabetes types from infection and from developing adverse outcomes is unclear [20]. Our study found that among people with diabetes who were obese or who had normal weight, booster vaccination did not seem provide protection against symptomatic infection. Whether the null association in the latter group might be in part attributable to type 1 diabetes requires further investigations.

The effectiveness of vaccination in shortening NCT was more consistent than in preventing symptomatic infection. A clear gradient association between more doses of vaccine and shorter NCT was seen and the magnitude of shortened NCT was considerable. The three-dose regimen was associated with approximately-two days shorter NCT given the mean NCT of the study sample was seven days. NCT can be considered as a proxy for duration of viral shedding. Duration of viral shedding is an important determinant of SARS-CoV-2 transmission and treatment and for choosing appropriate control and prevention measures [21,22]. Due to the

Table 3
Associations of vaccine doses with symptomatic infection and negative conversion of viral RNA by diabetes and age.

	Symptomatic infection*, odds ratio (95 % CI)					Negative conversion time†, difference (95 % CI), days
	Overall	Systemic	Respiratory	Gastrointestinal	Sensory	
Diabetes						
All adults						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
1 dose	0.88 (0.47, 1.74)	0.73 (0.41, 1.30)	0.85 (0.48, 1.54)	1.15 (0.60, 2.11)	1.35 (0.57, 2.93)	−0.80 (−1.69, 0.11)
2 doses	0.61 (0.44, 0.83)	1.08 (0.82, 1.42)	1.06 (0.80, 1.39)	1.34 (1.01, 1.79)	0.10 (0.06, 0.16)	−1.07 (−1.49, −0.66)
3 doses	0.46 (0.33, 0.62)	0.80 (0.61, 1.05)	0.82 (0.62, 1.07)	1.25 (0.95, 1.66)	0.12 (0.08, 0.20)	−1.55 (−1.96, −1.14)
18–44 years						
2 vs 0 doses	NA	NA	NA	NA	NA	−2.15 (−4.39, −0.15)
3 vs 0 doses	NA	NA	NA	NA	NA	−2.25 (−4.50, −0.26)
45–64 years						
2 vs 0 doses	0.65 (0.43, 0.96)	1.13 (0.79, 1.61)	1.10 (0.77, 1.56)	1.43 (0.97, 2.16)	0.03 (0.01, 0.08)	−0.59 (−1.12, −0.08)
3 vs 0 doses	0.47 (0.32, 0.70)	0.84 (0.59, 1.18)	0.84 (0.59, 1.18)	1.55 (1.06, 2.32)	0.08 (0.04, 0.16)	−1.09 (−1.61, −0.59)
≥65 years						
2 vs 0 doses	0.58 (0.31, 1.06)	1.10 (0.65, 1.84)	1.05 (0.62, 1.77)	1.51 (0.94, 2.47)	0.26 (0.12, 0.54)	−1.23 (−2.08, −0.40)
3 vs 0 doses	0.65 (0.36, 1.13)	1.05 (0.65, 1.69)	1.23 (0.75, 1.99)	1.21 (0.77, 1.92)	0.21 (0.10, 0.43)	−2.74 (−3.53, −1.97)
Without diabetes						
All adults						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
1 dose	0.88 (0.72, 1.09)	0.81 (0.67, 0.99)	1.03 (0.84, 1.25)	0.83 (0.67, 1.04)	0.80 (0.62, 1.14)	−0.09 (−0.40, 0.21)
2 doses	0.71 (0.62, 0.81)	0.95 (0.84, 1.08)	1.06 (0.93, 1.19)	1.07 (0.94, 1.22)	0.12 (0.09, 0.16)	−0.61 (−0.80, −0.42)
3 doses	0.45 (0.39, 0.51)	0.62 (0.55, 0.70)	0.67 (0.60, 0.76)	0.80 (0.71, 0.91)	0.08 (0.06, 0.11)	−1.71 (−1.89, −1.52)
18–44 years						
2 vs 0 doses	0.65 (0.52, 0.80)	0.98 (0.80, 1.20)	1.16 (0.94, 1.42)	1.39 (1.10, 1.78)	0.06 (0.04, 0.09)	−0.46 (−0.77, −0.16)
3 vs 0 doses	0.38 (0.30, 0.47)	0.60 (0.49, 0.73)	0.67 (0.55, 0.82)	0.87 (0.69, 1.11)	0.06 (0.04, 0.09)	−1.53 (−1.83, −1.23)
45–64 years						
2 vs 0 doses	0.83 (0.69, 1.01)	1.05 (0.88, 1.27)	1.20 (1.00, 1.43)	0.89 (0.74, 1.09)	0.13 (0.09, 0.18)	−0.60 (−0.87, −0.32)
3 vs 0 doses	0.58 (0.48, 0.70)	0.75 (0.63, 0.89)	0.85 (0.71, 1.01)	0.85 (0.70, 1.02)	0.07 (0.05, 0.09)	−1.74 (−2.01, −1.48)
≥65 years						
2 vs 0 doses	0.81 (0.54, 1.19)	0.95 (0.66, 1.33)	0.78 (0.54, 1.12)	1.2 (0.9, 1.61)	0.54 (0.29, 1.33)	−0.60 (−1.19, −0.01)
3 vs 0 doses	0.52 (0.36, 0.73)	0.68 (0.49, 0.93)	0.58 (0.41, 0.81)	0.84 (0.64, 1.11)	0.27 (0.11, 0.66)	−1.69 (−2.23, −1.17)

