Insecticide resistance monitoring and management in India

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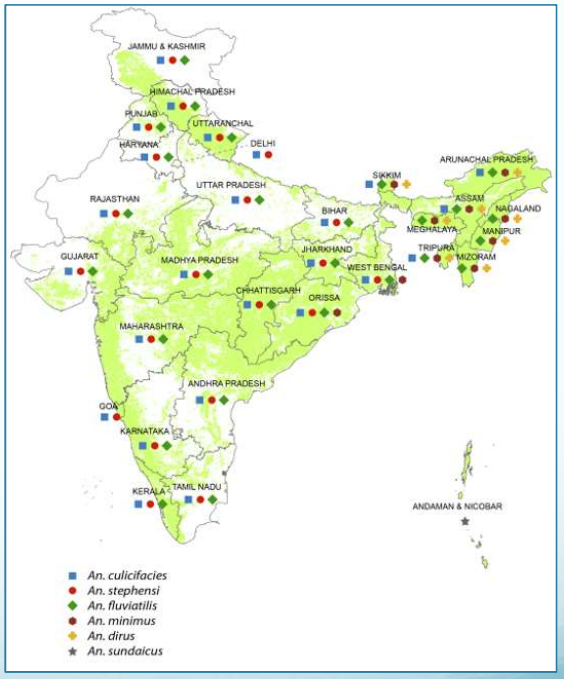
Major issues of concern

- Portfolio of public health insecticides is limited
- High reproduction rate and short life-cycle of mosquitoes spread R-genes fast
- Increase of selection pressure reducing effectiveness
  - Collateral effects of use of pesticides in agriculture
  - Sub-standard insecticide applications
    - Use of poor quality/counterfeit (illegal) insecticides
    - Non-judicious use of insecticides

Scale of the resistance problem in India

- Notable control failures during the malaria eradication era – DDT, dieldrin, malathion
- Non-reversible DDT R in *An. culicifacies*
- PY resistance widespread; R-frequency is <10%
- IR data are limited
  - Major focus is on malaria vectors
  - Multiple malaria vectors in different settings
  - Much less attention on *Aedes*, *Phlebotomus*, *Culex spp.*
  - In future, high intensity resistance & stronger mechanisms may pose threat to malaria control



Major aims of insecticide resistance management strategies

- Preventing loss of the epidemiological impact in field (effectiveness vs. control failure)
  - Prolonging effectiveness of insecticides and acaricides
  - Countering the development of resistance
- Developing alternative tools, strategies and policies
- Building national capacity for IRM
- Creating evidence base for alternative policies
- Mobilize resources

Main insecticide resistance mechanisms

- Modifying the target-site (e.g. due to *kdr* gene mutation affecting acetylcholinesterase or voltage-gated sodium channels)
- Metabolic resistance by detoxifying insecticides (using e.g. esterases, oxidases, monoxygenases and glutathione S-transferases)
- Behavioural resistance (deterrence/exophily)
- Cuticular resistance due to reduced insecticide penetration

