# 新型冠状病毒信息简报

第 40 期（2020 年 4 月 27 日报）

上海科技大学免疫化学研究所

生物医学大数据平台和高通量筛选平台领衔编译制作

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## 1. 2020 年 4 月 26 日疫情

数据来源：WHO

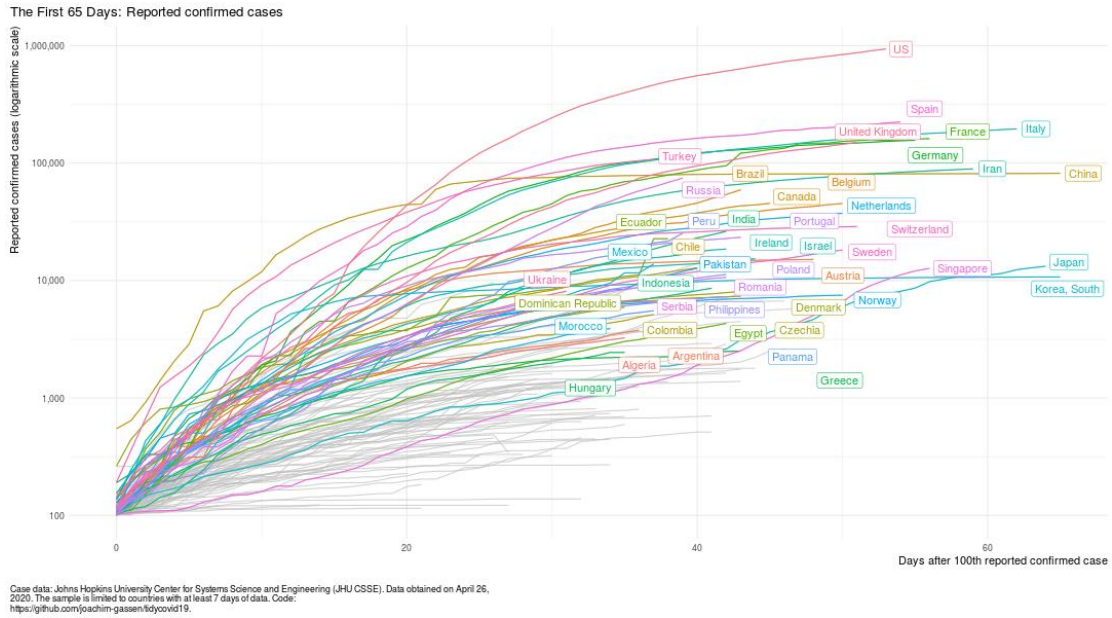
发布时间：2020 年 4 月 26 日北京时间下午 4 点

链接：

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

根据 WHO 提供的数据，2020 年 4 月 26 日全球累计确诊新型冠状病毒病人 2804796 例，当日新增确诊 84900 例，累计死亡 193710 例，当日新增死亡 6006。

中国累计确诊 84338 例，累计死亡 4642 例，当日新增确诊 14 例，新增死亡 0 例。




重点国家确诊数量曲线（https://jgassen.shinyapps.io/tidycovid19/，数据截止 4 月 26 日北京时间下午 4 点）


全国新型冠状病毒肺炎新增确诊病例分布图（4月26日，来源：http://2019ncov.chinacdc.cn/2019-nCoV/）

## 2. 废水中 SARS-CoV-2 RNA 滴度可预测 COVID-19 在低流行区出现——首次在西班牙未经处理的废水中检测到 SARS-CoV-2

SARS-CoV-2 RNA titers in wastewater anticipated COVID-19 occurrence in a low prevalence area——First detection of SARS-CoV-2 in untreated wastewater in Spain

**来源：** medRxiv
**发布时间：** 2020-04-25
**链接：** https://www.medrxiv.org/content/10.1101/2020.04.22.20075200v1
**第一作者：** Walter Randazzo
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**DOI 或 PUBMED ID：** https://doi.org/10.1101/2020.04.22.20075200
**编译者：** 宋张悦

**中文摘要：**

截至 2020 年 4 月 21 日，严重急性呼吸系统综合征冠状病毒 2 型(SARS-CoV-2)已在西班牙造成 20 多万 COVID-19 病例，导致 20800 多人死亡。COVID-19 患者粪便中 SARS-CoV-2 RNA 的脱落已经被广泛报道。因此，研究人员调查了 SARS-CoV-2 RNA 在 6 个污水处理厂(WWTPs)的发生情况，这些处理厂服务于穆尔西亚(西班牙)区的主要城市，而穆尔西亚是一个低流行区。首先，用猪冠状病毒(猪流行性腹泻病毒，PEDV)和门病毒(MgV)对氢氧化铝吸附-沉淀浓度法进行了测试。试验结果表明，该方法对进水和出水样品的平均回收率分别为 10.90%和 10.85%，对 PEDV 和 MgV 的平均回收率分别为 3.29%和 6.19%。然后，利用该方法监测 2020 年 3 月 12 日至 4 月 14 日期间，共收集 42 个进水样本、18 个二级和 12 个三级处理出水样本中 SARS-CoV-2 的发生情况。通过实时定量 PCR (RT-qPCR)诊断试剂盒（经美国 CDC 验证，靶向病毒核衣壳 N 基因的三个目标区域），研究人员估算未经处理的废水中 SARS-CoV-2 RNA 滴度的平均定量为 5.29 log 基因组拷贝/L。此外，研究人员还检测了所有二级和三级处理的水样，结果均为阴性，这表明目前污水处理厂污水消毒处理能够去除 SARS-CoV-2 RNA。将这一环境监测数据与全市公布的 COVID-19 病例进行了比较，结果显示，在许多采样了废水的城市中，在地方或国家当局报告第一例病例之前，SARS-CoV-2 就已在人群中传播。在 COVID-19 传播的早期阶段检测到废水中的 SARS-CoV-2，强调了这一策略作为在特定人群中感染的早期预警的相关性。此时，市政当局可以立即实施这种环境监测，作为一种工具，旨在帮助当局协调撤离战略，逐步解除对冠状病毒的封锁。
在法国巴黎进行的一项类似的研究表明，在疫情指数增长开始之前就发现了病毒基因组（详见 2020 年 4 月 18 日第 31 期简报第 2 条“巴黎废水中 SARS-CoV-2 的时间进程定量检测与 COVID-19 确诊病例相关”）。然而，本研究的结果表明，SARS-CoV-2 可在第一例确诊病例数周前检测到。废水中 SARS-CoV-2 RNA 的早期检测可以对即将到来的危险发出警报，给管理者一个宝贵的时间来协调和实施行动，以减缓疾病的传播。

**Abstract:**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused more than 200,000 reported COVID-19 cases in Spain resulting in more than 20,800 deaths as of April 21, 2020. Faecal shedding of SARS-CoV-2 RNA from COVID-19 patients has extensively been reported. Therefore, we investigated the occurrence of SARS-CoV-2 RNA in six wastewater treatments plants (WWTPs) serving the major municipalities

within the Region of Murcia (Spain), a low prevalence area. Firstly, an aluminum hydroxide adsorption-precipitation concentration method was tested using a porcine coronavirus (Porcine Epidemic Diarrhea Virus, PEDV) and mengovirus (MgV). The procedure resulted in average recoveries of 10.90% and 10.85% in influent water and 3.29% and 6.19% in effluent water samples for PEDV and MgV, respectively. Then, the method was used to monitor the occurrence of SARS-CoV-2 from March 12 to April 14, 2020 in influent, secondary and tertiary effluent water samples. By using the real-time RT-PCR (RT-qPCR) Diagnostic Panel validated by US CDC that targets three regions of the virus nucleocapsid (N) gene, we estimated quantification of SARS-CoV-2 RNA titers in untreated wastewater waters of 5.29 log genomic copies/L on average. Moreover, we tested as negative all secondary and tertiary treated water samples, highlighting that current water disinfection treatments applied in the analyzed WWTP are able to remove SARS-CoV-2 RNA. This environmental surveillance data were compared to declared COVID-19 cases at municipality level, revealing that SARS-CoV-2 was circulating among the population even before the first cases were reported by local or national authorities in many of the cities where wastewaters have been sampled. The detection of SARS-CoV-2 in wastewater in early stages of the spread of COVID-19 highlights the relevance of this strategy as an early indicator of the infection within a specific population. At this point, this environmental surveillance could be implemented by municipalities right away as a tool, designed to help authorities to coordinate the exit strategy to gradually lift its coronavirus lockdown.

