Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection

基于人群并按年龄分层的 COVID-19 病毒血清流行病学调查方案

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方案概要

基于人群的 COVID-19 年龄分层血清流行病学调查方案	
研究人群	普通人群的年龄分层便利样本
潜在结果及分析	以下估计值: •特定年龄的感染程度 •累计感染率 •感染罹患率 •无症状感染比例 •病死率
研究设计	按年龄分层的普通人群前瞻性人群便利样本
研究时间	该调查可以采用横断面调查方式，也可以采用前瞻性队列研究的连续抽样方式
从参与者那里获得的最少信息及样本	数据收集: 流行病学数据包括: 临床症状 样本: 用于血清流行病学推断的血清样本

Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection	
Study population	Age-stratified convenience sample from general population
Potential output and analysis	Estimates of: • Extent of age-specific infection • Cumulative incidence of infection • Infection attack rates • Fraction of asymptomatic infection • Case fatality ratio
Study design	Prospective population-based convenience sample from the general population, stratified by age
Study duration	The investigation can be conducted as a cross-sectional investigation, or can include serial sampling as a prospective cohort study
Minimum information and specimens to be obtained from participants	Data collection: Epidemiological data including: clinical symptoms Specimens: Serum samples to inform seroepidemiological inferences

WHO, in collaboration with technical partners, has developed a series of enhanced surveillance protocols, that are harmonized to help provide detailed insight into the epidemiological characteristics of COVID-19. Other COVID-19 investigations and studies protocols currently available include:

- Household transmission investigation protocol for COVID-19 virus infection

- Protocol for assessment of potential risk factors for COVID-19 infection among health care workers in a health

世卫组织与技术伙伴合作制定了一系列强化监测规程，这些规程经过协调有助于对 COVID-19 流行病学特征有更为详细的了解。现如今有关 COVID-19 其他的一些调查和研究方案包括:

- COVID-19 病毒感染家庭内传播调查方案

- 在卫生保健环境中评估医务工作者

care setting

- Surface sampling of COVID-19 virus: A practical "how to" protocol for health care and public health professionals

感染 COVID-19 潜在风险因素研究方案

- 物体表面采集 COVID-19 病毒的标本：卫生保健和公共卫生专业人员的实用"how to"方案

All WHO protocols for COVID-19 are available on the [WHO website](#) together with the technical guidance documents. This currently includes case definitions, laboratory guidance, infection prevention and control and travel advice

世卫组织有关 COVID-19 的所有方案和技术指导文件均可在 [WHO website](#) 查阅。目前包括病例定义、实验室指导、感染预防和控制以及旅行建议。

1 背景

The detection and spread of an emerging respiratory pathogen are accompanied by uncertainty over the key epidemiological and serologic characteristics of the novel pathogen and particularly its ability to spread in the human population and its virulence (case-severity). This is the case for the COVID-19 virus, first detected in Wuhan city, China in December 2019 (1).

新出现的呼吸道病原体的检测和传播伴随着对这种新病原体的主要流行病学和血清学特征的不确定性，特别是其在人群中传播的能力及其毒性（病例严重程度）。这是 2019 年 12 月在中国武汉市首次发现的 COVID-19 病毒（1）。

To date initial surveillance has focused primarily on patients with severe disease, and, as such, the full spectrum of the disease, including the extent and fraction of mild or asymptomatic infections that do not require medical attention are not clear. Estimates of the case fatality ratio, and other epidemiological parameters, will likely be lower than current crude mortality estimates once the full spectrum of disease is able to be included in the denominator. In addition, the role of asymptomatic or subclinical infections in human-to-human transmission of COVID-19 virus is not well understood and it is not yet clear whether those who are reported as asymptomatic may be able to transmit the virus to other individuals.

迄今为止，最初的监测都主要集中在重症患者身上。因此，该疾病的全部病谱，其中不需要医疗护理的轻度或无症状感染病例的范围和比例尚不清楚。因此，一旦将全系列病谱纳入分母，对于病死率和其他流行病学参数的估计可能会低于现今粗死亡率的估计。此外，无症状或亚临床感染在 COVID-19 病毒人际传播中的作用尚不了解，目前尚不清楚报道中无症状感染者是否能够将病毒传播给其他人。

With a novel coronavirus, initial seroprevalence in the population is assumed to be negligible due to the virus being novel in origin. Therefore, surveillance of antibody seropositivity in a population can allow inferences to be made about the extent of infection and about the cumulative incidence of infection in the population

因为新型冠状病毒是一种新型病毒，人群中的初始血清阳性率被认为是可忽略不计的。因此，在人群中监测抗体血清阳性可以推断人群感染程度和感染累积发病率。

The following protocol has been designed to investigate the extent of infection, as determined by seropositivity in the general population, in any country in which COVID-19 virus

下列方案旨在任何报告感染 COVID-19 病毒国家开展调查，由一般人群的血清阳性率所确定的感染程度。各国可

infection has been reported. Each country may need to tailor some aspects of this protocol to align with public health, laboratory and clinical systems, according to capacity, availability of resources and cultural appropriateness. However, using a standardized protocol such as this one below, epidemiological exposure data and biological samples can be systematically collected and shared rapidly in a format that can be easily aggregated, tabulated and analyzed across many different settings globally for timely estimates of COVID-19 virus infection severity and attack rates, as well as to inform public health responses and policy decisions. This is particularly important in the context of a novel respiratory pathogen, such as COVID-19 virus.