* Estimates were obtained from logistic regressions, adjusting for age, sex, body mass index, and number of comorbidities.
† Estimates were obtained from Poisson regressions, adjusting for age, sex, body mass index, number of comorbidities, and symptomatic infection.

immune evasion capabilities, high transmissibility and reinfection possibility of emerging variants of concern such as Omicron, ongoing advocation for full vaccination and importantly increasing the booster vaccination rate are critical to improve protection from COVID-19 and to reduce transmission [23].

Vaccine effectiveness decreased among older adults and adults with comorbidities [24,25]. Results of this study indicate that among older adults with obesity or diabetes, booster vaccination was not associated with a lower risk of symptomatic infection. Furthermore, the benefits in lowering risk of symptomatic infection appeared to be greater in young versus middle-aged and older adults. This does not mean that booster vaccination was not helpful, because it was consistently associated with a substantially shorter NCT. In fact, in many subgroups, the shortening of NCT in older adults was greater than that in young adults with booster vaccination. Vaccine hesitancy is a known phenomenon among elderly people, in particular those with comorbidities, due to safety and efficacy concerns [26,27]. Our study supported booster vaccination to all adults regardless of age, weight status and diabetes with one exception to accelerate viral shedding. Among young adults with obesity, booster vaccination was not significantly associated with a shorter NCT. This is the first study to examine the association between vaccination and COVID-19 outcomes in young people by BMI and thus this could be simply a chance finding. From the policy-making standpoint, this "counterintuitive" finding would not comprise the benefit of the rapid mass roll-out of the third dose for COVID-19 prevention and control.

Consistent with the literature, symptoms of the upper respiratory tract and systemic symptoms were more common in Omicron infected people than gastrointestinal and sensory symptoms [24]. Different symptoms may predict differential severity of infection [28]. However, the association between vaccination and specific types of symptoms has not been well studied. Prevalence of sensory symptoms was the lowest, but its inverse association with vaccination was most consistent across all strata and also the strongest among all four symptoms. The mechanisms underlying this association are not clear. For systemic and respiratory symptoms, they were more likely to be related to old age and comorbidities instead of vaccination.

Limitations should be noted. First, most data were self-reported including BMI and diabetes. Misclassification was likely. Second, the number of vaccine doses received largely depended on vaccine type which was not collected in this study, but inactivated vaccines were dominant in China. Third, this study did not include uninfected people as a comparison group. The comparison was between asymptomatic infection and symptomatic infection. Fourth, this study did not include cases with severe infection and thus the benefit of vaccination in reducing risk of severe infection was not studied. Nonetheless, the vast majority of the cases were asymptomatic and had mild symptoms in Shanghai [12]. Fifth, this is a single center study and thus whether the study sample was representative remained uncertain. However, we analyzed hospitalized people in a largest makeshift hospital in Shanghai which accepted infected people from all districts in Shanghai. Sixth, date of the last vaccine dose was not available and thus the waning of vaccine effectiveness was not studied. Seventh, this study could not distinguish diabetes type and was underpowered to use 30 kg/m^2 to define obesity. However, it is well-established that Asians develop cardiometabolic risk at a lower BMI than Caucasians [15].

In conclusion, adults with diabetes and overweight/obesity had a higher risk of symptomatic infection and prolonged NCT compared with adults with normal weight and without diabetes, but this association was primarily attributed to underlying comorbidities. Booster vaccination but not full vaccination was associated a lower risk of symptomatic infection or a shorter NCT or both regardless of weight status, diabetes status, and age.

Table 4
Associations of weight and diabetes status with symptomatic infection and negative conversion of viral RNA.