### 3. 转载：一个专业养老院内的症状前 SARS-CoV-2 感染以及传播

Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility

**原文来源：**NEJM

**发布时间：**2020-04-24

**文章报道中文链接：**https://mp.weixin.qq.com/s/F7XHmGOsPCxwBEZ8upwJuw（已全文翻译）

**原文章链接：**https://www.nejm.org/doi/full/10.1056/NEJMoa2008457

**第一作者：**M.M. Arons, K.M. Hatfield

**通讯作者：**CDC COVID-19 Investigation Team

**通讯作者单位：**美国 CDC

**DOI 或 PUBMED ID：**10.1056/NEJMoa2008457

**中文摘要：**

**背景**

专业养老院内 SARS-CoV-2 会迅速传播。当我们在一个专业养老院内确认了一名 Covid-19 患者后，我们分析了其传播，并评估了在该机构居民中进行基于症状的筛查是否充分和有效。

**方法**

我们进行了两个系列的时点感染率调查，间隔 1 周。在该调查中，征得居民同意后，我们开展了鼻咽以及口咽拭子 SARS-CoV-2 检测，包括 rRT-PCR，病毒培养，以及基因组测序。我们记录了在检测之前 14 天出现症状的情况。无症状但病毒检测为阳性的居民会在 7 天后被重新评估。有 SARS-CoV-2 感染的居民被根据症状分成 4 类：典型症状者（发烧，咳嗽，呼吸困难），仅有非典型症状者，症状前或无症状者。

**结果**

在该专业养老院出现第一个阳性病例后的 23 天，89 个居民中 57 人（64%）出现 SARS-CoV-2 病毒阳性。在参与时点感染率调查的 76 个居民中， 48 人（63%）病毒检测为阳性。在这 48 个居民中，27 人（56%）在检测时无症状；24 人后来出现症状（至出现症状中位时间为 4 天）。在这 24 个症状前居民中，rRT-PCR 的中位循环值为 23.1，从 17 个居民中发现了活病毒。截止到 4 月 3 号，在 57 个感染了 SARS-CoV-2 的居民中，11 人住院治疗（其中 3 人在重症监护室），另外 15 人去世（死亡率为 26%）。在 34 个被测序的居民中，27 人（79%）的病毒序列可以分为两个聚类，其间仅有一个核苷酸的差异。

**结论**

有证据表明该专业养老院发生了 SARS-CoV-2 迅速而广泛的传播。一多半的阳性居民在检测时还是无症状者，但非常可能已具备传播能力。在 SARS-CoV-2 已经进入该机构后，控制传染的策略如果仅仅集中在有症状居民不足以防止其传播。

**Abstract:**

**BACKGROUND**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can spread rapidly within skilled nursing facilities. After identification of a case of Covid-19 in a skilled nursing facility, we assessed transmission and evaluated the adequacy of symptom-based screening to identify infections in residents.

**METHODS**

We conducted two serial point-prevalence surveys, 1 week apart, in which assenting residents of the facility underwent nasopharyngeal and oropharyngeal testing for SARS-CoV-2, including real-time reverse-transcriptase polymerase chain reaction (rRT-PCR), viral culture, and sequencing. Symptoms that had been present during the preceding 14 days were recorded. Asymptomatic residents who tested positive were reassessed 7 days later. Residents with SARS-CoV-2 infection were categorized as symptomatic with typical symptoms (fever, cough, or shortness of breath), symptomatic with only atypical symptoms, presymptomatic, or asymptomatic.

**RESULTS**

Twenty-three days after the first positive test result in a resident at this skilled nursing facility, 57 of 89 residents (64%) tested positive for SARS-CoV-2. Among 76 residents who participated in point-prevalence surveys, 48 (63%) tested positive. Of these 48 residents, 27 (56%) were asymptomatic at the time of testing; 24 subsequently developed symptoms (median time to onset, 4 days). Samples from these 24 presymptomatic residents had a median rRT-PCR cycle threshold value of 23.1, and viable virus was recovered from 17 residents. As of April 3, of the 57 residents with SARS-CoV-2 infection, 11 had been hospitalized (3 in the intensive care unit) and 15 had died (mortality, 26%). Of the 34 residents whose specimens were sequenced, 27 (79%) had sequences that fit into two clusters with a difference of one nucleotide.

**CONCLUSIONS**

Rapid and widespread transmission of SARS-CoV-2 was demonstrated in this skilled nursing facility. More than half of residents with positive test results were asymptomatic at the time of testing and most likely contributed to transmission. Infection-control strategies focused solely on symptomatic residents were not sufficient to prevent transmission after SARS-CoV-2 introduction into this

facility.

**4. 赛沛 Xpert Xpress、雅培 ID Now 与罗氏 cobas 在 SARS-CoV-2 快速检测性能上的比较**

Comparison of Cepheid Xpert Xpress and Abbott ID Now to Roche cobas for the Rapid Detection of SARS-CoV-2

来源：biorxiv
发布时间：2020-04-22
链接：https://www.biorxiv.org/content/10.1101/2020.04.22.055327v1
第一作者：Marie C. Smithgall
通讯作者：Daniel A. Green
通讯作者单位：纽约哥伦比亚大学欧文医学中心病理与细胞生物学系
DOI 或 PUBMED ID：Preprint
编译者：孔娟
中文摘要：

SARS-CoV-2 的大流行对快速大规模诊断检测产生了前所未有的迫切需求，本研究将最近授权的两种 SARS-CoV-2 快速检测方法赛沛 XpertXpress 和雅培 ID Now 与罗氏 cobas SARS-CoV-2 检测方法进行了比较。研究中共测试了 113 个鼻咽拭子，其中包括罗氏 cobas 检测的全部 $C_t$ 值范围内的 88 个阳性样本。与罗氏 cobas 检测相比，雅培 ID Now S 及赛沛 Xpert 阳性一致率分别为 73.9%、98.9%，阴性一致率分别为 100%、92.0%。两者在中度和高度病毒荷载样本种阳性一致率均达到 100%（PCR 扩增循环数 $C_t$ 值<30）。然而，对于 $C_t$ 值>30 的患者，ID Now 识别率为 34.3%，Xpert 为 97.1%。

概括来说 Xpert 分析显示，在包括低水平阳性在内的整个测试 $C_t$ 值范围内，与 cobas 分析高度一致。相比之下，雅培 ID Now 即时检测法可靠地检测出 $C_t$ 值<30 的样本，但未检测出 $C_t$ 值>30 大多数的样本。这些发现强调了雅培 ID Now 立即诊断法对于低水平阳性及经运输介质稀释的样本中一个重要限制，需要进一步的研究来评估雅培 ID Now 在鼻咽拭子样本中的即时检测功能。

Abstract：

The SARS-CoV-2 pandemic has created an urgent and unprecedented need for rapid large-scale diagnostic testing to inform timely patient management. This study compared two recently-authorized rapid tests, Cepheid Xpert Xpress SARS-CoV-2 and Abbott ID Now SARS-CoV-2 to the Roche cobas SARS-CoV-2 assay. A total of 113 nasopharyngeal swabs were tested, including 88 positives spanning the full range of observed Ct values on the cobas assay. Compared to cobas, the overall positive agreement was 73.9% with ID Now and 98.9% with Xpert. Negative agreement was 100% and 92.0% for ID Now and Xpert respectively. Both ID Now and Xpert showed 100% positive agreement for medium and high viral concentrations (Ct value<30). However, for Ct values >30, positive agreement was 34.3% for ID Now and 97.1% for Xpert. These findings highlight an important limitation of ID Now for specimens collected in viral or universal transport media with low viral concentrations. Further studies are needed to evaluate the performance of ID Now for direct swabs

**5. 可用于临床的 AI 系统使用 CT 数据为 COVID-19 提供准确诊断、定量测量和预后**

Clinically Applicable AI System for Accurate Diagnosis, Quantitative Measurements

and Prognosis of COVID-19 Pneumonia Using Computed Tomography

**来源：** CELL

**发布时间：** 2020-04-26

**链接：**

https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00656.pdf

**第一作者：** 张康

**通讯作者：** 张康

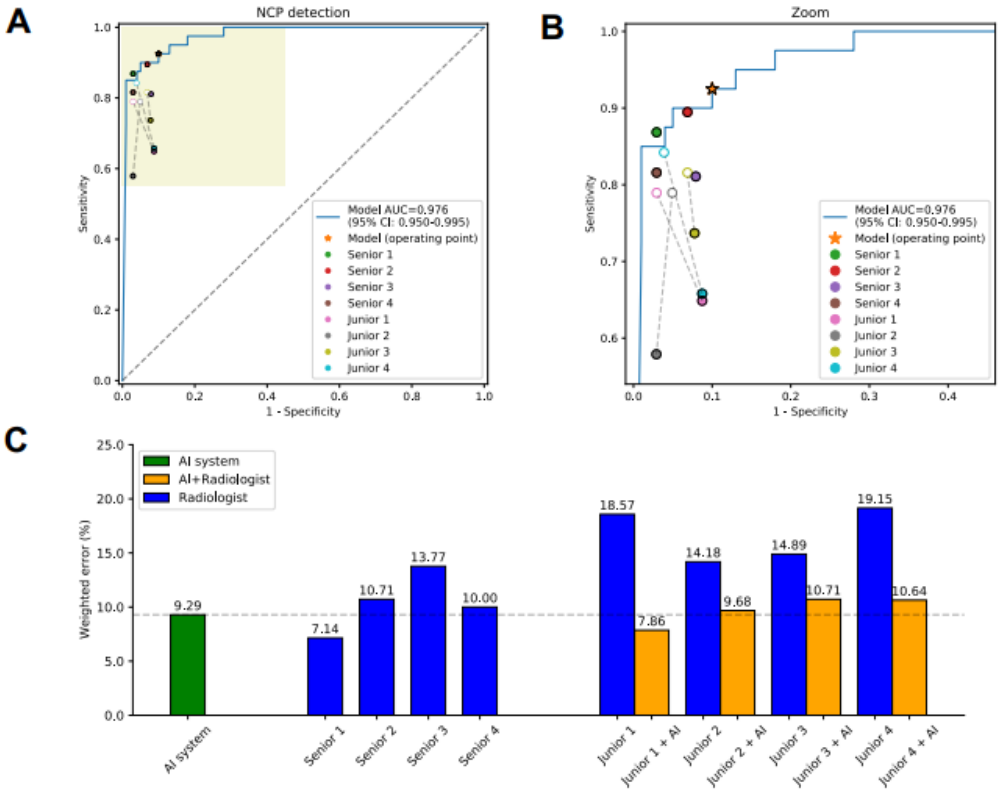
**通讯作者单位：** 澳门大学，华西医科大学，中国科学院广州生物医药与健康研究院