Comments for the user's consideration are provided in purple text throughout the document as the user may need to modify methods slightly because of the local context in which this study will be carried out.

能需要根据能力、资源可用性和文化适宜性，调整该方案的某些方面使其与公共卫生、实验室和临床系统相一致。然而，使用下文这样的标准化协议，可以系统快速地收集和分享流行病学接触数据和生物样本，其格式可以在全球许多不同环境中方便地进行汇总、列表和分析，以便及时估计 COVID-19 病毒感染的严重程度和罹患率，并为公共卫生应对措施和政策决定提供信息。这对于一种新的呼吸道病原体显得尤为重要，如 COVID-19。

供使用者参考的注解意见在整个文档中以紫色文本形式显示，因为使用者可能需要根据当地研究背景稍做修改。

1.1 目标

There are two primary objectives for this seroepidemiological investigation:
1. To determine the extent of infection in the general population and age-specific infection cumulative incidence, as determined by seropositivity
2. To determine the fraction of asymptomatic or subclinical infections
Seroepidemiological investigations provide the opportunity to evaluate secondary objectives, such as, but not limited to:
1. To determine risk factors for infection by comparing the exposures of infected and non infected individuals
2. To more accurately determine the case fatality ratio

本项血清流行病学调查主要有两个目标：
1. 根据血清阳性率确定一般人群中的感染程度和年龄特异性感染累积发病率
2. 确定无症状或亚临床感染的比例

血清流行病学调查提供了评价次级目标的机会，包括但不限于：
1. 通过比较感染者和非感染者的暴露情况来确定感染的危险因素
2. 更准确地评估病死率

COMMENT: Little is currently known about COVID-19 virus antibody kinetics. Asymptomatic infected persons may clear the virus more quickly than do symptomatic patients and antibody titers in the 5 former are likely to be lower, if they seroconvert at all, than in infected patients exhibiting symptoms. These are considerations for the interpretation of any COVID-19 virus seroepidemiological investigation.

注解：目前对 COVID-19 病毒抗体动力学了解甚少。如果血清转化完全，无症状的感染者可能比有症状的患者更快地清除病毒，抗体效价也更低。这些考虑因素完全基于对所有 COVID-19 病毒血清流行病学调查的解释。

2 研究步骤

2.1 研究设计

The seroepidemiological investigation for COVID-19 virus infection is a population-based, age-stratified prospective study. It is intended to provide key epidemiological and serologic characteristics of COVID-19 virus.

COVID-19 病毒感染的血清流行病学调查是一项以人群为基础、按年龄分层的前瞻性研究。旨在提供 COVID-19 病毒的主要流行病学和血清学特征。关于如何实施这项研究有三种可能性：

There are three possibilities for how this study can be implemented:
1) Cross-sectional investigation
2) Repeated cross-sectional investigation in the same geographic area (but not necessarily the same individuals each time)
3) Longitudinal cohort study with serial sampling of the same individuals each time

关于如何实施这项研究有三种可能性：
1）横断面调查
2）在同一地理区域反复进行横断面调查(但每次不需要是同一批人)
3）每次对同一批人进行连续抽样的纵向队列研究

COMMENT: The first option will likely be the easiest to implement for countries to implement, while the third provides the most comprehensive information on extent of infection, as described below. The choice as to how this study will be implemented should be determined by feasibility and available capacity.

注解：第一个备选方案可能是各国最容易实施的方案，然而第三个备选方案提供了关于感染程度最全面的信息，如下文所述。然而，研究方案的实施选择应基于可行性和现有能力来决定。

The timing of the study will depend on the specific public health questions that need to be addressed. If serial sampling is to be conducted, it is best to initiate the investigation as quickly as possible. Serial sampling can then be conducted as long as possible, as determined by capacity and resources.

研究的时间取决于待解决的具体的公共卫生问题。如果要进行连续抽样，最好尽快展开调查。然后再根据能力和资源的确定，尽可能长时间地进行序列抽样。

For one-time cross-sectional investigations, there may be an interest in completing the investigation after the peak of transmission of the epidemic wave. However, a cross-sectional investigation, conducted at any time of the epidemic, will provide important information that can be used to inform public health responses.

对于一次性横断面调查，也许在疫情传播高峰后完成调查更有益处。然而，在疫情发生的任何时期开展的横断面调查都将为告知公共卫生对策提供重要信息。

For longitudinal cohort study with serial sampling, the epidemic curve from surveillance (daily number of new confirmed cases) can be used to adjust the frequency with which samples are collected to provide real-time estimates of seropositivity in the general population.

对于连续抽样的纵向队列研究，可以利用监测的流行曲线(每日新增确诊病例数)来调整样本采集的频率，从而实时估计一般人群的血清阳性率。

2.2 研究人群

The geographic scope of the investigation should first be defined. This may be limited to a local or regional investigation, or may be conducted as a national investigation. Within the geographic scope of the study, high incidence and low incidence areas should be identified. The selection of these areas should be informed by the latest information on COVID-19 virus circulation, available on the [WHO website](#).

