Mathematical Modeling of COVID-19 in Malawi

Quantifying the Potential Burden of Novel Coronavirus

May 19, 2020
Background
As of May 19, 2020, the 2019 Coronavirus (COVID-19) has:

- Spread rapidly, causing a global pandemic reaching 188 countries.
- Infected more than 4,900,000 people.
- Caused 325,000 deaths.
Although Malawi has only a few confirmed cases of COVID-19, there is little doubt that the disease can spread widely in the nation.

Sub-Saharan Africa has had a seemingly late, slow, or mild outbreak – perhaps due to connectivity to the rest of the globe, younger population, differing background risk, or lack of testing.

Although Malawi has only a few confirmed cases of COVID-19, there is little doubt that the disease can spread widely in the nation.

With minimal COVID-19 testing capacity, it is difficult to estimate the current and future trajectory of disease in Malawi.
COVID Modeling Malawi Timeline

- **March 17**: Kuunika Pivots Support to COVID Response
- **March 21**: Baseline Epi and Risk Models Completed and Shared
- **March 31**: District and TA Estimates Modeled
- **April 8**: Mitigation Scenarios Modeled
- **April 27**: District Reports Created and Distributed
- **TBD**: Model Calibration with Additional Data Sources
- **May 25**: Dynamic Models Finalized and Released
- **Today**: Dynamic Models Finalized and Released
Kuunika Support for COVID Response
Areas of digital health support:

**Digital Platforms**
- Mobile application for point of entry, case-based surveillance, contact tracing, laboratory, and case management data collection.
- USSD, SMS, WhatsApp Chatbot and mobile application for risk communication and follow-up

**Data Analytics**
- Epidemiological, Risk, and Economic Vulnerability Model
- High frequency data collection for syndromic surveillance
- Internal data dashboards
- Deploy Palantir Foundry for a COVID-19 data pipeline

**Knowledge Translation & Support**
- Public COVID-19 website
- Emergency Operational Center infrastructure support, operational guidelines, Incident Management System software, and command hotline
- National help desk for COVID-19 mobile application
Epi Modeling Approach
Methods – Approach

One day time-step
One day time-step, starting with first introduced case to day 365.

Susceptible-Exposed-Infected-Recovered (SEIR)
Created SEIR deterministic and compartmental model.

Infectious while asymptomatic
 Individuals are assumed to be infectious in the exposed (asymptomatic) period.

Mild, Hospitalized, or Critical sub-state
 Persons in the infected state can either be in either mild, hospitalized, or in critical care - with the latter susceptible to death.

No births or non-COVID-19 deaths
There are no births or non-COVID-19 related deaths and no additional imported cases than the index case.

Key parameters
Scenario analyses conducted on key parameters.
Methods - Model Structure

Susceptible (S) → Exposed (E) → Mild (M) → Hospitalized (H) → Critical Care (C) → Recovered (R)

Infected

Dead (D)

https://github.com/CooperSmith-org/malawi-covid-work
Methods - Model Parameters

**CHALLENGE**
Malawi does not yet have extensive clinical data on COVID-19 patients

**ASSUMPTION**
Malawi will have a different fatality rate of COVID-19 due to its substantially younger population than places hardest hit (and with data) with COVID-19 mortality.*

*Advanced age is the greatest predictor for poor COVID-19 outcomes*
Update on the quality of evidence for model parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CS Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_0$</td>
<td>2.2</td>
</tr>
<tr>
<td>Infectious Period</td>
<td>5.2 days</td>
</tr>
<tr>
<td>Time to Hospitalization</td>
<td>6 days</td>
</tr>
<tr>
<td>Hospitalized Time - Severe Cases</td>
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<tr>
<td>Hospitalized Percent</td>
<td>3.0%–7.0%</td>
</tr>
</tbody>
</table>