**DOI 或 PUBMED ID：** 10.1016/j.cell.2020.04.045

**编译者：** 蒋立春

**中文摘要：**

该研究采用一个包括了来自于 4154 个病人的 6752 次 CT 一共 617,775 CT 切片图，构建了一个可以区别 COVID-19 和一般肺炎从而诊断 COVID-19 的 AI 系统。除了中国医院的数据，研究者们也用来自国外的 CT 数据对模型进行了测试。特别是当医疗系统过载时，这个 AI 系统可以起到辅助放射科医生和主治医生进行快速诊断。这个 AI 系统还鉴定除了和 COVID-19 引起的肺部损坏相关的临床标记物。这个 AI 系统和临床数据结合能提供准确的临床预后，可以帮助医生更好地规划早期临床管理将医疗资源进行优化。该研究的数据和代码可以在 http://ncov-ai.big.ac.cn/download?lang=en 下载或者联系作者获取，旨在帮助全球医生更好抗击 COVID-19 疫情。



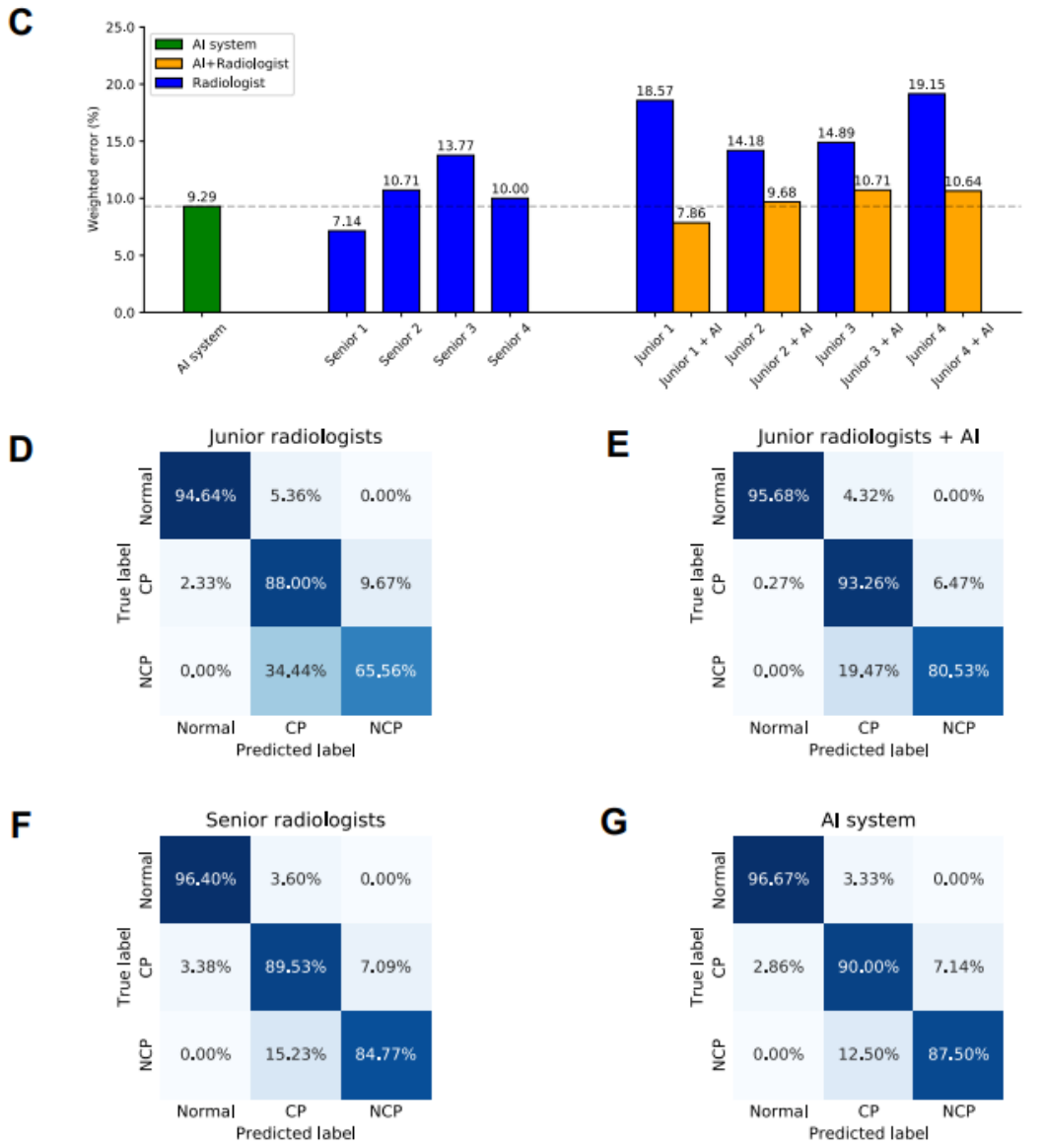



Figure 5. Comparisons of diagnostic performance between our AI model and practicing radiologists. (A and B) The performance of our AI system and eight practicing radiologists (four junior level and four senior level). Receiver operating characteristic (ROC) curve for diagnosis of NCP versus other classes. Filled dots denote junior and senior radiologists' performance, while the hollow dots denote the performance of junior group with AI assistance. Dashed lines linked the paired performance values of each junior radiologist. (C) Weighted error results based on penalty scores (See Figure S5). (D-G) Confusion matrices of multiclass classification. (D) Confusion matrix of the mean diagnostic performance of four junior radiologists. (E) Confusion matrix of the mean diagnostic performance of four junior radiologists with AI assistance. (F) Confusion matrix of the mean diagnostic performance of four senior radiologists. (G) The AI system demonstrated performance comparable to that of senior practicing radiologists. Accuracy = 90.71%, sensitivity = 92.50%, specificity = 90.00%, AUROC = 0.9756 (95% CI: 0.9496-0.9948).

**Abstract:**
Many COVID-19 patients infected by SARS-CoV-2 virus develop pneumonia (called novel coronavirus pneumonia, NCP) and rapidly progress to respiratory failure. However, rapid diagnosis and identification of high-risk patients for early intervention are challenging. Using a large computed Tomography (CT) database from 4,154 patients, we developed an AI system that can diagnose NCP and differentiate it from other common pneumonia and normal controls. The AI system can assist radiologists and physicians in performing a quick diagnosis especially when the health system is overloaded. Significantly, our AI system identified important clinical markers that correlated with the NCP lesion properties. Together with the clinical data, our AI system was able to provide accurate clinical prognosis that can aid clinicians to consider appropriate early clinical management and allocate resources appropriately. We have made this AI system available globally to assist the clinicians to combat COVID-19.

## 6. 一个基于全基因组测序的快速经济的敏感度高的 SARS-CoV-2 诊断方法

A rapid, low cost, and highly sensitive SARS-CoV-2 diagnostic based on whole genome sequencing

**来源：**biorxiv
**发布时间：**2020-04-25
**链接：**https://www.biorxiv.org/content/10.1101/2020.04.25.061499v1
**第一作者：**Brian Glenn St Hilaire
**通讯作者：**Erez Lieberman Aiden,Aviva Presser Aiden
**通讯作者单位：**Baylor College of Medicine, USA etc
**DOI：**
**编译者：**蒋立春
**中文摘要：**
该研究报道了利用高通量测序 SARS-CoV-2 扩增子进行检测的实验方案。数据分析方面，作者结合了参考基因组依赖的数据比对以及从头组装方法。作者采用梯度稀释方法，对检测的灵敏度进行了策略。作者们发现该方法可以准确的鉴定 84genome/ml 的病毒 RNA。这个精确度比 FDA 批准的几乎所有方法精度都更高。在更高的病毒 RNA 浓度下，可以对病毒基因组进行有效地组装，很多时候可以做到没有空缺，并且保证序列的准确性。基因组组装得到的数据除了对疾病进行检测，同时得到的基因组序列可以帮助分析病毒的传播以及更好助力疫苗和药物研发（目前核酸检测里更常规是采用 RT-PCR 方法，只针对特定位点进行扩增，并且得不到基因序列信息）。采用作者们报道的实验和数据分析系统 POLAR（低价的针对病原的组装和重测序），一个人在 8 小时实验里可以处理 192 个样品，包括测序数据分析时间在内，可以 24 小时完成一轮检测，每个病人的费用约为 30 美金（注：根据湖北省集中采购中标的公开信息，基于 RT-PCR 的检测试剂盒最低价格约为 20 人民币）。
**编者注：**EREZ Lieberman Aiden 教授是上科大免疫化学所访问助理教授