Core malaria vector control interventions

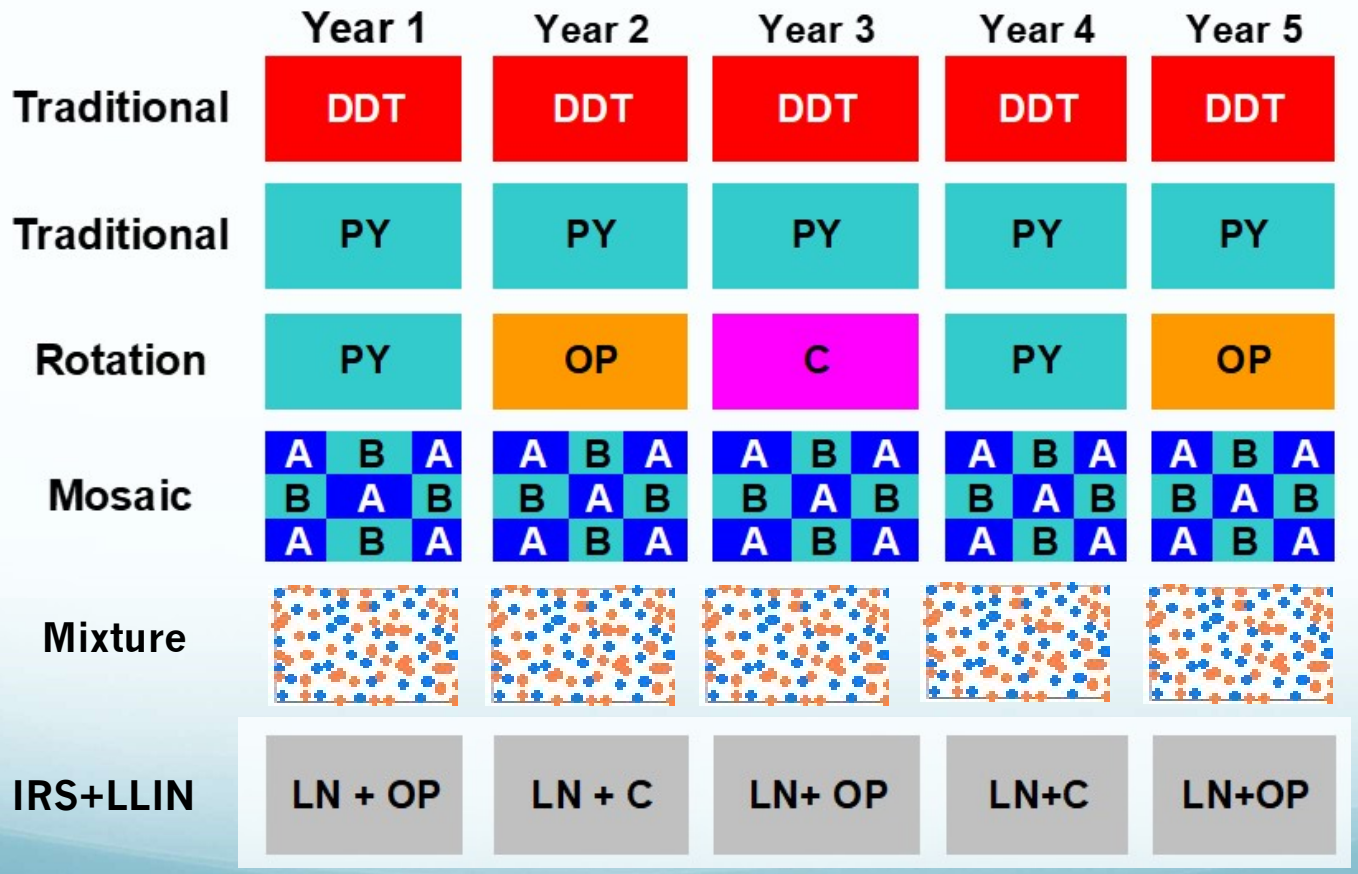
- LLINs/ITNs
- IRS
- Larviciding: supplementary intervention in areas where breeding habitats are few, fixed and findable and vector ecology is well understood

