Surviving SARS-CoV-2: Lessons From 40+ Years of HIV Research

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Four Prevention Opportunities

Cohen et al., JCI, 2008
Cohen et al., JIAS, 2008

- Behavioral, Structural
- Vaccines
  - ART PrEP
  - Microbicides
- Vaccines
  - ART PEP
- Treatment Of HIV to Reduce Infectivity

UNEXPOSED

EXPOSED
  - ( precoital/coital)
  - (postcoital)

INFECTED

YEARS

YEARS

YEARS

72h

HOURS
Current Guidelines

**ART for Everyone…Urgently**

- HIV replication has negative consequences
- Earlier ART prolongs survival (HPTN 052)
- ART blocks HIV transmission (HPTN 052)
- Early ART reduces the HIV latent reservoir

**ART is recommended for virtually all HIV-infected individuals, as soon as possible after HIV diagnosis**[a,b]

UNDETECTABLE = UNTRANSMITTABLE
Four Prevention Opportunities

**UNEXPOSED**
- Behavioral, Structural
  - Structural Circumcision
  - Condoms

**EXPOSED**
- **(precoital/coital)**
  - Vaccines
  - ART PrEP
  - Microbicides
  - bnAbs

- **(postcoital)**
  - Vaccines
  - ART PEP
  - bnAbs

**INFECTED**
- Treatment of HIV
- Reduced Infectivity

Cohen IAS 2008
New Technologies in HIV PrEP

Alternative Long-Acting ARV Strategies

• Once a month pill (Merck, Islatravir)
• Implants (Islatravir, Cabotegravir)
• Needles and Patches (Academic Centers)
• Sub Q Capsid Inhibitors (Gilead, Lencapravir)
50% of those infected develop NAbs
20% are broadly cross-reactive (bNAbs)

Mascola, Montefiori Ann Rev Imm (2010)
Two Randomized Trials of Neutralizing Antibodies to Prevent HIV-1 Acquisition

Combination prevention for COVID-19

The coronavirus disease 2019 (COVID-19) pandemic has produced the fear and disorder that invariably accompanies such an event. As such, it should also prompt consideration of our experience with HIV over the past 40 years. In dealing with HIV, the road to reducing infections with severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) and COVID-19, and ultimately mortality and morbidity, requires medical and nonmedical strategies. The most important lesson from tackling HIV is to use a combination of prevention strategies.

The first step to adopting the model of prevention for SARS-CoV-2 has already been taken—behavioral changes. This reflects a rapid but imperfect understanding of the transmission of this virus. At the beginning of the AIDS epidemic, changes in sexual behavior, treatment, prevention, and government interventions (including “square” BYT transmission) such as antiretroviral therapy and abstinence. For SARS-CoV-2, masks and gloves, hand hygiene, and “shelter in place” mandates have already demonstrated benefits. More efficient behavioral intervention requires better understanding of the rules governing SARS-CoV-2 transmission. What are the risks from exposure to respiratory droplets, airborne virus, and surface contamination? What constitutes an “episode” of SARS-CoV-2 transmission? Evidence suggests that “transmission” of SARS-CoV-2 is related to transmission of an HIV. At this stage, it is premature to introduce combination antiretroviral therapy, as the same benefits—for example, decreases in transmission—may be available as a result of behavioral changes. This reflects a rapid but imperfect understanding of the transmission of this virus. At the beginning of the AIDS epidemic, changes in sexual behavior, treatment, prevention, and government interventions (including “square” BYT transmission) such as antiretroviral therapy and abstinence. For SARS-CoV-2, masks and gloves, hand hygiene, and “shelter in place” mandates have already demonstrated benefits. More efficient behavioral intervention requires better understanding of the rules governing SARS-CoV-2 transmission. What are the risks from exposure to respiratory droplets, airborne virus, and surface contamination? What constitutes an “episode” of SARS-CoV-2 transmission? Evidence suggests that “transmission” of SARS-CoV-2 is related to transmission of an HIV. At this stage, it is premature to introduce combination antiretroviral therapy, as the same benefits—for example, decreases in transmission—may be available as a result of behavioral changes.

