INTEGRATED DISEASE SEROSURVEYS

Leveraging existing population-representative sampling frames

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COVID-19 pandemic has exposed the weaknesses in our existing disease surveillance systems

Systems were hampered by: inadequate diagnostic capacity, fragmented data systems, incomplete data, sub-optimal governance

Information on mortality and causes of death is important for designing disease prevention programs

- Only 8 African countries have compulsory death registration systems
- Reliance on surveys, model estimates, and small studies
- Completeness of data
  - >50% of deaths occur outside of facilities, meaning they are less likely to be counted
  - Different data collection instruments used across settings; >50% of SSA countries only have paper death records

Now is the time to assess what failed and act boldly to implement improvements

References
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6815655/
DISEASE SURVEILLANCE VISION

An integrated surveillance system to support the detection and response of the next pandemic and improve routine disease surveillance.

1 Population-representative surveillance foundation / population surveillance and vital statistics
   Civil registration and vital statistics (CRVS) or a sample registration system (SRS) & a mortality deep dive (confirming cause of death and disease burden)

2 Notifiable disease and IDSR-like surveillance
   Community based surveillance, electronic case reporting, syndromic and notifiable disease surveillance, and rapid investigative response teams

3 Pathogen surveillance including sequencing
   Laboratory reporting, genomic analysis to identify a pathogen and novel variants / strains, sewage and septic surveillance

4 Specialized programs
   Population immunity surveillance and vaccine effectiveness

5 Data integration
   Interoperable with common meta-data and privacy protection

6 National Public Health Institute
   Central surveillance coordination and decision making, incl. modeling, forecasting, and analytics

Surveillance component
Types of surveillance programs and elements included within it
### CORE PRINCIPLES FOR INTEGRATED DISEASE SURVEILLANCE*

<table>
<thead>
<tr>
<th>Principles</th>
<th>Implications</th>
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<tbody>
<tr>
<td>1 Population-based foundation - CRVS or sample registration system</td>
<td>Denominators for rates and burden</td>
</tr>
<tr>
<td>2 Laboratory testing adequately scaled to the threat</td>
<td>Cases accurately tracked</td>
</tr>
<tr>
<td>3 All digital with unique health identifiers and core metadata</td>
<td>Systems interconnect and privacy protected</td>
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<tr>
<td>4 Data transparency and automated reporting to NPHI</td>
<td>Full visibility at NPHI and WHO if PHEIC</td>
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<tr>
<td>5 Adequate financing</td>
<td>Countries determine adequate % of GDP needed</td>
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*As described in a commentary published in the Lancet*
NEED POPULATION REPRESENTATIVE PLATFORMS TO SERVE AS THE FOUNDATION

Benefits of a sample registration systems

• Nationally and sub-nationally representative data of entire population
  • Household sampling frame
  • Continuous data collection
  • Capturing births, pregnancies, and deaths
• Disease agnostic
• Stepping-stone to full CRVS
• Government led

Figure 1: Map of Sierra Leone showing enumeration areas, regions, and numbers of study deaths
• 1 province (Zambezia)
• Representative sample of households from COMSA clusters
• Target 2,900 individuals of all ages
• Five dried blood spots (50 µL each for four spots, plus 60 µL on separate TropBio card for serology, total 260 µL) on barcoded filter paper
  • Serum extracted, multiplex bead assay on eluate (one DBS can be used to determine antibody responses to up to 50 antigens)
  • Testing by Mozambique National Institute of Health (INS) using Luminex and CDC Atlanta
• Calculate provincial-level age-group-specific seropositivity (IgG antibodies to COVID, malaria, selected NTDs, measles, rubella, tetanus, and Hep A, B, C, E)
• Interest from USAID/Mozambique and INS in adding HIV – we are exploring this option and expanding target age group to adults
COMSA Mozambique

Pathogens and antigens available to be included in MagPix custom IgG panels developed by CDC and LSTMH