Effectiveness of LLINs in the face of resistance

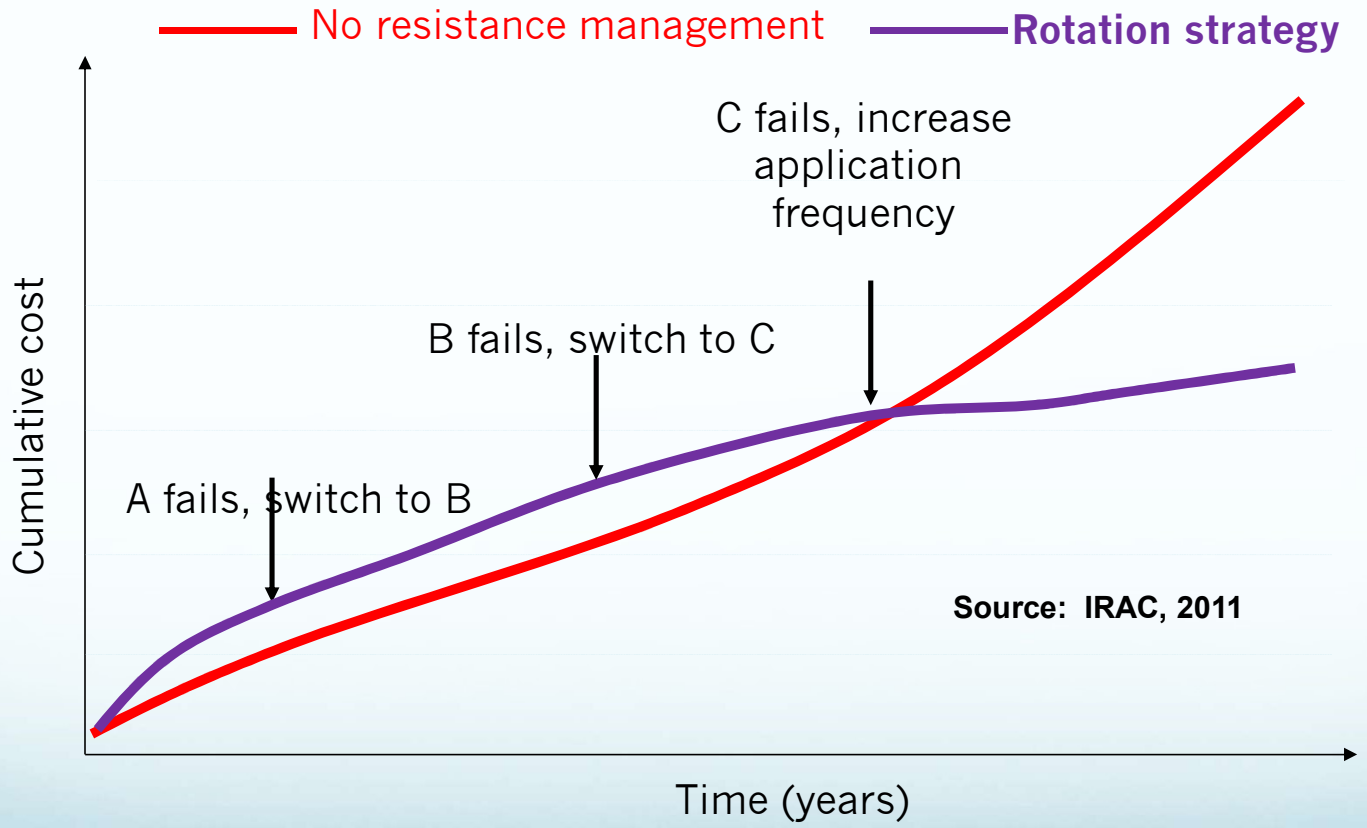
- ITNs provide personal and community protection when used by most people in an area.
- WHO Study*: pyrethroid LLINs continue to play a significant role in malaria control in the face of emerging insecticide resistance.
  - scale up use of LLINs for **community protection** without changing current policy
  - pyrethroid-LLINs continue to provide **personal protection** against malaria
  - this protection was no different between areas of varying levels of pyrethroid resistance
  - higher levels of resistance caused some loss of community protection of LLIN use, although there was no evidence of an associated increase in malaria incidence.
- Synergist PBO in nets
  - can increase the efficacy of pyrethroids in LLINs in all **but** highly resistant mosquito populations
  - this impact may vary in different regions, based on resistance intensity and mechanisms
- **Conclusions**
  - available evidence from field does not yet justify a complete switch from pyrethroid-only LLINs to PBO-LLINs in all settings;
  - the evidence is sufficient to justify limited, pilot "exploratory" implementation of PBO-LLINs, if accompanied by robust evaluation of the impact (entomological + epidemiological).