IFR

- Age-Standardized Rate Using:
  - 0-9: 0.0016%
  - 10-19: 0.007%
  - 20-29: 0.031%
  - 30-39: 0.084%
  - 40-49: 0.16%
  - 50-59: 0.60%
  - 60-69: 1.90%
  - 70-79: 4.30%
  - 80+: 7.80%

- TA-Specific Age-Standardized Rates: 0.16% - 0.36%

Review of 21 estimates ranging from 1.9 to 6.5 (2/3rds range from 2–3)
### Update on the quality of evidence for model parameters

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<td>TA-Specific Age-Standardized Rates: 0.16% - 0.36%</td>
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- **Review of 22 estimates for a range of 3.1 to 7.5 days**
- **Review of 52 estimates with a median of 5 and 7 days for hospitalization and ICU respectively (12 days total for ICU)**
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- No known review of these parameters, but treatment trial data produce similar estimates.

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Wide variety of both empirical and model-based estimates in literature. Range in **one review of 0.49-1.01%** and **0.3-1.4% in another**.
Methods - Estimation of Malawi-Specific Parameters

1. Standardize the age distribution of cases in Malawi relative to a setting with widespread testing*

2. Estimate weighted average hospitalization rates and IFR using Verity et al. estimates of age-specific data (*Lancet Inf. Dis.*) at District & TA level

<table>
<thead>
<tr>
<th></th>
<th>Chitipa</th>
<th>Karonga</th>
<th>Nkhabay</th>
<th>Rumphi</th>
<th>Mzimba</th>
<th>Likoma</th>
<th>Mzuzu City</th>
<th>Kasungu</th>
<th>Nkhotakota</th>
<th>Ntchisi</th>
<th>Dowa</th>
<th>Salima</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization</td>
<td>3.0%</td>
<td>2.9%</td>
<td>3.1%</td>
<td>3.0%</td>
<td>3.2%</td>
<td>3.1%</td>
<td>2.6%</td>
<td>2.9%</td>
<td>2.8%</td>
<td>3.0%</td>
<td>3.1%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Critical Care</td>
<td>0.6%</td>
<td>0.6%</td>
<td>0.7%</td>
<td>0.6%</td>
<td>0.7%</td>
<td>0.6%</td>
<td>0.3%</td>
<td>0.5%</td>
<td>0.5%</td>
<td>0.6%</td>
<td>0.6%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Crit of Hosp</td>
<td>20.55%</td>
<td>19.56%</td>
<td>21.21%</td>
<td>19.50%</td>
<td>21.31%</td>
<td>20.11%</td>
<td>12.94%</td>
<td>18.13%</td>
<td>19.14%</td>
<td>20.01%</td>
<td>20.08%</td>
<td>20.27%</td>
</tr>
<tr>
<td>IFR</td>
<td>0.37%</td>
<td>0.34%</td>
<td>0.39%</td>
<td>0.34%</td>
<td>0.40%</td>
<td>0.36%</td>
<td>0.19%</td>
<td>0.31%</td>
<td>0.32%</td>
<td>0.35%</td>
<td>0.36%</td>
<td>0.35%</td>
</tr>
<tr>
<td>IFR of Crit</td>
<td>59.12%</td>
<td>59.04%</td>
<td>59.15%</td>
<td>59.04%</td>
<td>59.15%</td>
<td>58.99%</td>
<td>58.25%</td>
<td>58.93%</td>
<td>58.99%</td>
<td>59.04%</td>
<td>59.05%</td>
<td>59.04%</td>
</tr>
<tr>
<td>IFR of Hosp</td>
<td>12.15%</td>
<td>11.55%</td>
<td>12.55%</td>
<td>11.51%</td>
<td>12.61%</td>
<td>11.86%</td>
<td>7.54%</td>
<td>10.69%</td>
<td>11.29%</td>
<td>11.82%</td>
<td>11.86%</td>
<td>11.97%</td>
</tr>
</tbody>
</table>

*Age-specific INCIDENCE is unknown in any setting, but this is a key driver of age-standardized rates
Methods - Co-Morbidity Prevalence

Crude and Age-Standardized Prevalence of Select COVID-19 Severity of Disease Risk Factors by Country

US       Korea       Malawi

No additional adjustments to incidence, hospitalization, or survival due to distribution of known co-morbidities
The bulk of data on COVID-19 cases has been in HICs, which do not have prevalence of many infections seen in Africa.