“HIV has taught us that multiple concomitant prevention strategies are essential.”

Science. 2020 May 8;368(6491):551.
Three Entities with Distinct Roles in COVID-19 Response

**Operation Warp Speed**
- USG body responsible for strategic approach, coordination and resource allocation

**Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)**
- NIH established Public-private partnership for coordinating COVID-19 response

**COVID-19 Prevention Network**
- NIH Funded networks - Phase 3 trial execution
CoVPN Clinical Sites
COVID-19: Four Prevention Opportunities

**UNEXPOSED**
- Behavioral, Structural
  - Masks
  - Distance
  - Air

**EXPOSED**
- Vaccines

**EXPOSED**
- PrEp, PEP

**INFECTED**
- Treatment Prevents?

**YEARS?**

**Full Immunit?y**

**96 hours?**

**Hours?**
637 million people travelled in National Day holiday (Oct. 1 - 8) in all parts of China

The Bund of Shanghai

The Forbidden City of Beijing

The West Lake of Hangzhou

The Beach of Qingdao
## COVID-19 Vaccines in the US

<table>
<thead>
<tr>
<th>Company</th>
<th>Platform</th>
<th>Product</th>
<th>Vaccination dose/schedule</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>moderna</strong></td>
<td>mRNA</td>
<td>mRNA: encodes 2P-stabilized Spike, TM, FI</td>
<td>2 doses at 100 µg (0, 28 days)</td>
<td>EUA</td>
</tr>
<tr>
<td><strong>Biontech/Pfizer</strong></td>
<td>mRNA</td>
<td>mRNA: encodes stabilized SARS-CoV-2 Spike</td>
<td>2 doses at 30µg (0, 21 days)</td>
<td>EUA</td>
</tr>
<tr>
<td><strong>AstraZeneca</strong></td>
<td>Ad Vector</td>
<td>Replication incompetent ChAdOx1 wild type Spike; ΔF; TM</td>
<td>2 doses at $5 \times 10^{10}$ vp, (0, 28 days)</td>
<td>Under Review</td>
</tr>
<tr>
<td><strong>Janssen</strong></td>
<td>Ad Vector</td>
<td>Replication Incompetent Ad26; stabilized Spike; ΔF; TM</td>
<td>1 dose at $5 \times 10^{10}$ vp</td>
<td>EUA</td>
</tr>
<tr>
<td><strong>Novavax</strong></td>
<td>Recombinant protein Adjuvanted</td>
<td>Baculovirus Expressed trimeric Stabilized Spike, ΔF; TM; trimerization domain; Matrix M</td>
<td>2 doses at 5 µg with Matrix M (0, 21 days)</td>
<td>Under Review</td>
</tr>
<tr>
<td><strong>GSK/Sanofi</strong></td>
<td>Recombinant protein Adjuvanted</td>
<td>Baculovirus Expressed trimeric Stabilized Spike, ΔF; TM; trimerization domain; AS03</td>
<td>5/15 µg +AS03 (0, 21 days)</td>
<td>??</td>
</tr>
</tbody>
</table>
Scaling Up Covid-19 Vaccination in Africa — Lessons from the HIV Pandemic

Jean B. Nachega, M.D., Ph.D., M.P.H., Nadia A. Sam-Agudu, M.D., John W. Mellors, M.D., Alimuddin Zumla, M.D., Ph.D., and Lynne M. Mofenson, M.D.