首先要明确调查的地理范围。可能是仅限于当地或区域性的调查，也可能作为全国性调查。在展开研究的地理范围内，应确定发病率高和低的地区。地区的选择可参考在 [WHO website](#) 上有关COVID-19 病毒传播的最新资料。

The study population should then be identified in at least one high incidence and one low incidence area through the random selection of households. For the purpose of this investigation, a household is defined as a group of people (2 or more) living in the same residence. In practice, the technical definition may vary due to social, political and cultural practices.

然后应在至少一个高发病率和一个低发病率地区确定研究人群并随机选择家庭。为了进行这项调查，家庭被定义为居住在同一住所的一群人(两个或两个以上)。实际上，由于社会、 政治和文化实践的不同，技术上的定义可能会有所不同。

Definitions of a household which may be used (but are not limited to):
• Two or more people living together in a domestic residence (residential institutions, such as boarding schools, dormitories, hostels or prisons will be excluded).
• A dwelling or group of dwellings with a shared kitchen or common opening onto a shared household space.

家庭可被定义为(但不限于):
• 两个或两个以上的人同住一个家庭住所(住宅单位，例如寄宿学校、宿舍、旅馆或监狱被排除在外)
• 共用厨房或共用家庭空间的一组住宅

All persons living in the household should be invited to participate in the study, including children to ensure age-specific attack rates can be calculated.

住在同一家庭的所有成员都应被邀请参加研究，其中包括儿童，以便确保能够计算出特定年龄的罹患率。

COMMENT: The distribution of household compositions in the population would be needed to calculate population, age-specific infection attack rates.

注解：需要获得人口中家庭成员的分布情况，以便计算人口、年龄特定的感染罹患率。

The random selection of households within a geographic area is one method of recruitment. Random digit dialing[1] , blood donors or other ongoing longitudinal cohort studies may also be used to identify and recruit individuals to participate in the investigation. The advantage of working with blood donors is that they are usually forthcoming to being contacted for future follow-up and you may be able to track long-term antibody dynamics. For COVID-19, the age-specific attack rates in blood

在研究地理区域内随机选择住户是一种招募方法。

随机数字拨号 [1]，献血者或其他正在进行的纵向队列研究也可用于识别和招募个体参与调查。与献血者一起工作的好处是：他们通常很乐意接受联系以便

donors are likely to be similar to that in the general population except for those with substantial comorbidities or elevated exposure (e.g. healthcare workers).

后续随访，而且可以长期跟踪抗体动态。对于 COVID-19 而言， 献血者的年龄特异性罹患率可能与一般人群类似， 但严重并发症及高暴露人群除外(例如医护人员)。

[1] Riley S, Kwok KO, Wu KM et al. Epidemiological characteristics of 2009 (H1N1) pandemic influenza based on paired sera from a longitudinal community cohort study. *PLoS Med*. 2011 Jun;8(6):e1000442

COMMENT: Plasma may be collected from a subset of participants so that the serologic assay results of the serum and plasma could be compared. This might be useful if sera and plasma give the same results as plasma are stored in many blood donor archives which could be used to retrospectively to estimate the infection attack rate.

注解：通过采集参与者的血浆，比较血清和血浆的血清学检测结果。如果血清和血浆显示相同结果，这将可能非常有用。因为血浆储在许多献血者存档处都有保存，可用于回顾性地估计感染罹患率。

Whichever method is used to identify and recruit participants, all attempts should be made to include participants over a range of ages in order to be able to determine and compare age-specific attack rates, although crude age-specific estimates will need to be adjusted for age structures in the population.

无论采用何种方法来确定和招募参与者，都应尽一切努力将不同年龄段的人群包括在内，从而确定和比较不同年龄段的罹患率，尽管需要根据人口的年龄结构来调整粗略的年龄分布。

COMMENT: Depending on which method of study recruitment is chosen, the group implementing the study may choose either to conduct home visits to collect data and specimens or to centralize data and specimen collection at one location, asking participants to travel to the location to participate in the study. Decisions as to how to implement the study should be determined by feasibility and resource (including personnel) availability.

注解：根据选择的研究招募方式，研究团队可以选择家访进行数据和样本收集，或在同一地点集中收集数据和样本，要求参与者前往该地点参与研究。关于如何实施这项研究的决定应该由可行性和资源(包括人员)的可用性来决定。

2.3 合格标准

Inclusion criteria: All individuals identified for recruitment into the investigation, irrespective of age.

纳入标准：不论年龄，所有被确定参加调查的人

Exclusion criteria: Refusal to give informed consent, or contraindication to venipuncture

排除标准：拒绝给予知情同意或有静脉穿刺禁忌症人群

2.4 数据收集

Each participant recruited into the investigation should be asked to complete a questionnaire which covers demographic and exposure information. An example of an investigation questionnaire which may be used can be found in the Appendix A. This questionnaire is not exhaustive and may need to be adapted to the local setting and outbreak characteristics, but it provides an outline as to the data to be collected in order to calculate the epidemiological parameters (see 4.3 Epidemiological parameters).

招募到的每位研究对象都需要完成一份包括人口学信息和暴露信息的问卷。附录 A 提供了一份可供使用的调查问卷示例。该问卷中的信息并不全面，可能需要根据当地情况和暴发特点进行调整，但是它提供了一个计算流行病学参数（参阅 4.3 流行病学参数）所需收集的数据的框架。

2.5 标本采集

A serum sample needs to be collected from each participant upon recruitment into the investigation.
The collection of serum samples should follow specimen collection guidance in the country.

