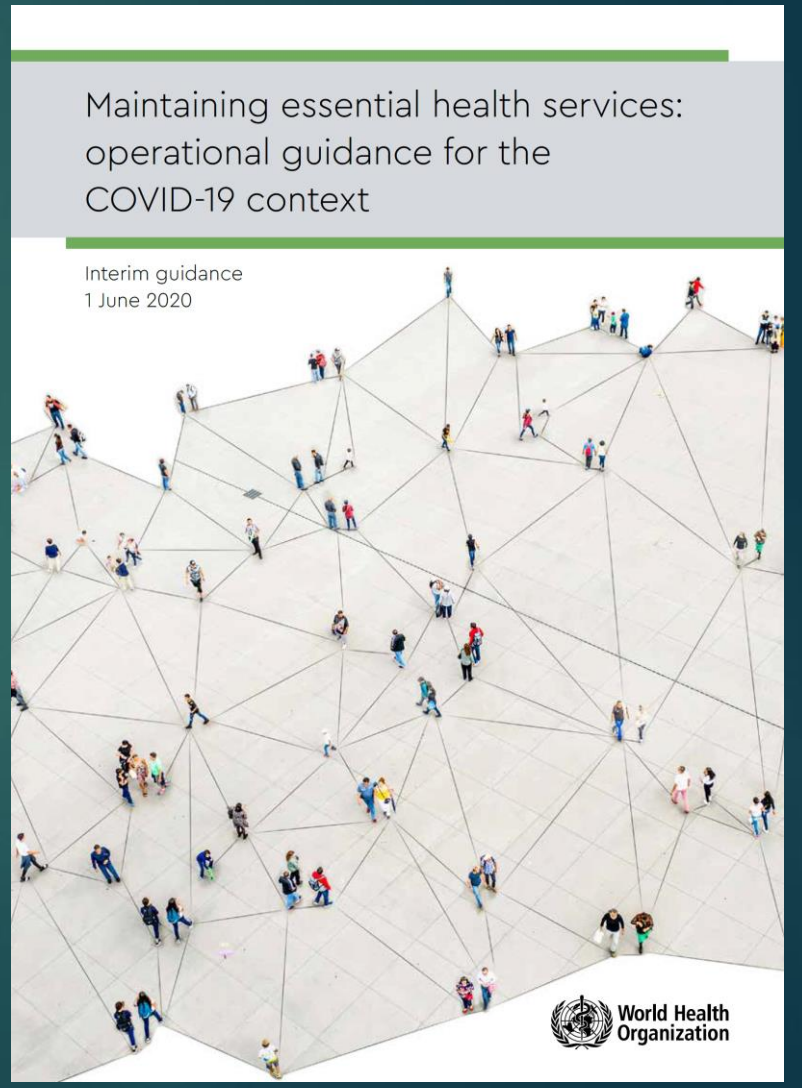
Risk-Benefit Analysis : Maintaining Essential RMNCAH Services vs. Risk of Covid-19 Infection

Comparison of **lives saved** through continued provision of essential services vs. **lives lost** due to increased exposure to the virus

1. **Mitigation strategies**
   - WHO June 2020 guidance document + country-defined

2. **Estimation of lives saved maintaining essential services**
   - Using LiST /Spectrum
   - Required: Estimates of impact of mitigation strategies on coverage (and effectiveness) of essential interventions

3. **Estimation of lives lost through increased risk of infection**
   - Required: Estimates of impact of mitigation strategies on risk of COVID-transmission
   - Risk to patient, caregiver (for children), and health care provider
   - Methodology example: LSHTM - Risk-benefit analysis immunization



Analysis Steps

1. **Determine interventions/intervention packages to include**
2. **Determine original coverage**
3. **Figure out impact of COVID on coverage of different interventions/intervention packages**
4. **Establish mitigation strategies**
5. **Estimate impact of mitigation strategies on coverage** (also added risk of COVID transmission for health worker and client)
6. **Calculate number of lives saved through improved coverage (using LiST Tool)**
7. **Carry out COVID risk analysis** to estimate number of lives lost in maintaining coverage of essential services
8. **Calculate benefit-risk ratios**