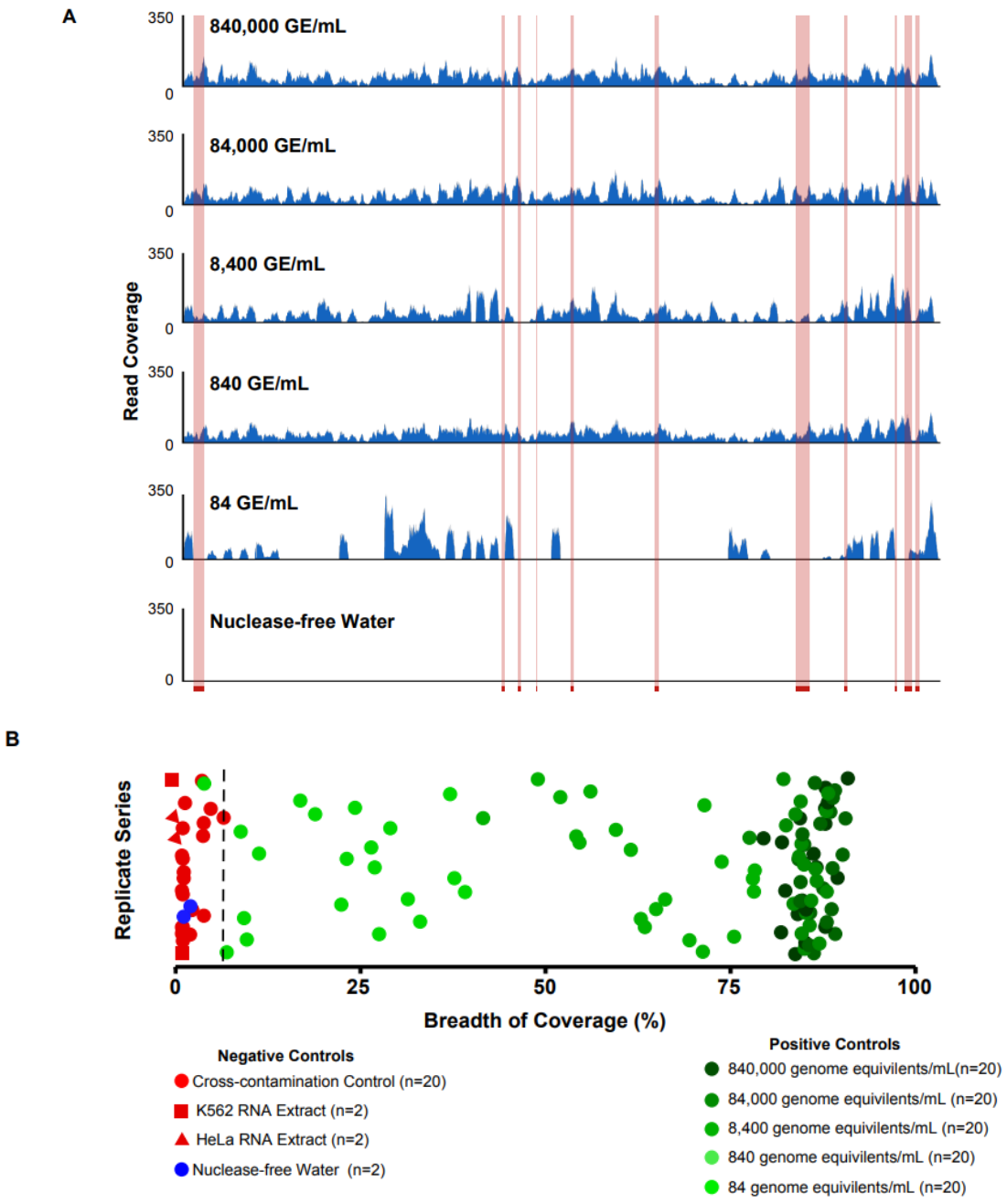



Figure 2. Polar Protocol Detects SARS-CoV2 in Dilute Samples. (A) Coverage tracks demonstrate sequencing depth across the SARS-CoV-2 genome produced by our protocol from samples with a range of starting SARS-CoV-2 genome concentrations. Red-highlighted regions represent virus sequence detected by qPCR-based COVID-19 diagnostics in use or development. (B) Scatter plot shows breath of coverage for all samples from all replicate dilution series. Dashed red line represents the empirically determined breadth of coverage threshold for positive samples.

**Abstract:**

Early detection of infection with SARS-CoV-2 is key to managing the current global pandemic, as evidence shows the virus is most contagious on or before symptom onset1,2 . Here, we introduce a low-cost, high-throughput method for diagnosis of

SARS-CoV-2 infection, dubbed PathogenOriented Low-Cost Assembly & Re-Sequencing (POLAR), that enhances sensitivity by aiming to amplify the entire SARS-CoV-2 genome rather than targeting particular viral loci, as in typical RT-PCR assays. To achieve this goal, we combine a SARS-CoV-2 enrichment method developed by the ARTIC Network (https://artic.network/) with short-read DNA sequencing and de novo genome assembly. We are able to reliably (>95% accuracy) detect SARS-CoV-2 at concentrations of 84 genome equivalents per milliliter, better than the reported limits of detection of almost all diagnostic methods currently approved by the US Food and Drug Administration. At higher concentrations, we are able to reliably assemble the SARS-CoV-2 genome in the sample, often with no gaps and perfect accuracy. Such genome assemblies enable the spread of the disease to be analyzed much more effectively than would be possible with an ordinary yes/no diagnostic, and can help identify vaccine and drug targets. Using POLAR, a single person can process 192 samples over the course of an 8-hour experiment, at a cost of ~$30/patient, enabling a 24-hour turnaround with sequencing and data analysis time included. Further testing and refinement will likely enable greater enhancements in the sensitivity of the above approach.

### 7. MINERVA：一个灵活的对临床样品进行全基因组深度测序的方法

MINERVA: A facile strategy for SARS-CoV-2 whole genome deep sequencing of clinical samples

**来源：** biorxiv

**发布时间：** 2020-04-25

**链接：** https://www.biorxiv.org/content/10.1101/2020.04.25.060947v1

**第一作者：** Chen Chen

**通讯作者：** Jianbinwang, Yanyi Huang, zenghui

**通讯作者单位：** 清华大学，北京大学，首都医科大学

**DOI 或 PUBMED ID：**

**编译者：** 蒋立春

**中文摘要：**

该研究中作者们开发了宏基因组 RNA 富集病毒测序方法（MINERVA），一个灵活的实际好用、稳定的对临床样品进行病毒基因组深度测序方法。该方法采用 Tn5 酶对 RNA/DNA 进行打断，建库之后针对病毒基因组进行富集捕获。作者在多位病人的鼻拭子、痰液以及大便样品中采用了该方法，从这些样品获得了 SARS-CoV-2 的全转录组以及全覆盖的基因组。同样测序量情况下，相比没有富集的常规宏基因组测序，该方法产生的数据深，覆盖度好。该方法兼容临床核酸抽提中使用载体 RNA（当样品量过少时，为了提高核酸抽提效果而加入到抽提体系里的无关 RNA，一般是简单序列 RNA 片段）。

**编者注：**

该文章方法和目前常规使用测序方法进行病原物检测的差异是引入 Tn5 使用。不了解使用 Tn5 酶打断和加接头后，试剂成本是否大幅度爬升。测序富集目前主要是两种方案：前文中的扩增子，以及本文中的探针富集。

Figure 1



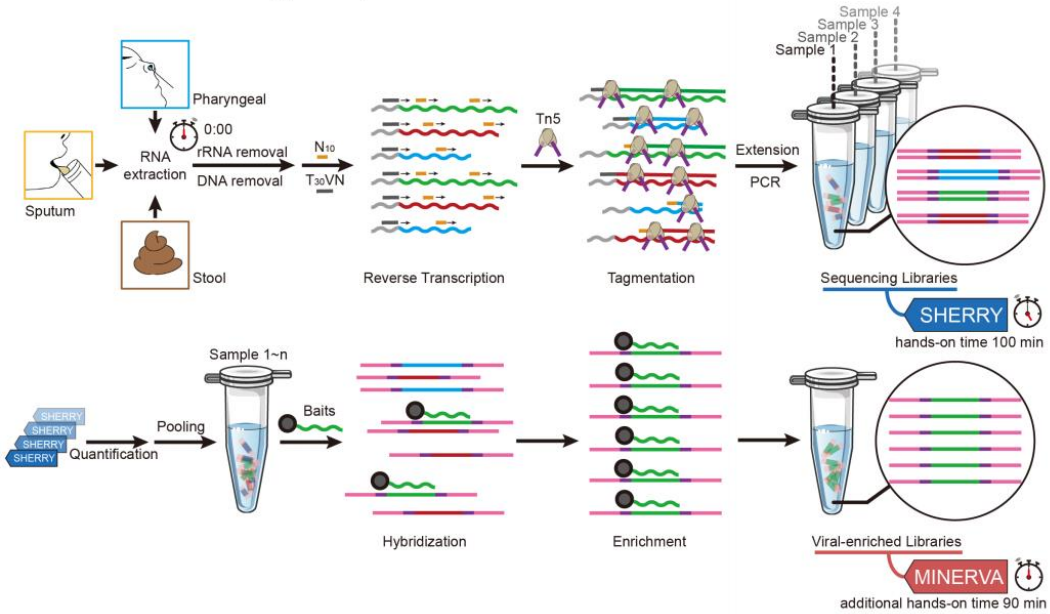



Figure 1. Scheme of MINERVA. RNA extracted from pharyngeal swabs, sputum and stool samples undergo rRNA and DNA removal before a SHERRY processing pipeline metagenomic sequencing library construction. Multiple libraries were then pooled for SARS-CoV-2 sequence enrichment.