Concerns regarding access to Covid-19 vaccines in Africa are reminiscent of concerns raised about responding to the HIV pandemic in the mid-1990s and early 2000s, when highly active antiretroviral treatment (ART) was accessible in high-income and ensure rapid and equitable access to vaccines in both high-
## Scaling Up Covid-19 Vaccination in Africa — Lessons from the HIV Pandemic

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<table>
<thead>
<tr>
<th>Area of Need</th>
<th>Lessons from HIV Response</th>
<th>Potential Applications in Covid-19 Pandemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health infrastructure and supply needs</td>
<td>Global Fund and PEPFAR funding were critical for HIV clinical care and local capacity building. Educating and training health care providers in HIV care and ART was essential. Community health and lay workers were indispensable for enhancing HIV testing, ART adherence, and retention in care in hard-to-reach communities.</td>
<td>Appropriate vaccine storage and transport. Protective equipment for health care workers in clinic settings. Adequate numbers of trained health care workers to safely provide injections and address patient concerns. Engagement and compensation of community health workers. Tracking systems for vaccines requiring multiple doses to ensure vaccine series completion.</td>
</tr>
<tr>
<td>Key populations and local epidemiology</td>
<td>Targeted programs were needed to identify groups at highest risk for HIV. Testing, treatment, and prevention had to be provided to difficult-to-reach populations.</td>
<td>Targeting limited vaccine supply toward populations at greatest risk. Tailoring response according to geographic region, infrastructure, and culture. Conducting surveillance to identify and reach high-risk populations (WHO Expanded Program on Immunization).</td>
</tr>
<tr>
<td>Prevention and treatment reluctance</td>
<td>Sustained and improved risk communication and education from trusted persons and institutions helped overcome fear and stigma surrounding contagion and ART side effects. Misconception that there is no reason for treatment if there are no symptoms had to be corrected. Convenience and side-effect profiles of ART regimens had to be improved. Misinformation, including from political leaders and media, had to be corrected.</td>
<td>Reducing stigma and fear of disease, isolation, and adverse effects of vaccines. Eliminating misconception that there is no reason for isolation if there are no symptoms. Addressing misinformation and disinformation about vaccines, including from political leaders, media, and social media. Recognizing the importance of risk communication by trusted voices in the community.</td>
</tr>
<tr>
<td>Communication and community involvement and engagement</td>
<td>Mobile testing units, community health workers (CHWs), community-based care, and efficient drug provision for treatment and prevention were implemented.</td>
<td>Tailoring education and risk communication to needs of local communities. Understanding community structures for vaccine communication and distribution. Involving CHWs for rapid, wide-scale, effective, and equitable vaccination.</td>
</tr>
<tr>
<td>Prevention and treatment in pregnant women and children</td>
<td>Years-long delays for inclusion in HIV drug studies and in access could have been minimized. Social determinants of health had to be identified.</td>
<td>Conducting timely trials of Covid-19 vaccines in pregnant women and children. Social determinants of infection disease and of vaccine acceptance and access will be important to identify and address.</td>
</tr>
</tbody>
</table>
COVID-19 mAb Applications for Prevention

Monoclonal Abs (mAbs):
- Offer immediate protection for those exposed or unvaccinated in high-risk settings
- Can be provided to people unlikely to respond to a vaccine, or allergic
- They could stop viral replication and block progression of disease
- *Can help predict requirements for a vaccine by identifying required titers of neutralizing antibodies*

Target Populations for mAbs:
- Nursing homes, both residents and attendants
- High incidence workplaces (e.g. meat packing plants)
- Index case contacts (e.g. household contacts)
## Emergency Use Authorization (EUA) Monoclonal Antibody Rx for COVID-19

**Adults**

- At least one of the following:
  - Are ≥65 years of age
  - A body mass index (BMI) ≥35
  - Chronic kidney disease
  - Diabetes
  - Immunosuppressive disease
  - Receiving immunosuppressive treatment

- ≥55 years of age AND have one of the following:
  - Cardiovascular disease
  - Hypertension
  - Chronic obstructive pulmonary disease
  - Other chronic respiratory disease