入组时，对每名研究对象采集一份血清标本，血清标本的采集应遵循国家标本采集指南。

 Table 1 describes when data and specimens should be collected according to the study design selected. If repeated sampling is to be conducted, whether as a repeated cross-sectional investigation, or as a longitudinal investigation, specimens should be collected at least 21 days apart.

表 1 描述了不同研究设计类型收集数据和采集标本的时间。无论是重复的横断面调查还是纵向调查，如果需要重复采样，两次采样之间至少需要间隔 21 天。

COMMENT: Other specimens (e.g. nasopharyngeal) may be collected to determine acute COVID-19 infection, as determined by the objectives of the investigation and the available resources and capacity.

注解：也可以采集其他标本（如鼻咽部的标本）来确诊 COVID-19 的急性感染，这取决于调查的目的和可用的资源及实际能力。

表 1：不同类型研究设计的数据收集和标本采集时间表

研究设计	基线	进一步招募和随访（基线调查后至少 21 天后）	对已招募的个体的定期随访（与招募时间间隔至少 21 天）		
横断面调查	数据收集和标本采集				
重复横断调查	数据收集和标本采集	数据收集和标本采集			
纵向队列调查	数据收集和标本采集		数据收集和标本采集	数据收集和标本采集	数据收集和标本采集

Figure 1: Schedule for data and specimen collection according to study design

Study design	Baseline	Further recruitment and follow-up (at least 21 days after baseline)	Regular follow-up of same individuals recruited (at least 21 days apart)		
Cross-sectional investigation	Data and specimen collection				
Repeated cross-sectional investigation	Data and specimen collection	Data and specimen collection			
Longitudinal cohort investigation	Data and specimen collection		Data and specimen collection	Data and specimen collection	Data and specimen collection

2.6 标本运输

All those involved in the collection and transportation of specimens should be trained in safe handling practices and spill decontamination procedures. For details regarding the transport of samples collected and infection control advice, please refer to case management algorithm and laboratory guidance in the country or WHO laboratory guidance, available on the WHO website.

所有参与标本采集和运输的人员均应该接受安全操作规范和溅出物无害化处理方面的培训。如果需要详细的标本运输和感染控制建议，请参阅各个国家的病例管理算法和实验室指南或者 WHO website 上的世界卫生组织实验室指南。

For each biological sample collected, the time of collection, the conditions for transportation and the time of arrival at the study laboratory will be recorded. Specimens should reach the laboratory as soon as possible after collection. If the specimen is not likely to reach the laboratory within 72 hours, specimens should be frozen, preferably at -80°C, and shipped on dry ice. It is, however, important to avoid repeated freezing and thawing of specimens. The storage of serum specimens in domestic frost-free freezers should be avoided, owing to their wide temperature fluctuations. Serum should be separated from whole blood and can be stored and shipped at 4°C or frozen to -20°C or lower and shipped on dry ice.

记录每个生物标本的采样时间、运输条件和到达实验室的时间。标本采集后应尽快送到实验室。如果无法在 72 小时内将标本送到实验室，应将标本冷冻（最好在-80°C 的条件下）起来并用干冰运输，但是应该避免反复冷冻和解冻标本。家用无霜冰箱的温度波动大，不能用来保存血清标本。应该将血清和全血分开。血清可在 4°C 条件下储存和运输，也可以冷冻至-20°C 或更低后用干冰运输。

Transport of specimens within national borders should comply with applicable national regulations. International transport of specimens should follow applicable international regulations as described in the WHO Guidance on Regulations for the Transport of Infectious Substances 2019-2020.

在国内运输标本时应遵守相应的国家法规，进行标本的国际运输时应遵循《世界卫生组织关于传染性物质运输的法规指南（2019-2020 年）》中的相应国际法规。

2.7 伦理考量

Ethical requirements will vary by country. In some countries, this investigation may fall under public health surveillance (emergency response) acts and may not require ethical approval from an Institutional Review Board.

伦理学的要求因国家而异。此类调查在一些国家属于公共卫生监测（应急响应）法的范畴，不需要经过伦理审查委员会的批准。

2.7.1 知情同意

The purpose of the investigation will be explained to all individuals identified for recruitment into the investigation. Informed consent will be obtained from all individuals willing to participate in the investigation before any procedure is performed as part of the investigation by a trained member of the investigation team. Consent for children under the legal age of consent will be obtained from a parent or legal guardian. Each participant must be informed that participation in the investigation is voluntary and that s/he is free to withdraw, without justification, from the investigation at any time without consequences and without affecting professional responsibilities.

应向所有拟招募的个体解释调查目的。在调查开始前，应由调查组内一名接受过训练的成员收集所有愿意参加调查的研究对象的知情同意书。未满法定年龄的儿童的知情同意书由其父母或法定监护人提供。必须告知每名研究对象：他/她是自愿参与调查，且随时可以无条件退出调查，这种退出不需要承担任何后果或专业责任。

COMMENT: The age of consent may vary by country. Check the

注解：知情同意的法定年龄因国家而

Informed consent will seek approval to collect blood and epidemiological data for the intended purpose of this investigation, that samples may be shipped outside of the country for additional testing and that samples may be used for future research purposes.