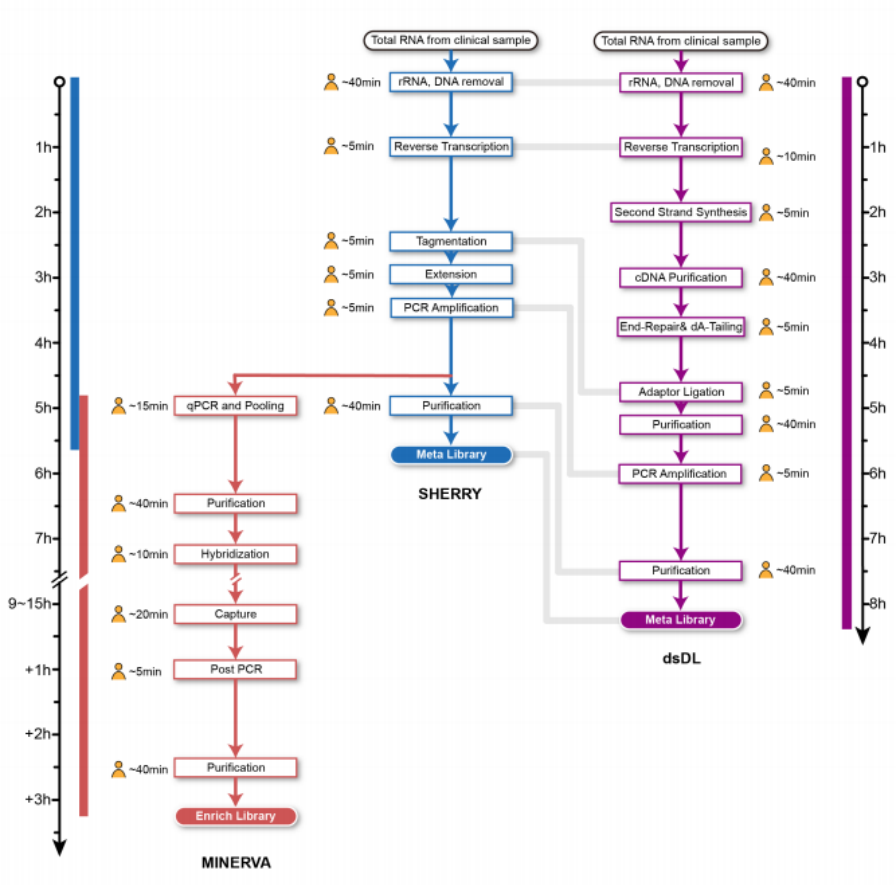


Figure S1. Comparison of workflow between MINERVA and the conventional dsDL strategy.

**Abstract**

The novel coronavirus disease 2019 (COVID-19) pandemic poses a serious public health risk. Analyzing the genome of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from clinical samples is crucial for the understanding of viral spread and viral evolution, as well as for vaccine development. Existing sample preparation methods for viral genome sequencing are demanding on user technique and time, and thus not ideal for time-sensitive clinical samples; these methods are also not optimized for high performance on viral genomes. We have developed MetagenomIc RNA EnRichment VirAl sequencing (MINERVA), a facile, practical, and robust approach for metagenomic and deep viral sequencing from clinical samples. This approach uses direct tagmentation of RNA/DNA hybrids using Tn5 transposase to greatly simplify the sequencing library construction process, while subsequent targeted enrichment can generate viral genomes with high sensitivity, coverage, and depth. We demonstrate the utility of MINERVA on pharyngeal, sputum and stool samples collected from COVID-19 patients, successfully obtaining both whole metatranscriptomes and complete high-depth high-coverage SARS-CoV-2 genomes from these clinical samples, with high yield and robustness. MINERVA is compatible with clinical nucleic extracts containing carrier RNA. With a shortened hands-on time from sample to virus-enriched sequencing-ready library, this rapid, versatile, and clinic-friendly approach will facilitate monitoring of viral genetic variations during outbreaks, both current and future.

## 8. 一项关于 COVID-19 住院患者与先前流感住院患者特征比较的国际研究

**An international characterisation of patients hospitalised with COVID-19 and a comparison with those previously hospitalised with influenza**

来源：medRxiv
发布时间：2020-04-22
链接：https://www.medrxiv.org/content/10.1101/2020.04.22.20074336v1
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DOI 或 PUBMED ID：Preprint
分类:流行病学
编译者：张鹏伟
中文摘要：

背景:为了更好地了解 2019 年重度冠状病毒病患者（COVID-19）的概况，作者对住院 COVID-19 的患者进行了特征分析，并将其与先前住院过流感的患者进行了比较。
方法:作者报告了 2019 年 12 月至 2020 年 4 月在美国（哥伦比亚大学欧文医学中心[CUIMC]、斯坦福医学研究数据库[STARR-OMOP]、，以及退伍军人事务部[VA OMOP]）和韩国健康保险审查与评估部（HIRA）的 COVID-19 住院的患者的特征（人口统计、既往情况和药物使用情况）。

将 COVID-19 住院患者与先前在 2014-19 年度流感住院患者进行了比较。
结果：纳入因 COVID-19 住院治疗的患者 6,806 名（美国：1,634 名，韩国：5,172 名）。在美国，患者多数为男性（VA OMOP：94%，STARR-OMOP：57%，CUIMC：52%），但在 HIRA 中女性为多数（56%）。年龄资料因数据来源而异。根据数据的来源哮喘患病率范围为 7%至 14%，糖尿病患病率为 18%至 43%，高血压病患病率为 22%至 70%，而 9%至 39%的患者在住院前 30 天正在服用作用于肾素-血管紧张素系统的药物。与 52,422 名因流感住院的人相比，在美国的 COVID-19 患者更可能是男性、更年轻、合并症较少、用药较少。
结论：在 COVID-19 住院患者中，合并症和药物使用率很高。但是，在美国，COVID-19 患者更有可能是男性，更年轻，而且似乎比通常接受流感的患者更健康。
Abstract:
Background: To better understand the profile of individuals with severe coronavirus disease 2019 (COVID-19), we characterised individuals hospitalised with COVID-19 and compared them to individuals previously hospitalised with influenza.
Methods: We report the characteristics (demographics, prior conditions and medication use) of patients hospitalised with COVID-19 between December 2019 and April 2020 in the US (Columbia University Irving Medical Center [CUIMC], STAnford Medicine Research data Repository [STARR-OMOP], and the Department of Veterans Affairs [VA OMOP]) and Health Insurance Review & Assessment [HIRA] of South Korea. Patients hospitalised with COVID-19 were compared with patients previously hospitalised with influenza in 2014-19.
Results: 6,806 (US: 1,634, South Korea: 5,172) individuals hospitalised with COVID-19 were included. Patients in the US were majority male (VA OMOP: 94%, STARR-OMOP: 57%, CUIMC: 52%), but were majority female in HIRA (56%). Age profiles varied across data sources. Prevalence of asthma ranged from 7% to 14%, diabetes from 18% to 43%, and hypertensive disorder from 22% to 70% across data sources, while between 9% and 39% were taking drugs acting on the renin-angiotensin system in the 30 days prior to their hospitalisation. Compared to 52,422 individuals hospitalised with influenza, patients admitted with COVID-19 were more likely male, younger, and, in the US, had fewer comorbidities and lower medication use.
Conclusions: Rates of comorbidities and medication use are high among individuals hospitalised with COVID-19. However, COVID-19 patients are more likely to be male and appear to be younger and, in the US, generally healthier than those typically admitted with influenza.

## 9. SARS-CoV-2 自扩增 RNA 脂质纳米颗粒疫苗可诱导与 COVID-19 康复患者等效的临床前抗体滴度和病毒中和力

Self-amplifying RNA SARS-CoV-2 lipid nanoparticle vaccine induces equivalent preclinical antibody titers and viral neutralization to recovered COVID-19 patients
来源：biorxiv
发布时间：2020.04.25
文章链接：https://www.biorxiv.org/content/10.1101/2020.04.22.055608v1
第一作者：Paul F. McKay
通讯作者：Robin J. Shattock
通讯作者单位：伦敦帝国理工学院传染病系

DOI: https://doi.org/10.1101/2020.04.22.055608
编译者：张怡
中文摘要：
SARS-CoV-2 在几个月内蔓延为全球大流行，这推动了一种可迅速增产的疫苗的开发。文中作者提出了一种编码 SARS-CoV-2 刺突蛋白的自扩增 RNA（编者注），其被脂质纳米颗粒包裹作为疫苗，并在伪病毒中表现出稳健的中和能力，可以得到数量成比例的特定 IgG，而且其数量高于 COVID-19 康复患者。这些数据为深入了解疫苗设计和免疫原性评估提供了思路，使其能够快速转化为临床应用。