<table>
<thead>
<tr>
<th>Pathogen/Disease</th>
<th>Antigen</th>
</tr>
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<tbody>
<tr>
<td><em>P. falciparum</em></td>
<td>MSP-1(19), PfAMA1, Gexp18, GLURP R2, Etramp5 Ag1, Rh4.2, CSP</td>
</tr>
<tr>
<td><em>P. vivax</em></td>
<td>PvMSP119, PvDBPRII, PvRBP2b</td>
</tr>
<tr>
<td><em>P. ovale</em></td>
<td>PoMSP119</td>
</tr>
<tr>
<td><em>P. malariae</em></td>
<td>PmMSP119</td>
</tr>
<tr>
<td>Measles</td>
<td>Whole virus</td>
</tr>
<tr>
<td>Rubella</td>
<td>Whole virus</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Toxoid</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Toxoid</td>
</tr>
<tr>
<td><em>Strongyloides stercoralis</em></td>
<td>NIE</td>
</tr>
<tr>
<td><em>Onchocerca volvulus</em></td>
<td>OV16</td>
</tr>
<tr>
<td><em>Taenia solium</em></td>
<td>ES33, T24H</td>
</tr>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td>pgp3, CT694</td>
</tr>
<tr>
<td><em>Treponema pallidum</em></td>
<td>Rp17, TmpA</td>
</tr>
<tr>
<td><em>Wuchereria bancrofti</em></td>
<td>Wb123, Bm14, Bm33</td>
</tr>
<tr>
<td><em>Schistosomiasis</em></td>
<td>SEA, Sm25</td>
</tr>
<tr>
<td>Dengue virus</td>
<td>Dengue 1 NS1, Dengue 2 NS1, Dengue 3 NS1, Dengue 4 NS1</td>
</tr>
<tr>
<td>Chikungunya virus</td>
<td>ChikE1 (envelope protein)</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>Cp23, Cp17</td>
</tr>
<tr>
<td><em>Giardia lamblia</em></td>
<td>VSP3, VSP5</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>Spike RBD, Nucleocapsid</td>
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Pilot in Zambezia Province
Lessons learned

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Opportunities</th>
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<tr>
<td>• Social mobilization needed to be increased to overcome community hesitancy with blood collection</td>
<td>• Used HIV and malaria rapid diagnostic tests to provide immediate results to participants</td>
</tr>
<tr>
<td>• Significant delays in procuring supplies for specimen collection and laboratory caused field and testing delays</td>
<td>• Integration of multiple pathogens provides rich epidemiological picture</td>
</tr>
<tr>
<td>• Conducting fieldwork in the context of COVID-19</td>
<td></td>
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<tr>
<td>• Difficult terrain complicated logistics for getting specimens to the laboratory</td>
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Healthy Sierra Leone (HCS) Dried blood spot study: Goal and approach

• Investigate the prevalence of exposure (antibodies) to various pathogens including COVID-19 infection using the COMSA platform

• COMSA sample frame: 46 enumeration areas in Bo District with ~8,000 people: ~4000 urban adults, ~3000 rural adults, ~1000 kids): 17 dedicated Surveyors

• To date: all urban and 1500 rural adults completed, rest plus kids to be completed by Aug 1, 2023

• Teams of two trained field staff enumerate/consent households and implement a general health check up about current health, blood pressure, exercise, smoking, alcohol, mental health concerns, and COVID experience

• Anthropometric measurements- two x BP, height, weight, waist hip ratio, body impedance (fat) and grip strength

• Collect DBS samples (5 spots Whatman paper for central Multiplex analyses), plus anemia/diabetes instant results

• Participants representative for age, smoking, BMI, BP vs whole of Sierra Leone
Malawi- Study Design

• The data collection was conducted in 7 districts
  o Kasungu, Dowa, Lilongwe, Dedza, Machinga, Zomba and Blantyre

• Data collection commenced on 27th December 2021 and completed on 17th January 2022

• The target number of household members to be enrolled in the 7 districts was 5,948.
  o Of these, 79.2% were enrolled.