Step 1. Determine Packages/Interventions to Include in Analysis

Family Planning	FP - Pills
	FP - Condoms
	FP - Injectables
	FP - Implants
	FP - IUD
	FP - Female Sterilization
	FP - Male Sterilization
	FP - Traditional Methods
Antenatal Care	TT - Tetanus toxoid vaccination
	IPTp - Intermittent preventive treatment of malaria during pregn
	Syphilis detection and treatme
	~~Calcium supplementation~~
	Iron supplementation in pregnancy
	Multiple micronutrient supplementation in pregnancy
	Balanced energy supplementation
	Hypertensive disorder case management
	Diabetes case management
	Malaria case management
	MgSO4 management of pre-eclampsia
	PMTCT - Prevention of Mother-to-Child Transmission
Delivery Care	Clean birth practices
	Immediate assessment and stimulation
	Labor and delivery management
	Neonatal resuscitation
	Antenatal corticosteroids for preterm labor
	Antibiotics for pPRoM
	MgSO4 management of eclampsia
	AMTSL - Active management of the third stage of labor
	Induction of labor for pregnancies lasting 41+ weeks
	Maternal sepsis case management
	Clean Postnatal Practices
Newborn Care	Chlorhexidine
	Case management of premature babies
	Thermal care
	Kangaroo-Mother Care (KMC)
	Full supportive care of prematurity
	Case management of neonatal sepsis/pneumonia
	Oral antibiotics
	Injectable antibiotics
	Full supportive care

Take out of package

Packages/Interventions Included in LiST Impact Model

Breastfeeding	Breastfeeding
	Complementary feeding - Education only
	Complementary feeding - Supplementary feeding + Education
Vaccines	BCG - Single dose
	Polio - Three doses
	Pentavalent
	DPT - Three doses
	Hib - Three doses
	HepB - Three doses
	Pneumococcal - Three doses
	Rotavirus - Two doses
	Meningococcal A - Single dose
	Malaria vaccine - Three doses
	Measles - Single dose
Child Health	Vitamin A supplementation
	Zinc supplementation
	ORS - Oral Rehydration Solution
	Antibiotics for treatment of dysentery
	Zinc for treatment of diarrhea
	Oral antibiotics for pneumonia
	Vitamin A for treatment of measles
	ACTs - Artemisinin compounds for treatment of malaria
Malnutrition	SAM - treatment for severe acute malnutrition
	MAM - treatment for moderate acute malnutrition
Other	Improved sanitation - Utilization of latrines
	Improved water source
	Improved water source - Water connection in the home
	Hand washing with soap
	Hygienic Disposal of Children's stool
	ITN
	Folic acid supplementation/fortification
	Safe abortion services
	Post abortion case management
	Ectopic pregnancy case management
	Blanket iron supplementation/fortification

Make freestanding intervention

Step 2+3. Determine Coverage pre-COVID and with COVID

- **Determine original coverage for key interventions**
  - Either from national documents or extract from Spectrum/LiST model
- **Figure out coverage reduction/disruption under COVID**
  - HMIS data
  - For packages such as FP, antenatal care, etc. % reduction can be applied to all sub-interventions (e.g. folic acid supplementation, syphilis testing, etc.)

Step 4. Determine Mitigation Strategies

Coverage Reduction as a result of:	Mitigation Strategies
Shortage of health workers	Deliver several interventions in one visit, prioritize high-risk cases, provide several months of supplements or contraceptives at a time, taskshifting
Supply and equipment bottlenecks	Strengthen supply chain, involve private sector
Decreased demand due to fear of infection, financial barriers	Establish safe and efficient patient flow, provide PPE
	Suspend co-payments or user fees
Physical access restrictions, reduced transport availability	Telemedicine solutions

Step 5. Estimate impact of mitigation strategies on coverage and COVID transmission risk

Example Antenatal Care:

- Reduce required number of ANC visits, provide all relevant care in those reduced visits, provide woman with several months of micronutrient supplements at a time

Impact on coverage:

- Maintains pre-COVID coverage

Impact on effectiveness:

- Might keep effectiveness of ANC about the same

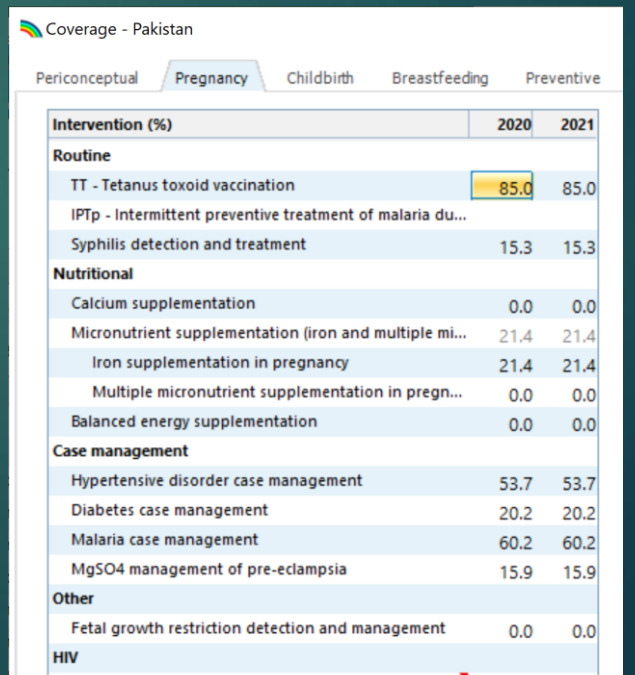
Impact on risk of COVID transmission:

- Redudes transmission risk as it reduces required number of trips to the health facility and contacts with a health care provider, reducing risk of transmission and risk of COVID mortality among pregnant women and health care providers

Step 6. Calculate number of lives saved through improved coverage

- All calculations in Excel except for this step
- Use of Spectrum/LiST tool to calculate number of lives saved
- Since LiST data entry relatively complex, Excel model will prep and arrange data so they can easily be copied into the LiSt tool (below)
- LiST results copied back into Excel model

		2020 With COVID	After Mitigation
Antenatal Care	TT - Tetanus toxoid vaccination	76.5	61.2
	IPTp - Intermittent preventive treatment of malaria during pregn	0.0	0.0
	Syphilis detection and treatment	13.8	11.0
	Calcium supplementation	0.0	0.0
	Iron supplementation in pregnancy	19.3	15.4
	Multiple micronutrient supplementation in pregnancy	0.0	0.0
	Balanced energy supplementation	0.0	0.0
	Hypertensive disorder case management	48.4	38.7
	Diabetes case management	18.2	14.6
	Malaria case management	54.2	43.4
	MgSO4 management of pre-eclampsia	14.3	11.4
	PMTCT - Prevention of Mother-to-Child Transmission	0.0	0.0



Intervention (%)	2020	2021
Routine		
TT - Tetanus toxoid vaccination	85.0	85.0
IPTp - Intermittent preventive treatment of malaria du...		
Syphilis detection and treatment	15.3	15.3
Nutritional		
Calcium supplementation	0.0	0.0
Micronutrient supplementation (iron and multiple mi...	21.4	21.4
Iron supplementation in pregnancy	21.4	21.4
Multiple micronutrient supplementation in pregn...	0.0	0.0
Balanced energy supplementation	0.0	0.0
Case management		
Hypertensive disorder case management	53.7	53.7
Diabetes case management	20.2	20.2
Malaria case management	60.2	60.2
MgSO4 management of pre-eclampsia	15.9	15.9
Other		
Fetal growth restriction detection and management	0.0	0.0
HIV		

Step 7. Calculate number of lives lost through excess COVID transmission risk

Excess Risk

- Additional infections/deaths among households that are attributable to a health facility visit, that would not have occurred during the course of the epidemic if not for the visit to the health facility.

- Excel model based on Abbas K. et al. 2020. Benefit-risk analysis of health benefits of routine childhood immunisation against the excess risk of SARS-CoV-2 infections during the COVID-19 pandemic in Africa. The Lancet Global Health.

Step 7. Calculate number of lives lost through excess COVID transmission risk

- Additional risk of infection incurred traveling to clinic, waiting at clinic and interacting with health care worker
- Also additional risk incurred by health care worker providing the intervention
- Depending on community prevalence and mitigation strategies in place

Excess Risk Calculation

Additional infections/deaths among households that are attributable to a vaccination visit/adult visit to a health facility, that would not have occurred during the course of the epidemic if not for vaccination/adult visit to a health facility.