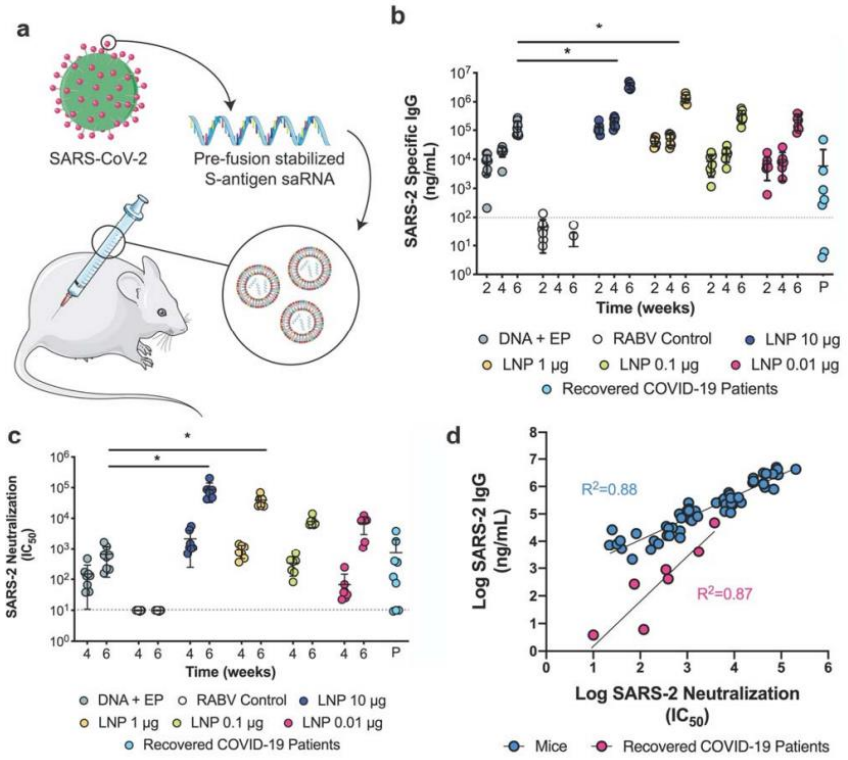


Figure 1. Antibody quantification and neutralization of a SARS-CoV-2 saRNA vaccinated mice compared to COVID-19 recovered patients. a) Schematic of vaccination of BALB/c mice with saRNA encoding pre-fusion stabilized spike protein in LNP, b) SARS-CoV-2 specific IgG responses in mice vaccinated with doses of LNP-formulated saRNA ranging from 0.01-10 µg of saRNA with n=7 and COVID-19 recovered patients with n=9, c) SARS-CoV-2 pseudotyped virus neutralization of sera from BALB/c mice vaccinated with doses of LNP-formulated saRNA ranging from 0.01-10 µg of saRNA with n=7 and COVID-19 recovered patients with n=9, d) Correlation between SARS-CoV-2-specific IgG and SARS-CoV-2 neutralization IC50 for vaccinated mice (n=7) and recovered COVID-19 patients (n=9). Electroporated pDNA (DNA + EP) was used as a positive control while saRNA encoding the rabies glycoprotein (RABV) in pABOL was used as a negative control (RABV control). * indicates significance of p
编者注：
关于为什么 RNA 可以自己扩增，作者提到“We used a plasmid vector to synthesize a self-amplifying RNA (saRNA) replicon, based on a Trinidad donkey Venezuelan equine encephalitis virus strain (VEEV) alphavirus genome.”详情见原文方法部分

Abstract
The spread of the SARS-CoV-2 into a global pandemic within a few months of onset motivates the development of a rapidly scalable vaccine. Here, we present a self-amplifying RNA encoding the SARS-CoV-2 spike protein encapsulated within a lipid nanoparticle as a vaccine and demonstrate induction of robust neutralization of a pseudo-virus, proportional to quantity of specific IgG and of higher quantities than recovered COVID-19 patients. These data provide insight into the vaccine design and evaluation of immunogenicity to enable rapid translation to the clinic.

## 10. 羟氯喹和阿奇霉素治疗新冠肺炎导致患者的 QT 间期延长

The QT interval in patients with COVID-19 treated with hydroxychloroquine and azithromycin

来源：Nature Medicine
发布时间：2020-04-24
链接：https://www.nature.com/articles/s41591-020-0888-2
第一作者：Ehud Chorin
通讯作者：Ehud Chorin，Lior Jankelson
通讯作者单位：美国纽约大学医学院
DOI 或 PUBMED ID：https://doi.org/10.1038/s41591-020-0888-2
编译者：刘焕珍
中文摘要：

使用羟氯喹和阿奇霉素治疗的新冠肺炎患者出现了明显的心电图异常，主要是 QTc 间期延长。研究人员查看了 84 例服用羟氯喹和阿奇霉素（HY/AZ）5 天的新冠肺炎患者的心电图，并追踪了他们的 QTc 间期。患者每天两次服用 HY，第一天每次剂量为 400mg，第二天开始每次剂量为 200mg。患者每天服用 500mg AZ。患者服用 HY/AZ 后，后续对患者进行心电图监测的平均时间为 4.3±1.7 天。
在治疗 3.6± 1.6 天时，QTc 435±24 ms 的基线平均值延长到 463±32 ms 的最大值平均值。11％患者的 QTc 严重延长至> 500ms，这些患者面临着较高的心律不齐和心脏性猝死风险。在这个高风险组中，QTc 的基线平均值从 447±30 ms 增加到 527±17 ms。任何患者都没有发生尖端扭转型室速（一种多形性室性心动过速）的风险。4 例患者死于多器官功能衰竭，无心律失常证据，无严重 QTc 延长。有 16 名患者已出院，仍有 64 名患者在医院。
研究者发现接受 HY/AZ 治疗的新冠肺炎患者的 QTc 显著延长。9 名严重 QTc 间期延长的患者中有 5 名患者的 QTc 基线正常。因此，研究者建议接受 HY/AZ 治疗的新冠肺炎患者，尤其是合并症患者和接受其他延长 QT 间期药物治疗的患者，应重复随访 QTc。
Abstract:
We reviewed the charts and followed the corrected QT (QTc) interval in a consecutive cohort of 84 patients receiving the combination of hydroxychloroquine and azithromycin (HY/AZ). HY and AZ were administered orally for 5 days.HY was given at a dose of 400 mg twice daily on the first day, followed by 200 mg twice daily. AZ was given at a dose of 500 mg per day. The average time of electrocardiograph (ECG) follow-up after HY/AZ exposure was 4.3 ± 1.7 days.
We observed prolongation of the QTc from a baseline average of 435 ± 24 ms (mean ± s.d.) to a maximal average value of 463 ± 32 ms ($P < 0.001$ (one-sample t-test)),

which occurred on day 3.6 ± 1.6 of therapy (Fig. 1). In a subset of nine (11%) of those patients, the QTc was severely prolonged to >500 ms, a known marker of high risk of malignant arrhythmia and sudden cardiac death. In this high-risk group, the QTc increased from a baseline average of 447 ± 30 ms to 527 ± 17 ms ($P < 0.01$ (one-sample t-test)). There were no torsades de pointes events recorded for any patients, including those with a severely prolonged QTc. Four patients died from multi-organ failure, without evidence of arrhythmia and without severe QTc prolongation. 64 patients remained admitted and 16 patients were discharged.
In our work, we found that in patients with COVID-19 who were treated with HY/AZ, the QTc was significantly prolonged. In our cohort, five of nine patients with severe QTc prolongation had a normal QTc at baseline. We therefore suggest that the QTc should be followed repeatedly in patients with COVID-19 who are treated with HY/AZ, particularly in those with co-morbidities and in those who are treated with other QT-prolonging medications.
文章分类：临床试验

## 11. 高、低剂量二磷酸氯喹辅助治疗 SARS-CoV-2 感染住院患者的随机临床研究

**Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection A Randomized Clinical Trial**

来源：JAMA Netw Open.
发布时间：2020-04-24
链接：https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765270
第一作者：Mayla Gabriela Silva Borba, MD
通讯作者：Marcus Vinícius Guimarães Lacerda, MD
通讯作者单位：巴西亚马逊大学
DOI 或 PUBMED ID：10.1001/jamanetworkopen.2020.8857
编译者：张丽双
中文摘要：
在治疗重症新型冠状病毒肺炎(COVID-19)时，两种不同剂量的二磷酸氯喹(CQ)方案的安全性和有效性如何？
方法：在这个巴西团队做的 IIb 期 81 例 COVID-19 重症患者的平行双盲随机临床试验中[高剂量组（600 毫克/次，每天两次，共 10 天），低剂量组（450 毫克/次，第一天 2 次/天，之后 4 天 1 次/天)]，入组 81 例重症患者[高剂量组 41 例(50.6%)，低剂量组 40 例(49.4%)]。入选患者的平均（SD）年龄为 51.1（13.9）岁，大多数（60[75.3%]）为男性。高剂量组平均年龄更大(平均 54.7[13.7]岁 vs 47.4[13.3]岁)和基础心脏疾病更多(5/28[17.9%]vs 0)。低剂量组 40 例(77.5%)和高剂量组 41 例(75.6%)中，分别有 31 例(77.5%)和 31 例(75.6%)检测到病毒 RNA。
结果：在第 13 天之前，高剂量组（16/41）的致死率为 39.0%，低剂量组（6/40）的致死率为 15.0%。高剂量组 QTc 间期大于 500ms（心率失常）（7/37[18.9%]）多于低剂量组（4/36[11.1%]）。27 例患者中仅有 6 例（22.2%）在第 4 天呼吸分泌物呈阴性。由于样本量有限，研究无法表明任何整体治疗效果。
结论：这个 CloroCovid-19 试验的初步发现表明，出于心脏毒性和致死率增加方面的安全性

担忧，特别是对于接受阿奇霉素和奥司他韦治疗的患者，不建议使用高剂量的氯喹治疗重症COVID-19。

Abstract:

**Importance** There is no specific antiviral therapy recommended for coronavirus disease 2019 (COVID-19). In vitro studies indicate that the antiviral effect of chloroquine diphosphate (CQ) requires a high concentration of the drug.

Objective To evaluate the safety and efficacy of 2 CQ dosages in patients with severe COVID-19.

**Design, Setting, and Participants** This parallel, double-masked, randomized, phase IIb clinical trial with 81 adult patients who were hospitalized with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was conducted from March 23 to April 5, 2020, at a tertiary care facility in Manaus, Brazilian Amazon.

**Interventions** Patients were allocated to receive high-dosage CQ (ie, 600 mg CQ twice daily for 10 days) or low-dosage CQ (ie, 450 mg twice daily on day 1 and once daily for 4 days).

**Main Outcomes and Measures** Primary outcome was reduction in lethality by at least 50% in the high-dosage group compared with the low-dosage group. Data presented here refer primarily to safety and lethality outcomes during treatment on day 13. Secondary end points included participant clinical status, laboratory examinations, and electrocardiogram results. Outcomes will be presented to day 28. Viral respiratory secretion RNA detection was performed on days 0 and 4.