- These conditions could be a detriment to survival.
- Diseases which could plausibly harm COVID-19 patients include HIV & TB.

What improvements in case fatality are due to health system quality in advanced economies?

- Malawi has 17 ventilators nationwide (1 per million) – a potentially life-saving piece of equipment for patients – hinting that case-fatality could be higher
- Reductions in other health service delivery, including HIV, TB, malaria, and MNCH treatment could lead to aggregate declines in life expectancy

Many Uncertainties

- Unknown Co-morbid Risk Factors
- Health System Capacity and Spillovers

Uncertainties
Important Considerations with No Evidence Currently Available

Contextual Contributors to COVID-19 Severity & Mortality

- Poverty
- Clean Water
- Malnutrition
- Unknown Prophylaxis
- Non-ICU Hospital Care
Sensitivity Analysis

Probabilistic sensitivity analysis
- Random draws of key model parameters using a normal distribution with a mean of the baseline value and assumed standard deviation
- 1,000 simulations performed, with 2.5% and 97.5% to identify the interval
- Parameters include:
  - Incubation period
  - Hospitalized time
  - Hospitalization rate
  - ICU rate
  - Mortality rate
  
- IN PROGRESS
Mitigation Scenarios
<table>
<thead>
<tr>
<th>Policy</th>
<th>Contact Reduction Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase 0 - Unmitigated</strong></td>
<td></td>
</tr>
<tr>
<td>No policies in place (Baseline)</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Phase 1 – Early Stage Outbreak (Current Stage)</strong></td>
<td></td>
</tr>
<tr>
<td>Social Distancing</td>
<td>Rotational Work Schedules</td>
</tr>
<tr>
<td><strong>Phase 2 - Additional Population Guidelines</strong></td>
<td></td>
</tr>
<tr>
<td>Work From Home – If Possible (Essential personnel excepted)</td>
<td>Movement Limited to Essential Activities (Groceries, Food, Pharmacies, etc), Max. gatherings of 10 people</td>
</tr>
<tr>
<td><strong>Phase 3 – Enforced Pop Restrictions</strong></td>
<td></td>
</tr>
<tr>
<td>Shelter in Place</td>
<td>Restrict Movements to essential activities (food/pharmacies), Close most businesses</td>
</tr>
<tr>
<td><strong>Phase 4 – Fully Enforced Country Wide Lockdown (Strict)</strong></td>
<td></td>
</tr>
</tbody>
</table>
Novel Approach – Leverage Google Location Services to Derive Contact Reduction Estimates

Google Mobility Reports

- Retail & Recreation (Incl. Places of Worship)
- Transit Stations (Incl. Bus Depots)
- Places of Work
- Grocery & Pharmacy (Incl. Markets)
- Parks (excl. from analysis)

Mobility trends for each of the above-mentioned categories vs. a baseline to assess response to policy guidelines

Source: https://www.google.com/covid19/mobility/
Novel Approach – Leverage Google Location Services to Derive Contact Reduction Estimates

Recommended Policies for Malawi were taken

Identified Countries Following Phase 1-3 Policy Guidelines (Currently)

Reductions rates for each country by category were established

Weighted average for each country was used to develop a range for each Phase (1-3)

Note: No country fit well into Phase 4 as of yet and was therefore excluded. An aspirational target was estimated for modeling purposes.
Novel Approach – Leverage Google Location Services to Derive Contact Reduction Estimates (Appendix)