	Symptomatic infection*, odds ratio (95 % CI)					Negative conversion time†, difference (95 % CI), days
	Overall	Systemic	Respiratory	Gastrointestinal	Sensory	
Normal weight + no diabetes	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
Overweight + no diabetes						
Model 1	0.98 (0.93, 1.02)	0.98 (0.94, 1.03)	0.97 (0.93, 1.01)	0.94 (0.89, 0.99)	1.10 (0.91, 1.33)	0.15 (0.08, 0.21)
Model 2	0.98 (0.94, 1.02)	0.98 (0.94, 1.03)	0.97 (0.93, 1.01)	0.94 (0.89, 0.98)	1.15 (0.95, 1.40)	0.15 (0.09, 0.21)
Model 3	0.95 (0.91, 0.99)	0.96 (0.91, 1.00)	0.94 (0.9, 0.99)	0.91 (0.87, 0.96)	1.09 (0.90, 1.33)	0.12 (0.06, 0.18)
Obesity + no diabetes						
Model 1	1.00 (0.88, 1.14)	1.03 (0.90, 1.16)	1.03 (0.9, 1.16)	1.03 (0.89, 1.18)	0.53 (0.24, 1.01)	0.33 (0.15, 0.52)
Model 2	1.00 (0.88, 1.14)	1.02 (0.90, 1.16)	1.02 (0.9, 1.16)	1.02 (0.89, 1.18)	0.53 (0.24, 1.01)	0.31 (0.13, 0.49)
Model 3	0.90 (0.79, 1.02)	0.92 (0.81, 1.05)	0.93 (0.82, 1.07)	0.95 (0.82, 1.09)	0.45 (0.20, 0.87)	0.19 (0.01, 0.38)
Normal weight + diabetes						
Model 1	1.24 (1.04, 1.48)	1.15 (0.97, 1.37)	1.17 (0.98, 1.39)	0.96 (0.79, 1.16)	1.64 (0.88, 2.78)	0.31 (0.06, 0.56)
Model 2	1.17 (0.98, 1.40)	1.10 (0.92, 1.31)	1.11 (0.94, 1.33)	0.93 (0.77, 1.13)	1.52 (0.81, 2.62)	0.18 (−0.07, 0.43)
Model 3	0.99 (0.83, 1.19)	0.95 (0.79, 1.13)	0.98 (0.82, 1.17)	0.83 (0.68, 1.01)	1.24 (0.66, 2.17)	−0.02 (−0.28, 0.23)
Overweight + diabetes						
Model 1	1.34 (1.23, 1.45)	1.24 (1.15, 1.35)	1.30 (1.20, 1.40)	1.17 (1.07, 1.27)	1.74 (1.33, 2.27)	0.44 (0.33, 0.56)
Model 2	1.28 (1.18, 1.39)	1.19 (1.10, 1.29)	1.24 (1.14, 1.34)	1.13 (1.04, 1.23)	1.74 (1.32, 2.29)	0.33 (0.21, 0.44)
Model 3	1.08 (0.98, 1.18)	1.02 (0.93, 1.11)	1.08 (0.99, 1.18)	1.00 (0.91, 1.10)	1.41 (1.03, 1.90)	0.11 (−0.02, 0.23)
Obesity + diabetes						
Model 1	1.38 (1.18, 1.63)	1.33 (1.14, 1.56)	1.35 (1.16, 1.59)	1.19 (1.01, 1.39)	2.17 (1.34, 3.33)	0.47 (0.24, 0.70)
Model 2	1.34 (1.14, 1.58)	1.29 (1.10, 1.51)	1.32 (1.12, 1.55)	1.16 (0.98, 1.37)	2.22 (1.36, 3.45)	0.40 (0.17, 0.62)
Model 3	1.12 (0.95, 1.33)	1.10 (0.93, 1.29)	1.14 (0.97, 1.35)	1.02 (0.86, 1.21)	1.77 (1.07, 2.81)	0.16 (−0.07, 0.40)

* Estimates were obtained from logistic regressions, adjusting for age, sex (Model 1), doses of vaccine (Model 2), and number of comorbidities (Model 3).
† Estimates were obtained from Poisson regressions, adjusting for age, sex (Model 1), doses of vaccine (Model 2), number of comorbidities, and symptomatic infection (Model 3).

Table 5
Associations of vaccine doses with symptomatic infection and negative conversion of viral RNA by weight and diabetes status.