Results Out of a predefined sample size of 440 patients, 81 were enrolled (41 [50.6%] to high-dosage group and 40 [49.4%] to low-dosage group). Enrolled patients had a mean (SD) age of 51.1 (13.9) years, and most (60 [75.3%]) were men. Older age (mean [SD] age, 54.7 [13.7] years vs 47.4 [13.3] years) and more heart disease (5 of 28 [17.9%] vs 0) were seen in the high-dose group. Viral RNA was detected in 31 of 40 (77.5%) and 31 of 41 (75.6%) patients in the low-dosage and high-dosage groups, respectively. Lethality until day 13 was 39.0% in the high-dosage group (16 of 41) and 15.0% in the low-dosage group (6 of 40). The high-dosage group presented more instance of QTc interval greater than 500 milliseconds (7 of 37 [18.9%]) compared with the low-dosage group (4 of 36 [11.1%]). Respiratory secretion at day 4 was negative in only 6 of 27 patients (22.2%).

**Conclusions and Relevance** The preliminary findings of this study suggest that the higher CQ dosage should not be recommended for critically ill patients with COVID-19 because of its potential safety hazards, especially when taken concurrently with azithromycin and oseltamivir. These findings cannot be extrapolated to patients with nonsevere COVID-19.

Trial Registration ClinicalTrials.gov Identifier: **NCT04323527**

## 12. 肠道菌群可能是影响健康个体对COVID-19易感性的因素

Gut microbiota may underlie the predisposition of healthy individuals to COVID-19

**来源：**mdeRxiv

**发布时间：**2020-04-25

**链接：**https://www.medrxiv.org/content/10.1101/2020.04.22.20076091v1

**第一作者：**Wanglong Gou，Yuanqing Fu，Liang Yue，Geng-dong Chen，Xue Cai，Menglei Shuai，Fengzhe Xu（contributedequally）
**通讯作者：**Yu-ming Chen，Tiannan Guo，Ju-Sheng Zheng
**通讯作者单位：中山大学，西湖大学，西湖大学**
**DOI 或 PUBMED ID：**
**编译者：**宋珂
**中文摘要：**

COVID-19 疫情正在全球范围扩散，但患者对病症严重程度的敏感性却表现出很大差异。急需科学家找出导致差异的关键因素。本文中，作者使用 20 种可以预测严重 COVID-19 患者病程的血液蛋白质组生物标志物，构建了蛋白质组风险评分系统（编者注）。作者发现，在国内的 990 例未感染人群中，该蛋白质组风险分数主要与老年人群中的促炎细胞因子呈正相关性，而在较年轻的人群中，则未发现相关性。作者进一步发现，借助机器学习模型，可以利用一套核心的肠道菌群数据，在 301 名个体中准确地预测上述蛋白质组生物标志物。而且，这些肠道菌群的特征与另一组中 366 名个体的促炎细胞因子具有高度相关性。粪便代谢组学分析表明，存在与氨基酸相关的关联肠道菌群与炎症的潜在通路。这项研究表明，肠道菌群可能是影响正常个体对严重 COVID-19 易感性的因素。

**Figure 2**

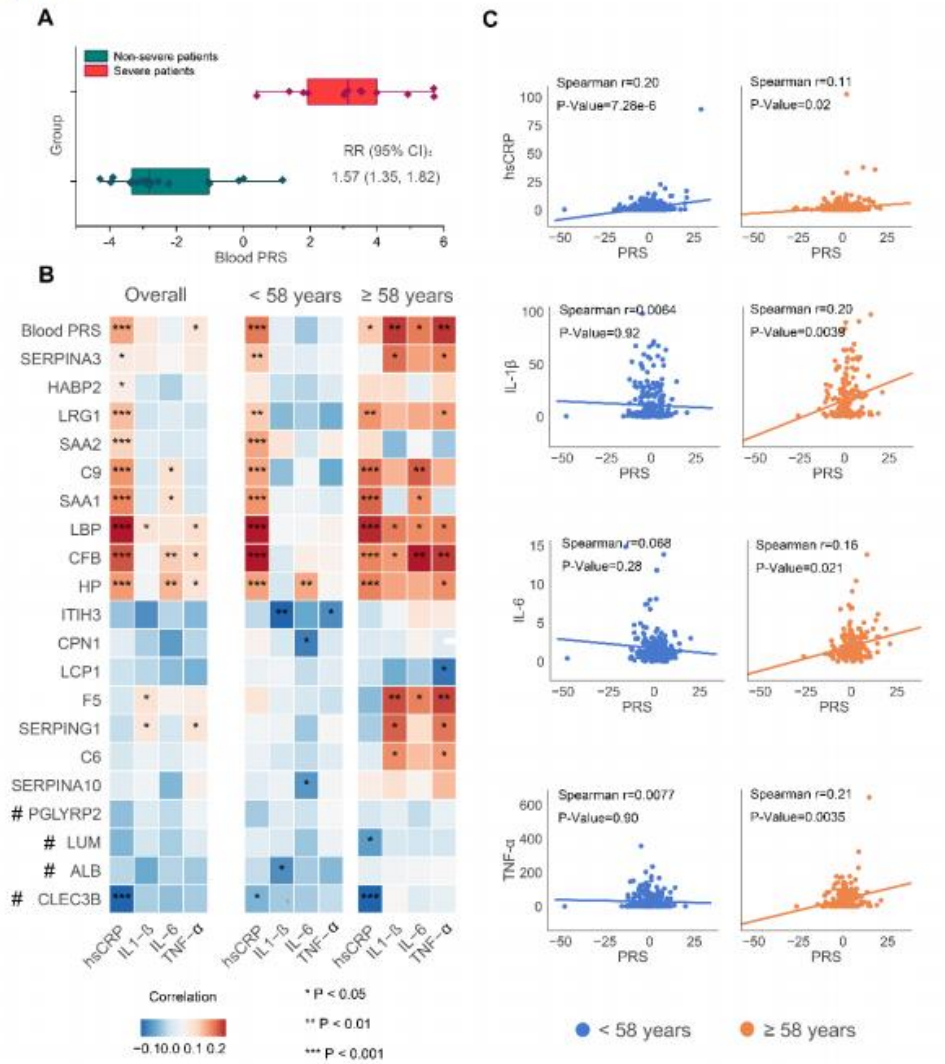


Figure 2. Predictive proteomic profile for severe COVID-19 is correlated with

pro-inflammatory factors among healthy individuals. (A) The associations of COVID-19-related blood proteomic biomarkers and proteomic risk score (PRS) with host inflammatory markers. 990 participants were involved in this analysis. # protein down-regulated in severe patients, else, up-regulated. (B) The correlation of the above blood proteomic biomarkers and PRS with host inflammatory markers stratified by the median age of participants (<58 years or ≥58 years )