知情同意书上应将征求研究对象的同意，也就是同意血液和流行病学数据的收集以达到本调查的预期目的，标本有可能被运到国外进行进一步的检测，也可能用于将来的研究目的。

2.7.2 受试者的风险和收益

This investigation poses minimal risk to participants, involving the collection of a small amount of blood. The primary benefit of the study is indirect in that data collected will help improve and guide efforts to understand extent of COVID-19 virus infection and may prevent further transmission of the virus.

本调查涉及少量血液的采集，给受试者带来的风险很小。受试者主要获得一些间接的益处，也就是所收集的数据有助于改善和指导人们了解 COVID-19 的感染程度，并可能阻止病毒的进一步传播。

2.7.3 保密性

Participant confidentiality will be maintained throughout the investigation. All subjects who participate in the investigation will be assigned a study identification number by the investigation team for the labelling of questionnaires and specimens. The link of this identification number to individuals will be maintained by the investigation team and the Ministry of Health (or equivalent) and will not be disclosed elsewhere

整个调查过程都会保护研究对象的隐私。调查团队会给每名研究对象一个研究识别号，该识别号用于对问卷和标本进行标记。该识别号与研究对象之间的链接将由调查团队和卫生部门共同维护，不会被泄露到其他地方。

If the data is shared by the implementing organization to WHO or any agency or institution providing support for data analysis, data shared will include only the study identification number and not any personably identifiable information.

如果实施调查的机构将数据共享给世界卫生组织或任何提供数据分析支持的机构，共享的数据将仅包含研究标识号，而不包含任何可以识别个人身份的信息。

Article 45 of the IHR (2005) describes the "treatment of personal data".[2] Person identifiable data collected under the IHR should be kept confidential and processed anonymously, as required by national law. However, such data may be disclosed for assessments and management of public health risks, provided the data are processed fairly and lawfully

《国际卫生条例（2005）》第 45 条描述了"个人数据的处理"。根据《国际卫生条例》，应对所收集的可识别个人身份的数据进行保密，并按照国家法律的要求进行匿名化处理。但是，在保证数据处理过程公平和合法的条件下，可以将这类数据用于公共卫生风险评估和管理。

2.7.4 预防调查人员感染 COVID-19

All personnel involved in the investigation need to be trained in infection prevention and control procedures (standard contact

所有参与调查的人员都需要接受感染预防和控制程序的培训（国家或当地指

and droplet precautions, as determined by national or local guidelines). These procedures should include proper hand hygiene and the correct use of surgical masks, if necessary, not only to minimize their own risk of infection when in close contact with individuals with COVID-19 infection, but also to minimize the risk of spread among other participants in the investigation.

南中所制定的标准的接触传播和飞沫传播预防措施）。这些程序应包括恰当的手卫生和必要时外科口罩的正确使用。这不仅是为了最大程度地降低调查员与 COVID-19 感染者密切接触时的自身感染风险，也是为了最大程度地降低他们在调查过程中将病毒传播给其他研究对象的风险。

WHO technical guidance on infection prevention and control specific to COVID-19 can be found on the [WHO website.](WHO website)

在 WHO website 上有 COVID-19 感染预防和控制的技术指南。

3 实验分析

Laboratory and biosafety guidance for COVID-19 can be found on the [WHO website.](WHO website)

针对 COVID-19 的实验室和生物安全指南可以在 WHO website 上获得。

Serologic assays specific to COVID-19 are currently under development / in the process of evaluation. The protocols or SOPs will be published on the WHO website once they become available. Cross reactivity to other coronaviruses may be an issue and should be considered in the interpretation of data. Multiple assays may be required to confirm a seropositive for COVID-19 virus.

针对 COVID-19 的血清学分析目前正在评估。一旦方案或标准操作流程可用，将在 WHO 官网上发布。分析过程中对其它冠状病毒的交叉反应可能存在，因此在数据呈现中应当考虑其影响。为了能够确保 COVID-19 的血清反应呈阳性，应当做多次分析。

Laboratory procedures involving sample manipulation must be carried out in a biosafety cabinet (BSC).

所有实验操作包括样品处理都应该在生物安全柜（BSC）中进行。

3.1 血清学检测

Serum samples should be screened for the presence of COVID-19 virus specific antibodies using serological testing. Tests for both IgM and IgG should be carried out using an enzyme linked immunosorbent assay (ELISA) or immunofluorescence. If a sample is positive for either IgM or IgG a plaque reduction neutralization test (PRNT) should be done.

应通过血清学检测筛选血清样本是否存在 COVID-19 病毒特异性抗体。IgM 和 IgG 的检测应采用酶联免疫吸附试验（ELISA)或免疫荧光法。如果样本的 IgM 或 IgG 呈阳性，则应进行空斑减少中和试验（PRNT）。

ELISA testing should be carried out in a facility with at least biosafety level 2 (BSL-2) capacity.

ELISA 应在至少具有生物安全 2 级（BSL-2）的设施中进行。

3.2 中和抗体存在的确认

A PRNT can be carried out on samples that were positive for COVID-19 specific IgM or IgG antibodies to confirm the presence of neutralizing antibodies.