Country		Pakistan			
Variable		**Mean**	**Min**	**Max**	**Comment**
Number of children receiving vaccination/adults receiving health intervention x	I	20,000	20,000	20,000	
Number of visits for vaccination/health intervention x	v	1	1	3	
Reproduction number for SARS-CoV2	R_0	2.5	1.6	3.6	Expected number of cases directly generated by one case in a population where all individuals are susceptible to infection
Duration of period at risk (in months)	T	6	5	6	Length of community spread. After this period, between 40% and 70% of the population will have been infected (corresponds to herd immunity required for R_0 between 1.6 and 3.6
Proportion of SARS-CoV2 infected population at end of risk period	Θ	60%	38%	72%	
Duration of infectiousness (day)	Ψ	7	4	11	Number of days an infected individual spreads the virus on average
Risk ratio of a vaccinator being infected and infectious vs. another community member	I1	2.5	1	4	Higher risk of being infected (between 1 and 4 times) because of higher frequency of exposure to other people Community member: 6 contacts per day Vaccinator: 21 potentially infectious contacts per day
Risk ratio potentially infectious contact of a vaccinator transmitting vs. another community member	I2	0.62	0.25	1	Lower risk of onward transmission (between 0.25 and 1 times) because most of their contacts with vaccinees are brief, and they have enhanced risk awareness and use corresponding protective measures including basic respiratory hygiene and personal protective equipment as available
Average number of transmission-relevant contacts of a community member per day	N	6	2	10	
Number of non-vaccinator contacts of child and carer during their travel to the vaccine clinic and in the waiting room	n	5.5	1	10	
Prevalence among community members on any given day (ΘΨ / T)	po	2.3%	1.0%	4.4%	Assumes reasonably flat epidemic curve, total cases spread out over months of community spread as specified above
Prevalence among health care provider on any given day (I1xpo)	pv	5.8%	1.0%	17.6%	Higher risk due to increased number of potentially infectious contacts
Probability of transmission given potentially infectious contact with community members (R_0/NΨ)	t_0	6.0%	20.0%	3.3%	General risk of acquiring infection in the community
Probability of transmission given potentially infectious contact with vaccinators (I2xt_0)	t_v	3.7%	5.0%	3.3%	
For vaccination visits (child + caretaker):					
Probability for a SARS-CoV-2 infection for the whole household of a child who gets vaccinated $1-(1-t_v)^{2n_{pv}}(1-t_0)^{2n_{po}n}$	P	2.0%	0.001	0.032	One minus the probability of either the infant or the mother not being infected by either the vaccinator or anyone else on any of the vaccination visits
Probability for excess SARS-CoV-2 infection for the whole household of a child who gets vaccinated (Px (1-Θ))	P_EChild	0.8%	0.001	0.009	Probability of facility-visit related infection x Percent of population who has not gotten infected at the end of the risk period
For adult visits:					
Probability for a SARS-CoV-2 infection for the whole household of an adult seeking care	P_E	1.0%	0.001	0.017	One minus the probability of the adult not being infected by either the health care provider or anyone else on the visit or visits to the health facility
Probability for excess SARS-CoV-2 infection for the whole household of an adult seeking care (Px (1-Θ))	P_EAdult	0.4%	0.000	0.005	
Infection rate within household		100%			Assumption that if either child or caretaker gets infected they will infect all other household members, owing to the high secondary attack rates observed for family gatherings
Infection fatality rate					
Children (aged <20)	P	0.00161%	0.00019%	0.00586%	Based on Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infect Dis 2020; published online March 30. DOI:10.1016/S1473-3099(20)30243-7.
Adults (aged 20-59)	P	0.08464%	0.03936%	0.15629%	
Older adults (60+)	P	3.28379%	1.73737%	5.53980%	
Household Age Distribution					
Average Household Size		6.6			2017-18 DHS
Children (aged <20)		3.3			2017-18 DHS
Adults (aged 20-59)		2.9			2017-18 DHS
Older adults (60+)		0.4			2017-18 DHS

	Mean	Min	Max
Number of Excess Infections due to vaccination	**1053**	**85**	**1,171**
Number of Excess Deaths due to vaccination	**2.8**	**0.1**	**5.2**
Number of Excess Infections due to adult facility visit	**529**	**42**	**93**
Number of Excess Deaths due to adult facility visit	**2.8**	**0.1**	**5.2**