• Zomba, Blantyre, Machinga, Kasungu and Dedza all enrolled over 80% of their target number of individuals
High seroprevalence in adults and in females
Household cohort study in two communities serviced by health facilities where severe respiratory illness (SRI) and influenza-like illness (ILI) surveillance is conducted in South Africa, namely Pietermaritzburg (KwaZulu-Natal), and Mitchell's Plain (Western Cape).

- Study participants were identified using randomly selected GPS coordinates to identify households in the target areas.
- **HUTS-1**: November 2020 – April 2021
- **HUTS-2**: April – May 2022

### Laboratory Testing

- Serum samples collected for SARS-CoV-2 ELISA using the Roche Elecsys® Anti-SARS-CoV-2 assay
  - Anti-Nucleocapsid
  - Anti-Spike
- Plasma samples collected for HIV and viral load testing

**Seroprevalence**

- **4800 individuals**
COVID-19 Healthcare Utilisation and seroprevalence survey (HUTS-1), Nov 2020 – Apr 2021

Seroprevalence of Severe Acute Respiratory Syndrome Coronavirus 2 After the Second Wave in South Africa in Human Immunodeficiency Virus–Infected and Uninfected Persons: A Cross-Sectional Household Survey
High prevalence of antibodies against COVID-19 within the general population: Evidence from Nairobi and Kilifi

Key messages:
- By May 2022, 69% of individuals residing within the Kilifi Health and Demographic System (HDSS) and 91% residing within the Nairobi Urban HDSS had COVID-19 antibodies resulting from natural infection and/or vaccination, i.e., anti-spike IgG antibodies.
- The majority of HDSS residents with anti-spike IgG antibodies appear to have developed them as a result of natural infection, given that about 11% - 27% of the total number of residents sampled within the Kilifi HDSS and Nairobi Urban HDSS reported receiving one or more doses of COVID-19 vaccine by May 2022.
- The proportion of HDSS residents with anti-spike IgG antibodies was significantly higher in Nairobi, an urban setting, than in rural Kilifi.
- Seroprevalence by May 2022 represents a substantial increase from May 2021 when about 20% of the residents within the Kilifi HDSS and 40% within the Nairobi Urban HDSS had anti-spike IgG antibodies.
- Surveillance for COVID-19 antibodies among residents HDSS sites provides an opportunity to understand the extent COVID-19 spread and immunity within the general population in Kenya.
Building population-representative, Pathology-informed Mortality Surveillance platforms

• Building platforms to serve as the foundation for disease surveillance

Collecting better primary data → Countrywide integration → Improved global estimates for decision-making

MITS Surveillance Alliance
• ~5 sites MITS-VA feasibility projects
• MITS Kits
• Training and capacity building
• Data quality assurance of tissues samples

Child Health and Mortality Surveillance (CHAMPS)
• Most accurate cause-of-death data for children <5 years, using MITS
• Sub-nationally representative sites across 9 countries in Africa and South East Asia

Countrywide Mortality Surveillance for Action (COMSA)
• Sample registration system providing representative causes-of-death using verbal autopsy, all ages
• Subset of death w/MITS
• Integrated serosurveillance using dried blood spots

Institute for Health Metrics and Evaluation (IHME)
• Improved modeling of causes of death and global burden of disease
• Geospatial mapping to guide interventions and highlight data gaps

Africa CDC’s Mortality Surveillance Program Secretariat
• TA across Member States
• Developed continental mortality surveillance framework

Digital Mortality Tool Assessment
• Developing guidance and standards on mortality data collection

Post-COVID-19 Investments
Measuring excess-mortality

• Burial Site Surveillance
• Bangladesh
• Pakistan
• Mobile Phone Surveys
• Mozambique
• Bangladesh
• Burkina Faso
• Malawi
• HDSS Sites
• 18 sites across SSA and SEA (4 CHAMPS sites)
EXTRA SLIDES ON SAMPLE REGISTRATION SYSTEMS
COMSA is a country-led sample registration system