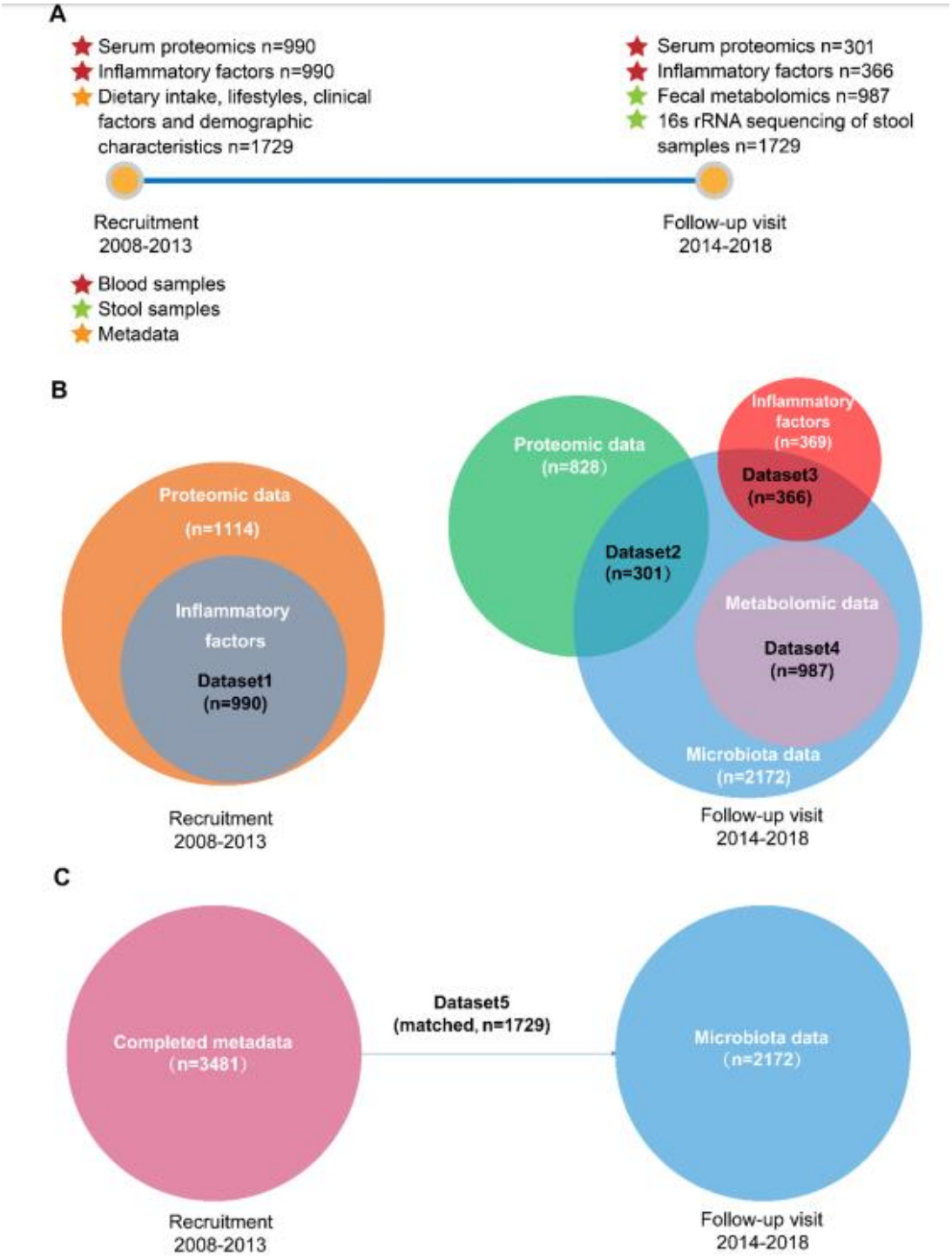


Figure S1. Timeline of the participants enrollment, follow-up visit and sample

collection in the Guangzhou Health and Nutrition Study. (A) At baseline, 4048 subjects provided completed metadata (required for analysis in the present study), and 1114 subjects provided blood samples (1114 for proteomic analysis and 990 for measurement of inflammatory factors). At follow-up visit, 2172 subjects provided stool samples (n=1729 for 16s rRNA sequencing; n=987 for metabolomic analysis) , among which 667 subjects provided blood samples (n=301 for proteomic analysis; n=366 for measurement of inflammatory factors). (B) Detail information about the number of participants in the dataset1-dataset4 used in the present study. (C) Detail information about the number of participants in the dataset5 used in the present study

编者注：

这个蛋白质组标志物是该研究中西湖大学 tiannan guo 课题组之前的一项工作报道的。我们 4 月 8 日简报第 9 条。原文链接：

https://www.medrxiv.org/content/10.1101/2020.04.07.20054585v1

**Abstract:**

The COVID-19 pandemic is spreading globally with high disparity in the susceptibility of the disease severity. Identification of the key underlying factors for this disparity is highly warranted. Here we describe constructing a proteomic risk score based on 20 blood proteomic biomarkers which predict the progression to severe COVID-19. We demonstrate that in our own cohort of 990 individuals without infection, this proteomic risk score is positively associated with proinflammatory cytokines mainly among older, but not younger, individuals. We further discovered that a core set of gut microbiota could accurately predict the above proteomic biomarkers among 301 individuals using a machine learning model, and that these gut microbiota features are highly correlated with proinflammatory cytokines in another set of 366 individuals. Fecal metabolomic analysis suggested potential amino acid-related pathways linking gut microbiota to inflammation. This study suggests that gut microbiota may underlie the predisposition of normal individuals to severe COVID-19.

## 13. 利用常见材料对 N95 口罩进行微波蒸汽净化

Microwave-Generated Steam Decontamination of N95 Respirators Utilizing Universally Accessible Materials

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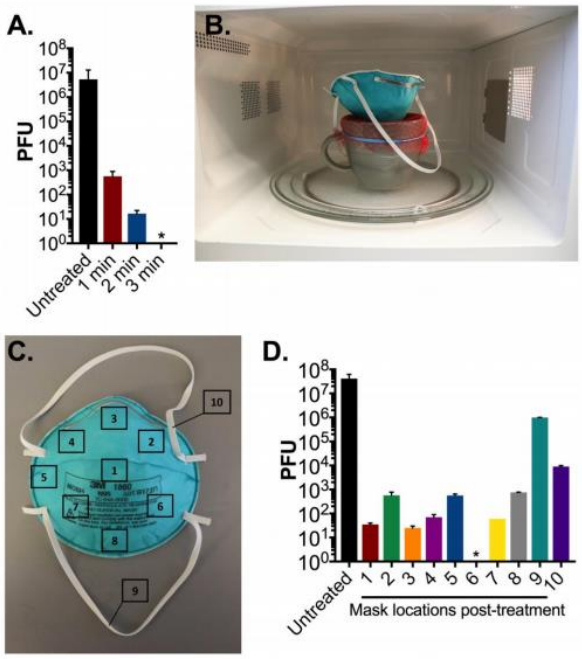
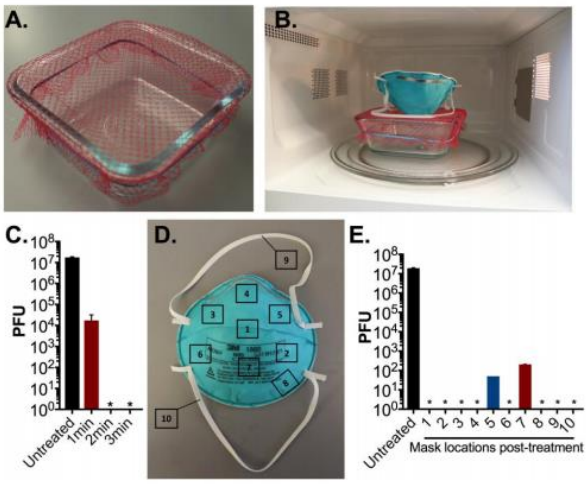
**中文摘要：**

SARS-CoV-2 的流行已经导致 N95 口罩严重的全球短缺，N95 口罩对于保护医护人员免受感染至关重要。鉴于当前供应链的局限性，必须确定有效的净化、再利用方法，从而保障 N95

口罩的库存。有效的净化是指在必须不影响口罩过滤性能或口罩贴面性能的情况下对 N95 口罩进行消毒。尽管有许多 N95 去污方法，但没有一种是普遍可操作的。该研究描述了一种微波产生的蒸汽净化方法，任意规模，不同地理位置的医疗系统都可用该方法对 N95 口罩进行进化。利用广泛可用的玻璃容器、商用生产网袋、橡皮筋和 1100W 商用微波炉，构建了一种有效、标准化和可重复使用的 N95 口罩净化方法（图一，图二）。利用这种方法杀灭 MS2 噬菌体，一种高度保守的 SARS-CoV-2 污染替代物，一次 3 分钟微波净化后，平均出现 6-log10 噬菌斑（PFU）（99.9999%）和最小 5-log10 噬菌斑（99.999%）减少（图一，图二）。值得注意的是，即使经过 20 个连续的微波蒸汽净化循环，定量口罩的贴面性和功能也得以保持。该方法为临床医生提供了一种有效的 N95 口罩净化和再利用的方法。




**图一 N95 decontamination by microwave generated steam over an open ceramic mug.** (A) Triplicate N95 coupons treated with $10^7$ PFU MS2 were placed on the mesh covered ceramic mug and treated for the indicated durations in an 1100W microwave. After treatment, phage was extracted from N95 coupons and quantified by plaque assay. (B) We next evaluated treatment of an entire N95 respirator on the mug decontamination system. (C) $10^7$ PFU of MS2 was spotted on 10 pre-marked sections of a whole N95 respirator as indicated. (D) After a 3-minute treatment in an 1100W microwave demarcated pre-treated segments measuring 1 $cm^2$ were excised from the respirator, and MS2 phage was then extracted and quantified by plaque assay. Triplicate untreated pre-cut N95 coupons were included as a control in all assays. Bars shown are mean and standard deviation of phage titers from each excised segment from a single respirator. * indicates no viable MS2 detected. Limit of detection of all assays is 10 PFU. Data shown are representative of three separate respirator experiments.




**图二 N95 decontamination with microwave-generated steam over an open glass container.** (A-B) Image of glass container decontamination system. A 17 cm x 17 cm glass container was filled with 60 ml of water, covered with mesh from a produce bag, secured with a rubber band. (C) Triplicate N95 respirator coupons inoculated with $10^7$ PFU MS2 phage, placed on the mesh-covered container, and treated for indicated times in an 1100W microwave. After treatment, MS2 phage was extracted from N95 coupons and quantified by plaque assay. (D) $10^7$ PFU of MS2 phage was spotted on 10 different pre-marked locations on a N95 respirator as indicated. (E) The whole N95 respirator was then treated for 3 minutes as shown in Fig. 3B in an 1100W microwave. Demarcated segments measuring 1 $cm^2$ encompassing the area of inoculation were excised from respirator, and MS2 phage was extracted and quantified by plaque assay. Triplicate untreated pre-cut N95 coupons were included as a control in all assays. Data shown are the mean and standard deviation of plaque titers from a single respirator and are representative of three separate experiments. In one experiment, no viable PFU were detected from all excised segments (data not shown). * indicates no viable MS2 was detected. Limit of detection of all assays is 10 PFU.

**Abstract:**

The SARS-CoV-2 pandemic has caused a severe, international shortage of N95 respirators, which are essential to protect healthcare providers from infection. Given the contemporary limitations of the supply chain, it is imperative to identify effective means of decontaminating, reusing, and thereby conserving N95 respirator stockpiles. To be effective, decontamination must result in sterilization of the N95 respirator without impairment of respirator filtration or user fit. Although numerous methods of N95 decontamination exist, none are universally accessible. In this work we describe a microwave-generated steam decontamination protocol for N95 respirators for use in healthcare systems of all sizes, geographies, and means. Using widely available glass containers, mesh from commercial produce bags, a rubber band, and a 1100W commercially available microwave, we constructed an effective, standardized, and reproducible means of decontaminating N95 respirators. Employing this methodology against MS2 phage, a highly conservative surrogate for SARS-CoV-2

contamination, we report an average 6-log10 plaque forming unit (PFU) (99.9999%) and a minimum 5-log10 PFU (99.999%) reduction after a single three-minute microwave treatment. Notably, quantified respirator fit and function were preserved, even after 20 sequential cycles of microwave steam decontamination. This method provides a valuable means of effective decontamination and reuse of N95 respirators by frontline providers facing urgent need.