### Example

<table>
<thead>
<tr>
<th>Policy/Behavior</th>
<th>SSA Specific Context</th>
<th>Reduction Range</th>
<th>Similar Countries</th>
<th>Reduction in Contact Rate</th>
<th>Retail &amp; Recreation</th>
<th>Grocery &amp; Pharmacy</th>
<th>Transit Stations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Zambia</td>
<td>-15%</td>
<td>-21%</td>
<td>-8%</td>
<td>-24%</td>
</tr>
<tr>
<td>Current situation</td>
<td></td>
<td>10 - 20%</td>
<td>Tanzania</td>
<td>-11%</td>
<td>-16%</td>
<td>-8%</td>
<td>-11%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mozambique</td>
<td>-18%</td>
<td>-26%</td>
<td>-13%</td>
<td>-29%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Kenya</td>
<td>-35%</td>
<td>-45%</td>
<td>-33%</td>
<td>-39%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Senegal</td>
<td>-37%</td>
<td>-44%</td>
<td>-31%</td>
<td>-50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nigeria</td>
<td>-28%</td>
<td>-39%</td>
<td>-25%</td>
<td>-34%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>South Africa</td>
<td>-65%</td>
<td>-79%</td>
<td>-60%</td>
<td>-80%</td>
</tr>
<tr>
<td>+ Additional Pop Guidelines</td>
<td></td>
<td>30 - 40%</td>
<td>Senegal</td>
<td>-37%</td>
<td>-44%</td>
<td>-31%</td>
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</tr>
<tr>
<td>Enforced Pop Restrictions</td>
<td></td>
<td>40 - 60%</td>
<td>Rwanda</td>
<td>-57%</td>
<td>-56%</td>
<td>-57%</td>
<td>-75%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Uganda</td>
<td>-41%</td>
<td>-50%</td>
<td>-36%</td>
<td>-59%</td>
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National-level Projections
The unmitigated scenario represents the worst case. Over the past weeks Malawi has released guidelines intended to reduce inter-personal contacts. The impact of these are modeled in the subsequent scenario analyses.
Scenario Outcomes – Infections & Deaths

### Infections

<table>
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<th>Day</th>
<th>Expected Trajectory</th>
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<tr>
<td>8 Mar.</td>
<td></td>
</tr>
<tr>
<td>18 Jun.</td>
<td></td>
</tr>
<tr>
<td>28 Sept.</td>
<td></td>
</tr>
<tr>
<td>7 Jan.</td>
<td></td>
</tr>
<tr>
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<td></td>
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### Deaths

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<tr>
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### Reductions

- **No Mitigation**
- **No Further Reduction From Current**
- **Additional Guidelines (30-40% Reduction in Mobility)**
- **Enforced Population Restrictions (40-60% reduction in mobility)**
- **Strict Enforcement of Lockdown (75% mobility reduction)**
Scenario Outcomes – Hospitalizations & Critical Care

### Hospitalizations

- **No Mitigation**
- **No Further Reduction From Current**
- **Additional Guidelines (30-40% Reduction in Mobility)**
- **Enforced Population Restrictions (40-60% reduction in mobility)**
- **Strict Enforcement of Lockdown (75% mobility reduction)**

### Critical Care

- **Expected trajectory given current policies and adherence**

#### Reduction

- Grey: No Mitigation
- Red: No Further Reduction From Current
- Blue: Additional Guidelines (30-40% Reduction in Mobility)
- Orange: Enforced Population Restrictions (40-60% reduction in mobility)
- Black: Strict Enforcement of Lockdown (75% mobility reduction)
Scenario Outcomes – Projected Reduction in **Infections** with Mitigation Scenarios

- **Without mitigation** we expect about **16 million infections**
- **Current** policies and adherence are projected to avert **1.7 million infections**
- Additional guidelines consistent with **Phase 2** scenario are projected to avert an additional **4.1 million infections**
- Enforced policies consistent with **Phase 3** scenario are projected to avert an additional **5.8 million infections**
- Strictly enforced policies consistent with **Phase 4** scenario are projected to avert an additional **3.9 million infections**
Calibration Considerations
### Calibration options

**Calibration**: adjustment of model parameters and inputs to achieve a projection which matches empirical data estimates of prevalence, incidence, or deaths.