	Symptomatic infection*, odds ratio (95 % CI)					Negative conversion time†, difference (95 % CI), days
	Overall	Systemic	Respiratory	Gastrointestinal	Sensory	
Normal weight + no diabetes						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
2 doses	0.69 (0.56, 0.84)	0.86 (0.71, 1.04)	0.98 (0.81, 1.18)	1.08 (0.88, 1.31)	0.11 (0.07, 0.17)	−0.46 (−0.74, −0.18)
3 doses	0.43 (0.35, 0.52)	0.57 (0.48, 0.69)	0.63 (0.52, 0.75)	0.76 (0.63, 0.92)	0.10 (0.07, 0.14)	−1.57 (−1.85, −1.29)
Overweight + no diabetes						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
2 doses	0.73 (0.61, 0.88)	1.07 (0.90, 1.27)	1.15 (0.97, 1.36)	1.11 (0.92, 1.33)	0.12 (0.09, 0.17)	−0.71 (−0.98, −0.44)
3 doses	0.47 (0.39, 0.56)	0.70 (0.59, 0.83)	0.74 (0.63, 0.87)	0.88 (0.74, 1.05)	0.07 (0.05, 0.09)	−1.81 (−2.07, −1.55)
Obesity + no diabetes						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
2 doses	0.94 (0.48, 1.78)	0.80 (0.41, 1.50)	1.10 (0.58, 2.03)	0.78 (0.43, 1.42)	0.49 (0.04, 11.56)	−1.09 (−2.06, −0.16)
3 doses	0.46 (0.24, 0.84)	0.42 (0.22, 0.77)	0.56 (0.30, 1.00)	0.65 (0.37, 1.16)	0.56 (0.08, 11.48)	−2.00 (−2.95, −1.10)
Normal weight + diabetes						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
2 doses	0.69 (0.27, 1.60)	1.29 (0.58, 2.80)	1.11 (0.49, 2.41)	3.13 (1.15, 10.98)	0.13 (0.03, 0.62)	−0.96 (−2.24, 0.24)
3 doses	0.50 (0.20, 1.14)	0.99 (0.45, 2.11)	0.85 (0.38, 1.82)	2.36 (0.88, 8.23)	0.07 (0.01, 0.37)	−1.49 (−2.74, −0.31)
Overweight + diabetes						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
2 doses	0.51 (0.34, 0.75)	0.96 (0.68, 1.33)	0.94 (0.67, 1.31)	1.15 (0.83, 1.60)	0.07 (0.04, 0.14)	−1.15 (−1.66, −0.66)
3 doses	0.39 (0.26, 0.56)	0.69 (0.50, 0.96)	0.73 (0.52, 1.01)	1.08 (0.79, 1.50)	0.12 (0.07, 0.22)	−1.63 (−2.12, −1.14)
Obesity + diabetes						
0 dose	[reference]	[reference]	[reference]	[reference]	[reference]	[reference]
2 doses	1.06 (0.51, 2.10)	1.55 (0.80, 2.95)	1.67 (0.86, 3.19)	1.71 (0.85, 3.70)	0.22 (0.07, 0.68)	−0.85 (−1.88, 0.13)
3 doses	0.80 (0.39, 1.55)	1.23 (0.65, 2.29)	1.27 (0.67, 2.36)	1.82 (0.92, 3.87)	0.16 (0.05, 0.49)	−1.27 (−2.27, −0.32)

* Estimates were obtained from logistic regressions, adjusting for age, sex, and number of comorbidities.
† Estimates were obtained from Poisson regressions, adjusting for age, sex, number of comorbidities, and symptomatic infection.

5. Research in context

5.1. Evidence before this study

We searched PubMed, Google Scholar and medRxiv from Jan 1, 2020 to May 31, 2022. Obesity and diabetes have been associated with increased severity of COVID-19 as well as prolonged viral shedding and thus chances of spreading SARS-CoV-2. However, we did not identify any study investigating the collective association of different weight and diabetes status on symptomatic infection and viral shedding. Furthermore, the effectiveness of vaccination on preventing symptoms after SARS-CoV-2 infection and reducing viral shedding may vary by weight status, diabetes status and age, but little data are available particularly among Asians whose cardiometabolic risk profiles and distribution of adipose tissue differ from Caucasians.

5.2. Added value of this study

Based on over 38,000 adults with confirmed SARS-CoV-2 infection in Shanghai, this is the first study to reveal that adults with diabetes and overweight/obesity had a higher risk of symptomatic infection and prolonged negative conversion time of viral RNA compared with adults with normal weight and without diabetes,

but this association was primarily attributed to underlying comorbidities. Booster vaccination but not full vaccination was associated a lower risk of symptomatic infection, a shorter negative conversion time or both, regardless of weight status and diabetes status, alone and in combination. Furthermore, the effectiveness of booster vaccination on preventing symptomatic infection and shortening negative conversion time did not attenuate with age.

5.3. Implications of all the available evidence

Approximately half of the global population are overweight, obese or diabetic. Findings of this study suggest that people regardless of body mass index, diabetes, and age should receive three doses of vaccine for preventing symptomatic infection with SARS-CoV-2 and for reducing transmission. Future efforts need to focus on increasing vaccination rate particularly booster doses for COVID-19 prevention and control.

6. Contributors

VWZ, XL, WZ, JZ and HW designed the study. VWZ and JR conducted the statistical analysis. VWZ wrote the initial draft of the manuscript. All authors revised the manuscript critically for important intellectual content and edited the final version of the manuscript. All authors approved the final version of the manuscript. VWZ, WZ, JZ and HW had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Data availability

Individual data related to this article were subject to ethical approval and cannot be made publicly available.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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