可以对 COVID-19 病毒特异性 IgM 或 IgG 抗体呈阳性的样本进行 PRNT，以确认是否存在中和抗体。

PRNT should be carried out in a facility with at least BSL-3 capacity.

PRNT 应在至少具有生物安全 3 级（BSL-3）的设施中进行。

3.3 样品储存

In the case that serum samples cannot be processed immediately, they should be stored at -80℃. It is recommended to aliquot samples prior to freezing, to minimize freeze thaw cycles.

如果不能立即处理血清样品，应将其储存在-80℃ 下。并建议在冷冻前对样品进行等分，以尽量减少冻融循环。

COMMENT: These recommendations are subject to changes as new, reliable serological assays become available.

注解：随着新的、可靠的血清学检测方法的出现，这些建议可能会发生变化。

COMMENT: If serological testing is not available in the country in which serum samples are collected, they may be stored or shipped to an international reference laboratory. WHO is able to facilitate communication with international referral laboratories in order for samples to be shipped for further testing.

注解：如果在收集血清样本的国家无法进行血清学检测，则可将样本储存或运至国际参考实验室。世卫组织能够与国际转诊实验室沟通，以便运送样本进行进一步检测。

4 数据分析

4.1 样本量

The figure below provides estimates of margin of error as a function of seroprevalence for 100, 200 and 300 samples. For a given seroprevalence rate p and sample size N, the expected margin of error corresponds to the expected width of the 95% confidence interval associated with the point estimate of p obtained using binomial likelihood.

下图提供了 100 个、200 个和 300 个样本的血清阳性率的误差幅度估计。对于给定的血清阳性率 p 和样本量 N，预期的误差幅度对应于使用二项似然法得到的 p 点估计的 95%置信区间的期望宽度。
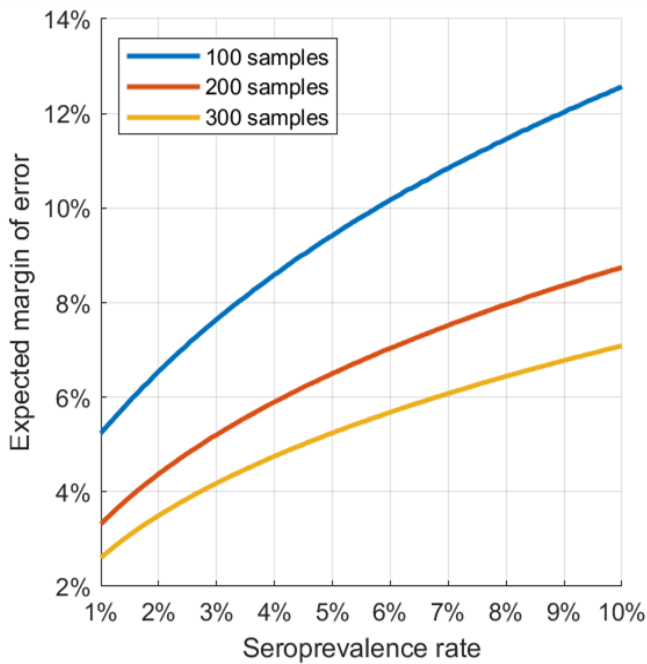
4.2 流行病学参数

下表提供了可作为本次调查的一部分的流行病学参数。

The table below provides an overview of the epidemiological parameters that can be measured as part of this investigation.

参数	定义 (括号内为其"简化"表达式)	得到数据来计算相关的参数的表格和问题	注释，限制
不同年龄组的发病率	不同年龄层对 COVID-19 病毒感染呈血清阳性的个体占比。		
不同年龄组累积发病率	不同年龄层中对病毒感染呈阳性反应的个体占比。		*比例应根据参与者年龄分层的差异和整体人口调整
有症状病例的比例(无症状部分)	感染 COVID-19 并有体征或症状的个体比例。		*分子是报告各种感染体征或症状(例如发烧、咳嗽)的人数，以及没有任何体征或症状的人数/比例（即无症状部分）；分母是所有参加监测的人。
对感染的血清学反应	血清中 COVID-19 病毒特异性抗体水平的变化(滴度升高)。		
最有风险的人群	最易受 COVID-19 病毒感染的群体(如年龄组、性别、职业)。		*可能只是一个早期信号，巢式病例对照研究可以用

			来评估感染的危险因素
重症比	某年龄组严重感染的比例，即感染引起严重疾病的概率，表示为重症数除以该年龄组病例总数的一个比例。		
病死率	感染 COVID-19 病毒后死亡个体的占比。		*可能需要延长随访时间以确定 COVID-19 感染患者的预后

Parameter	Definition (*in bracket*: "simplified" expression of it)	Form and questions where to get the data to calculate the parameters concerned	Comments, limitations
Age-specific attack rate	The proportion of individuals per age strata who show seropositivity for COVID-19 virus infection		
Age-specific cumulative incidence	The proportion of individuals per age strata who show seropositivity for virus infection		*Proportion should be adjusted for any difference in the age stratification of the participants and the overall population