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<th>Calibration Point</th>
<th>Challenge</th>
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<tr>
<td>COVID Diagnoses</td>
<td>Significantly limited testing means cases are underreported</td>
</tr>
<tr>
<td>COVID Deaths</td>
<td>Incomplete ascertainment of COVID-related deaths</td>
</tr>
<tr>
<td>Adjusted COVID Deaths</td>
<td>Incomplete ascertain of deaths of any cause impede estimation of excess deaths</td>
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**Why adjust COVID deaths?**
- Some analyses have pointed towards the potential under counting of COVID-19 mortality, even in high resource settings with extensive testing capacity. Using assumptions of infection fatality ratio, one could back-calculate the presumed number of infections from an accurate account of deaths.
Approach for estimating undetected COVID deaths

Estimated through comparing historic mortality trends

Source: The Economist
Estimating undetected COVID deaths in Malawi

Source: DHIS2

What is recorded?
- Inpatient Deaths
- Facility-level (linked to districts)
- Limited cause-of-death availability

What is missing?
- Maternal causes
- Deaths outside of hospital settings
- District hospital deaths
  - Attempting to get now

Summary:
- Total Deaths = 44,131
  - 2017 = 13,183
  - 2017 GBD Deaths = 129,000

Finding: No clear trend of increased inpatient mortality in Q1 of 2020 relative to the prior 3 years.
Estimating undetected COVID deaths in Malawi - Districts

Extension 1:
- Investigate deaths only at district level, focusing on districts with known COVID cases – primarily Lilongwe and Blantyre
- Similar results for Blantyre, which has a significant data reporting error which makes the trend difficult to interpret

Finding: Even more noise at the district level, difficult to ascertain any clear trend
Estimating undetected COVID deaths in Malawi - Facilities

Extension 2:
- Investigate deaths only among high burden facilities in districts with known COVID cases – primarily Lilongwe and Blantyre
- Similar results for Blantyre, which has a significant data reporting error which makes the trend difficult to interpret

Finding: No apparent trend
Discussion

• No apparent trend of increased inpatient mortality in Malawi in Q1 of 2020 among reporting facilities

• Potential reasons for no detected increase
  1. There is no/limited undetected COVID-19 mortality
  2. Increased COVID-19 mortality is offset by decreases in other causes of death (i.e. motor vehicle injuries)
  3. COVID-19 deaths are predominantly occurring outside of health facilities and aren’t measured
  4. Reporting delay in March
  5. To-be reported deaths in April and May will reveal an increase in undetected COVID-19 deaths

• Implications for modeling and calibration:
  • COVID deaths, crude or adjusted, are unlikely to be a reliable or robust calibration point for models
  • Additional data on surveillance of influenza like illnesses, verbal autopsy, sero-surveillance, and increased testing could aid in better projections of COVID-19

• Implications for policy:
  • Critically, absence of directly measured COVID-19 deaths does not rule out a current or future severe outbreak
Time-Varying Geographic Outbreak - Infections

Simulated infection curves indexed to first recorded case. Each line is a district.

Assumptions:
1. First recorded case is the first actual case
2. First recorded case resulted in community spread
3. Other districts have not yet had a case or community spread
4. Only modest reduction of contacts 15%

Dummy Data
Time-Varying Geographic Outbreak - Infections

Aggregate infection curve from district projections

Infections


0 100,000 200,000 300,000 400,000 500,000 600,000

Dummy Data
Time-Varying Geographic Outbreak - Infections

While the new, time-dependent projection still has a substantial peak, the result is far flatter and more plateaued than original projections.