**Pediatrics**

- Between 12-17 years of age AND at least one of the following:
  - BMI ≥85th percentile for their age and gender based on CDC growth charts
  - Sickle cell disease
  - Congenital or acquired heart disease
  - Neurodevelopmental disorders, for example, cerebral palsy
  - A medical-related technological dependence, (e.g., tracheostomy, gastrostomy, or positive pressure ventilation)
  - Asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.
BLAZE-2: POST-EXPOSURE PROPHYLAXIS

N=966 (666 staff; 300 residents)

STUDY DESIGN

- **Evaluation Period**
  - Bamlanivimab 4200 mg
  - 1:1 Randomization

- **Follow-Up Period**
  - Placebo

**Maximum 7-day window**

- Week 0
- Week 8
- Week 24

**Deployment & Screening**

- Confirmed Case at Site

**MOBILE RESEARCH UNITS**

To facilitate rapid prophylaxis and treatment of residents and facility staff, participants were enrolled prior to assessment of baseline SARS-CoV-2 status. This allowed for separate prevention and treatment analysis populations.
RESIDENTS WITH SYMPTOMATIC COVID-19
(Prevention Population)

Notes:
No significant effect in rate of COVID-19 diagnosis, which was relatively low, in staff.
Lower viral loads at time of detection among those getting the mAb

Phase 3 Clinical Trial of Casirivimab And Imdevimab as Passive “Vaccine” to Prevent COVID-19 in Household Contacts

- Household contacts of COVID-19 case (N=400 prelim analysis) randomized to CASI+IMDE 1,200 mg subQ vs Placebo

  • Passive vaccination with CASI+IMDE resulted in 100% prevention of symptomatic infection (8/223 placebo vs. 0/186 CASI+IMDE), and approximately 50% lower overall rates of infection (symptomatic and asymptomatic) (23/223 placebo vs. 10/186 CASI+IMDE)

  • Infections occurring with CASI+IMDE therapy were all asymptomatic
    - Infections occurring in the placebo group had, on average, more than 100-fold higher peak viral load.
    - Infections in the CASI+IMDE group lasted no more than 1 week, while approximately 40% of infections in the placebo group lasted 3-4 weeks.
    - No infected individuals in the CASI+IMDE group had high viral loads (>10^4 copies/mL) compared to 62% of the infected placebo group (13/21 placebo vs. 0/9 CASI+IMDE).

Variants: They’re Here

• Major variants

• **B.1.1.7** – UK -> More infectious, Maybe more severe disease

• **B.1.351** – South Africa -> Reduced protection by some vaccines (not Moderna or Pfizer), reduced effect of some COVID-19 antibody treatments

• **P.1** – Brazil -> shares E484K mutation with B.1.351

Epidemiology in India

Reported cases: ~22.7M  Deaths: ~246K

Vaccine coverage: 9.4% received 1 dose; 2.1% fully vaccinated

Vaccines available: Majority of vaccine administered (10:1) has been Covishield (Serum Institute of India, ChAdOx1), followed by Covaxin (Bharat Biotech, inactivated w/ Alhydroxiquim-II adjuvant)

Variants in India: B.1.617 > B.1.1.7 > B.1.351

Preliminary reports that B.1.617 growing at a rate similar to B.1.1.7 in India, suggesting that it may be more transmissible than ancestral variants. More data needed.
Molnupiravir: An Antiviral Agent for COVID-19

- A ribonucleoside analog that inhibits viral RNA replication by incorporation of the 5’-monophosphate metabolite (EIDD-1931) into the viral genome producing viral error catastrophe

- Active against SARS-CoV-2, SARS-CoV, MERS-CoV, and other human CoV (Also against influenza virus and others); EC50 = 0.17 µM

- 800 mg MOVBID inhibits replication in vivo

- Phase 3 treatment study underway

- Phase 3 TaSP study in protocol development
‘The Biggest Monster’ Is Spreading. And It’s Not the Coronavirus.

Apoorva Mandavilli | Aug. 3, 2020

www.nytimes.com › coronavirus-tuberculosis-aids-malaria
Thank you!

- To all study participants
- To all investigators
- To All Funders at NIH, BMGF and many, many industry partners