Symptomatic proportion of cases (asymptomatic fraction)	The proportion of individuals who show symptoms or signs of COVID-19 infection		*The numerators of interest are the numbers of those individuals reporting various signs and symptoms of infection (e.g. fever, cough) and the number/proportion of individuals reporting no signs or symptoms (i.e. the asymptomatic fraction); the denominator is the total number of individuals tested.
Serological response to infection	The change in serum level of specific antibodies to COVID-19 virus (*Increase in titre*)		
Population groups most at risk	The identification of groups who are most vulnerable to COVID-19 virus infection (e.g. age groups, gender, occupation)		*May only be an early signal, a nested case-control study could be conducted to evaluate risk factors for infection
Ratio of severe disease	The proportion of an age group with severe infection, divided by the probability that an infection resulted in a severe case, expressed as a proportion of the total number of people in that age group		
Case fatality ratio	The proportion of individuals with fatal outcome for COVID-19 infection		* May require extended follow-up to determine outcome of those with COVID-19 infection

5 结果报告

5.1 报告

Any investigation of this nature should include reporting on the following information:

(1) the number of households and the number of individuals included;

(2) the age and sex of all individuals included

(3) the time in the outbreak of sample collection and the antibody titre levels of each specimen collected

(4) the number of individuals with serologic evidence of COVID-19 virus infection. If sample size permits, these numbers should be stratified by age

(5) the number of individuals with serologic evidence of COVID-19 virus infection who have reported symptoms

任何这种性质的调查都应包括报告下列信息：

（1）包括家庭数量和个人数量；
（2）包括所有个人的年龄和性别；
（3）样本采集时间及采集样本的抗体滴度；
（4）有 COVID-19 病毒感染血清学证据的个体数。如果样本量允许，这些数字应按年龄分层；
（5）有 COVID-19 病毒感染血清学证据且报告症状的个人数量。

It is also important to fully document the study design, how individuals were recruited, and the serological assay and methods used to ensure that data can be pooled to increase power in estimating epidemiological parameters.

另外，充分记录研究设计、个人招募方式、血清学检测试剂和方法，以确保能够汇总数据以提高估计流行病学参数能力的方法也同样重要。

Ideally, information would be collected in a standardized format according to the questionnaires and tools in this generic protocol to assist with data harmonization and comparison of results (see forms in Appendix A).

理想情况下，应根据调查问卷和本通用流程中工具来收集标准格式的信息以协助数据整合和结果比较（见附录 A 中的表格）。

To enable results to be aggregated across study sites and across county sites and by extension, strengthen the statistical power of the results, it is expected that they are shared with WHO by sending individual, de-identified data to EarlyInvestigations-2019-nCoV@who.int. The data shared should include only the study identification number and not any personably identifiable information.

为了使结果能够跨地点、跨国家汇总，进一步加强结果的统计功效，我们希望可以发送个人的、去识别（不包含任何个人身份信息）的数据到 EarlyInvestigations-2019-nCoV@who.int 与世卫组织共享结果。共享的数据应仅包括研究识别号，而不应包括研究识别号任何可识别的个人信息。

6 参考信息

6.1 有关 COVID-19 的更多参考信息

WHO Situation reports（WHO 现状报告）

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/

Surveillance and case definitions （病例确定与监测）

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/surveillance-and-case-definitions

Laboratory guidance （实验指南）

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance

Clinical management（临床管理）

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/patient-management

Infection prevention and control （感染预防与控制）

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/infection-prevention-and-control

Risk communications（风险通报）

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/risk-communication-and-community-engagement

7 致谢

This generic protocol was adapted from the protocol entitled "Prospective longitudinal cohort study of influenza infection during epidemic periods" by the Consortium for the Standardisation for Influenza Seroepidemiology (CONSISE). CONSISE is a global partnership aiming to develop influenza investigation protocols and standardise seroepidemiology to inform public health policy for pandemic, zoonotic and seasonal influenza. This international partnership was created out of a need, identified during the 2009 H1N1 pandemic, for better (standardised, validated) seroepidemiological data to estimate infection attack rates and severity of the pandemic virus and to inform policy decisions.

该通用流程改编自流感血清流行病学标准化联合会（CONSISE）题为"流行期流感感染前瞻性纵向队列研究"的方案。CONSISE 是一个全球联合会，旨在为大流行、人畜共患病和季节性流感制定流感调查方案和标准化血清流行病学分析，从而指导公共卫生政策的制定。建立这一国际联合会是为了在 2009 年 H1N1 大流行期间确定需要更好的（标准化的、经验证的）血清流行病学数据，以估计大流行病毒的感染攻击率和严重程度，并为政策决定提供信息。

附录

Appendix A: Sample questionnaires - Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection
附录 A：样本问卷-基于人群并按年龄分层的 COVID-19 血清流行病学调查方案

Form 1: Report Form for all participants
表 1：所有参与者的报告表

Form 2: Laboratory results for all participants
表 2：所有参与者的实验室结果

附录

基于人群并按年龄分层的 COVID-19 血清流行病学调查方案

表 1：所有参与者的报告表

参与者识别码	

1. 数据采集者信息	
数据采集者姓名	
数据采集者所属机构	
数据采集者电话号码	
手机号码	
电子邮件	
表格完成日期（日/月/年）	＿＿＿＿/＿＿＿＿/＿＿＿＿
与消息提供者面谈日期（日/月/年）	＿＿＿＿/＿＿＿＿/＿＿＿＿