Additional diagnoses in new districts will further plateau the peak.
Sub-national Projections
District – Estimated Total Cases & Deaths in Current Scenario

### Infections

- Lilongwe
- Mzimba
- Lilongwe City
- Mangochi
- Blantyre City
- Dedza
- Kasungu
- Thyolo
- Zomba
- Dowa
- Mulanje
- Machinga
- Ntcheu
- Mchinji
- Chikwawa
- Blantyre
- Balaka
- Phalombe
- Salima
- Nkhotakota
- Chiradzulu
- Karonga
- Nsanje
- Ntchisi
- Chitipa
- Rumphi
- Mzuzu City
- Nkhata Bay
- Neno
- Zomba City
- Mwanza
- Likoma

### Deaths

- Lilongwe
- Mzimba
- Lilongwe City
- Mangochi
- Blantyre City
- Dedza
- Kasungu
- Thyolo
- Zomba
- Dowa
- Mulanje
- Machinga
- Ntcheu
- Mchinji
- Chikwawa
- Blantyre
- Balaka
- Phalombe
- Salima
- Nkhotakota
- Chiradzulu
- Karonga
- Nsanje
- Ntchisi
- Chitipa
- Rumphi
- Mzuzu City
- Nkhata Bay
- Neno
- Zomba City
- Mwanza
- Likoma
Traditional Authority – Infections & Deaths

*Additional graphics available for; Hospitalization & Critical Care – Due to similarities, they have been put in appendix. White areas are non-inhabited areas, national parks, lakes, and other unmapped areas.
Geographic Prioritization of Policies
Geographic Prioritization Outcomes – Infections & Deaths

<table>
<thead>
<tr>
<th>Date</th>
<th>Infections</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 Mar.</td>
<td>No Mitigation</td>
<td>No Further Reduction From Current</td>
</tr>
<tr>
<td>18 Jun.</td>
<td>Enforced Restrictions in Lilongwe, Blantyre, Chikwawa, &amp; Nkhotakota</td>
<td></td>
</tr>
<tr>
<td>28 Sept.</td>
<td>Enforced Restrictions in above + Salima, Mzuzu, Zomba, Mzimba, &amp; Mangochi</td>
<td></td>
</tr>
</tbody>
</table>

Number of People

Reduction

- No Mitigation
- No Further Reduction From Current
- Enforced Restrictions in Lilongwe, Blantyre, Chikwawa, & Nkhotakota
- Enforced Restrictions in above + Salima, Mzuzu, Zomba, Mzimba, & Mangochi
Without mitigation we expect about **1.6m infections**

Enforced policies in Lilongwe, Blantyre, Chikwawa, and Nkhotakota could reduce peak infections by **45%**

Enforced policies in further into Salima, Mzuzu, Zomba, Mzimba, & Mangochi could reduce peak infections by another **13%**

Without mitigation we expect about **50k infections**

Enforced policies in Lilongwe, Blantyre, Chikwawa, and Nkhotakota could reduce deaths by **25%**

Enforced policies in further into Salima, Mzuzu, Zomba, Mzimba, & Mangochi could reduce deaths by another **12%**
Key Takeaways and Next Steps
To-date, the COVID-19 outbreak in Malawi has not tracked closely to modeled trajectories. Possible reasons include:

- Limited testing and underdiagnosis
- Incomplete attribution of deaths
- Incorrect modeling assumptions
  - Timing and internal spread slower than expected

- Earlier versions of this epidemiological model assume simultaneous seeding and community spread across all districts in Malawi. True seeding, particularly in rural districts, may be significantly delayed

- **Timing** is everything for policy intervention

- **Hyper local data across sectors** should be used to guide “triggers” and local decision making
The Kuunika Program aims to institutionalize effective and efficient data systems, incentivize and support data use, and strengthen data governance. It is lead by the Quality Management Directorate within the Ministry of Health and Population Malawi and supported by Cooper/Smith and Luke International Norway with funding from the Bill and Melinda Gates Foundation.

For questions about this material please contact:
Tyler Smith

For questions about Kuunika please contact:
Director of Quality Management and Digital Health, Dr. Andrew Likaka

or

Kennedy Kanyimbo
Maganizo Monawe