- Led by national statistics organizations with close collaboration from ministries of health, national civil registration authorities, national public health institutes
  - Four years of BMGF support for external technical assistance
  - Low running costs
- Select representative enumeration areas across a country
  - Cover ~ 3-8% of entire population
  - Identify and report pregnancies outcomes and deaths (including stillbirths)
  - Conduct verbal autopsy (VA) on all deaths
  - Conduct MITS on some U5 deaths from COMSA (outside of CHAMPS site)
- Assemble all data across the country and calculate statistics at the national and subnational levels
  - National and subnational crude birth and death rates
  - Age-group specific mortality rates and cause-specific mortality fractions and rates
  - Use MITS-VA pairs from CHAMPS and COMSA to calibrate national VA-based COD
- Integrate with existing data systems and share data promptly and continuously with local, national, and international stakeholders
COMSA Mozambique- Births and deaths registered by place of residence

% Deaths

- Urban: 45.9
- Rural: 7.4

% Births

- Urban: 36.9
- Rural: 27.7

Urban with high registration compared to rural
COMSA Mozambique - Deaths registered by wealth quintiles

<table>
<thead>
<tr>
<th>Wealth Quintile</th>
<th>% Deaths</th>
</tr>
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<tbody>
<tr>
<td>Poorest</td>
<td>2.6</td>
</tr>
<tr>
<td>Second</td>
<td>4.9</td>
</tr>
<tr>
<td>Middle</td>
<td>6.3</td>
</tr>
<tr>
<td>Fourth</td>
<td>14.2</td>
</tr>
<tr>
<td>Wealthiest</td>
<td>56.3</td>
</tr>
</tbody>
</table>

Wealthiest with high registration compared to poorest households
Odds ratio of death registration by selected characteristics

- Age 5-14 vs U5
- Age 15-59 vs U5
- 60+ yo vs U5
- Male vs Female
- Employed vs Unemployed
- Pension vs Unemployed
- Other vs Unemployed
- Stud vs Unemployed
- Health facility vs home
- Other vs home
- lower vs poorest
- Q2 vs poorest
- Q4 vs poorest
- Wealthiest vs poorest
- Urban vs rural
Data collection and analysis

• Establish representative random sample of 700 clusters (~300 households each) nationally

• Recruit, train and equip a Community Surveillance Assistant (CSA) in each cluster to:
  • List population of the cluster
  • Identify and report pregnancies, pregnancy outcomes (live births, stillbirth, pregnancy loss), and deaths continuously

• Recruit, train and equip verbal autopsy (VA) data collectors based at provincial level to:
  • Follow up on all deaths for VA interviews on a continuous basis
  • Supervise the CSAs

• Calibrate national VA-based cause of death information using pathology-based gold standard cause of death information from CHAMPS sites and other sources of paired minimally invasive tissue sampling/VA data
Comsa Mozambique is now reporting births and deaths nationwide

700 clusters of ~300 households each

- ~800,000 people under active surveillance
- 38,000 annual births
- 2,600 annual under-five deaths
- Reporting births & deaths in all provinces (1,924 deaths reported to date)
  - 1,446 verbal autopsies completed
- Preliminary calibration analysis completed using 167 CHAMPS network MITS/VA pairs on 226 COMSA deaths (February 2019)
  - As CHAMPS network produces more MITS/VA pairs and they are incorporated into calibration, we expect to see some shifting of cause-specific mortality fraction estimates and improved accuracy of VA cause of death findings
Other uses for the EAs/sampling frame, beyond mortality and serosurveillance purposes

• COMSA sample drawn to be representative of the population of each province
• Cluster maps developed and digitized
• Population listing done, with GIS and phone numbers (needs regular update)
• In theory COMSA sample can accommodate all survey type data collection. Current examples include:
  • Rapid mortality mobile phone surveys (RAMMPS)
  • Study of COVID-19 impact on RMNCH