2. 参与者信息	
名	
姓	
性别	（ ）男 （ ）女 （ ）未知
出生日期（日/月/年）	＿＿＿＿/＿＿＿＿/＿＿＿＿
电话号码（手机）	
年龄（岁，月）	
邮箱	
居住国	
国籍	
种族（选填）	
职业	
你有没有接触过疑似或确诊感染 COVID-19 病毒的人？	（ ）有 （ ）无 （ ）未知 如有，接触日期：（日/月/年） ＿＿＿＿/＿＿＿＿/＿＿＿＿

Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection

Form 1: Report Form for all participants

Unique ID	

1. Data Collector Information	
Name of data collector	
Data collector Institution	
Data collector telephone number	
Mobile number	
Email	
Form completion date (DD/MM/YYYY)	__/__/__
Date of interview with informant (DD/MM/YYYY)	__/__/__

2. Identifier information	
First name	
Surname	
Sex	□ Male □ Female □ Not known
Date of Birth (DD/MM/YYYY)	__/__/__
Telephone (mobile) number	
Age (years, months)	
Email	
Country of residence	
Nationality	
Ethnicity (optional)	
Occupation	
Have you had contact with a anyone with suspected or confirmed COVID-19 virus infection?	□ Yes □ No □ Unknown If Yes, dates of last contact (DD/MM/YYYY): __/__/__

3. 症状史	
在过去（X）个月内，您是否有以下情况： 注：（X）为从 COVID-19 病毒出现到数据收集的时间段	
体温≥38°C	（ ）是 （ ）否
感到寒冷	（ ）是 （ ）否
感到疲劳	（ ）是 （ ）否
肌肉疼痛	（ ）是 （ ）否
喉咙痛	（ ）是 （ ）否
咳嗽	（ ）是 （ ）否
流鼻涕	（ ）是 （ ）否
气短（呼吸困难）	（ ）是 （ ）否
喘息（气喘）	（ ）是 （ ）否
胸痛	（ ）是 （ ）否
其他呼吸道疾病症状	（ ）是 （ ）否
头痛	（ ）是 （ ）否

恶心/呕吐	（ ）是 （ ）否 （ ）未知
腹痛	（ ）是 （ ）否 （ ）未知
腹泻	（ ）是 （ ）否 （ ）未知
这些症状严重到需要就医吗？	（ ）是 （ ）否 （ ）未知
这些症状是否导致您耽误工作/学习？	（ ）是 （ ）否 （ ）未知
这些症状需要您住院治疗吗？	（ ）是 （ ）否 （ ）未知

3. Symptom history

In the past (X) months, have you had any of the following:

COMMENT: (X) period to cover time since emergence of COVID-19 virus to date of data collection

Fever ≥38°C	□ Yes □ No
Chills	□ Yes □ No
Fatigue	□ Yes □ No
Muscle ache (myalgia)	□ Yes □ No
Sore throat	□ Yes □ No
Cough	□ Yes □ No
Runny nose (rhinorrea)	□ Yes □ No
Shortness of breath (dyspnea)	□ Yes □ No
Wheezing	□ Yes □ No
Chest pain	□ Yes □ No
Other respiratory symptoms	□ Yes □ No
Headache	□ Yes □ No
Nausea/vomiting	□ Yes □ No

Abdominal pain	□ Yes □ No	
Diarrhea	□ Yes □ No	
Did any of these symptoms require you to seek medical attention?	□ Yes □ No	□ Unknown
Did any of these symptoms require you to miss work or school?	□ Yes □ No	□ Unknown
Did any of these symptoms require you to be hospitalized?	□ Yes □ No	□ Unknown

基于人群并按年龄分层的 COVID-19 血清流行病学调查方案

表 2：实验室结果

根据样本采集计划和研究设计，需要为采集的每个血清样本填写此表。

19b. 血清学试验方法和结果（为采集的每个样本填写新表格）：	
实验室识别号	
采集日期（日/月/年）	（日/月/年）_____/_____/_____
收到样品日期（日/月/年）	（日/月/年）_____/_____/_____
样品类型	□血清 □其他，说明：
血清学检测类型	
血清学结果	□阳性□阴性□未知
COVID-19 病毒滴度	
结果日期（日/月/年）	_____/_____/_____
样品是否运至其他实验室确认	□是　□否

日期（日/月/年）	（日/月/年）_____/_____/_____
结果确认	□阳性□阴性□未知

Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection

Form 2: Laboratory results

This table will need to be completed for every serum sample collected, as determined by the chosen specimen collection schedule and design of the study.

19b. Serology testing methods and results (complete new table for each specimen collected):	
Lab identification number	
Date sample collected (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___
Date sample received (DD/MM/YYYY)	(DD/MM/YYYY)___/___/___
Type of sample	□ Serum □ Other, specify:
Type of serological assay	
Serology result	□ Positive □ Negative □ Unknown
COVID-19 virus titres	
Date of result (DD/MM/YYYY)	___/___/___
Specimen shipped to other laboratory for confirmation - Date (DD/MM/YYYY)	□ Yes □ No (DD/MM/YYYY)___/___/___
Confirmation result	□ Positive □ Negative □ Unknown

Note: This translation was not created by WHO. WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition.

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