Based on: Abbas K. et al. 2020. Benefit-risk analysis of health benefits of routine childhood immunisation against the excess risk of SARS-CoV-2 infections during the COVID-19 pandemic in Africa. The Lancet Global Health doi: 10.1016/S2214-109X(20)30308-9

Step 8. Calculate benefit-risk ratios

Morocco

	Lives Saved through Mitigation Measures	Lives Lost through Added COVID Infections	Benefit-Risk Ratio
Family Planning	8	(4)	2.1
Antenatal Care	64	(4)	17.5
Delivery Care	261	(9)	28.6
Newborn Care	1,125	(8)	145.1
Breastfeeding	--	--	--
Vaccines	212	(74)	2.8
Child Health	50	(6)	8.7
TOTAL	1,720	(105)	16.5

Key Findings Across Countries

- Overall Benefit-Risk Ratio across countries between 11.7 and 79.2, i.e. for every 11.7 to 79.2 lives gained due to increased RMNCA coverage, there was one excess COVID death.

- More specifically, for all countries and for all health packages, the benefit risk ratio was (in many cases significantly) above 1, i.e.,maintaining services saved more lives than were lost due to additional deaths caused by COVID acquired during contacts with the health system.

- The number of lives saved depended on a large number of factors and their interactions, mainly:
  - Interventions included (the more highly effective RMNCAH interventions included, the higher the impact)
  - Baseline coverage (the lower the initial coverage, the lower the impact of disruption and recovery)
  - Coverage disruption (the higher the initial disruption, the more impactful the potential recovery)
  - Number and impact of mitigation measures
  - HH size and age structure of population (COVID assumed to spread within family, older population suffering much higher fatality than children and younger adults)

High-Impact RMNACH Interventions

Health Packages with the Highest Benefit-Risk Ratios:

- Breastfeeding (low number of contacts with health system, extremely effective intervention, long-term impacts (1-2 years), large number of lives saved)
- Newborn care (highly effective interventions such as clean delivery care, newborn resuscitation and treatment of newborn sepsis/pneumonia)
- Delivery care (AMTSL, C-section and assietd vaginal delivery saving many lives)

Health Packages with Lower, but Still Positive Benefit-Risk Ratios:

- Child Health (in particular, when high-impact interventions such as ORS, ARI treatment included)
- Antenatal Care (main impact seen when tetanus toxid coverage is restored, many lives saved due to timely recognition of pregnancy complications not capcturd here, but under delivery and EmOC care)
- Vaccine (assumption that vaccination disruption is temporary, impact only calculated for one year, in which existing herd immunity does still provide protection, important that vaccination catch up after interruption)
- Family Planning – main impact on number of birth and pregnancies, not deaths

Mitigation Measures

Mitigation Measures Reducing Transmission Risk

- Some empirical studies available on effectiveness of mitigation measures, but wide range of estimates
- Most effective: Hygiene and social distancing measures, in particular masks and PPE with training of health care providers in correct usage
- Also effective: Move to e-/telehealth and move of selected services to community level/outreach teams

Mitigation Measures Improving Coverage

- No empirical, published data available at all
- Effort to try and err on the conservative side when estimating impact
- Total impact capped so WITH mitigation coverage did not exceed original baseline coverage by more than 2%
- Most measures working through restoration of confidence of population in safety of health facility visits
- Some measures increasing coverage through the fixing of supply side shortages (staff, supplies)
- Impact of any individual measures usually in the 1-5% range

Limitations of Risk-Benefit Exercise

- Recent and constantly shifting nature of the COVID-19 pandemic (second, third waves, new strains of the virus, vaccine development) makes estimates and predictions difficult
- Limited empirical evidence available to support estimates for the impact of mitigation measures on reduced transmission of COVID-19
- No evidence to support estimates for the impact of mitigation measures on increased coverage. These estimates must be communicated with this caution
- HMIS data of varying quality, problem of delayed or missing data, no data for breastfeeding
- New application of the LiST model (previously only used for gradual scale-up of coverage, never for disruption)
- LiST model only capable of producing annual estimates, which complicates what can be modeled