*http://who.int/malaria/publications/atoz/mpac-september2016-report.pdf

IRS approaches for resistance management



Cost of a rotational vector control programme



Resistance management using rotations is expected to be cost-saving in the long run

LLINs + IRS in the face of resistance – outcomes of a WHO study

- Area with pyrethroid resistance & bendiocarb susceptibility
  - Pyrethroid LLINs + IRS with **deltamethrin =** no additional protection
  - Pyrethroid LLINs + IRS with **bendiocarb** reduced malaria incidence by 50% relative to LLINs alone
  - Pyrethroid + **carbamate** IRS appeared to slow the emergence of pyrethroid resistance relative to LLINs only

Conclusion

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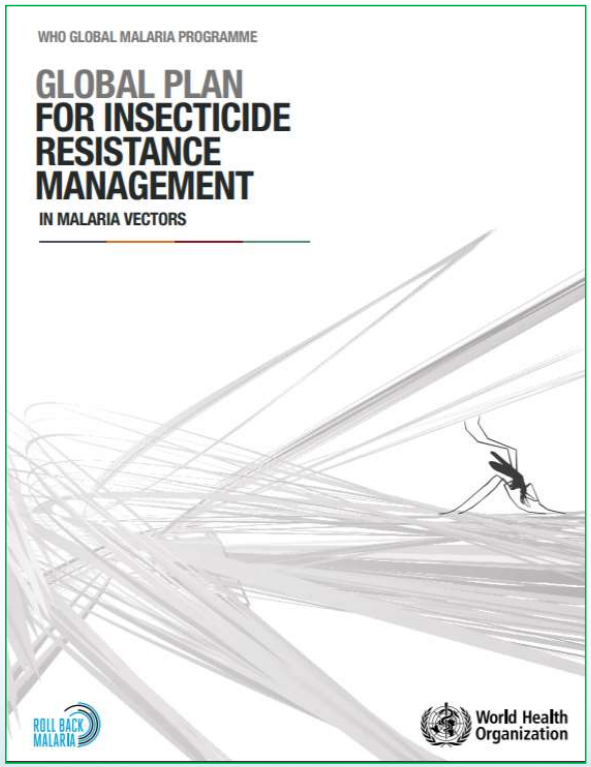
Adding IRS with an unrelated mode of actioncompound enhances the effectiveness of VC against malaria

WHO guidance documents



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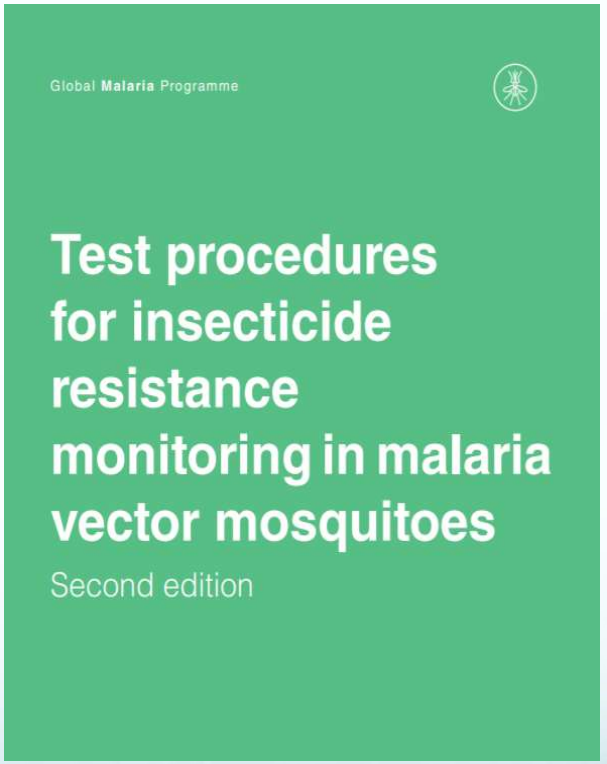

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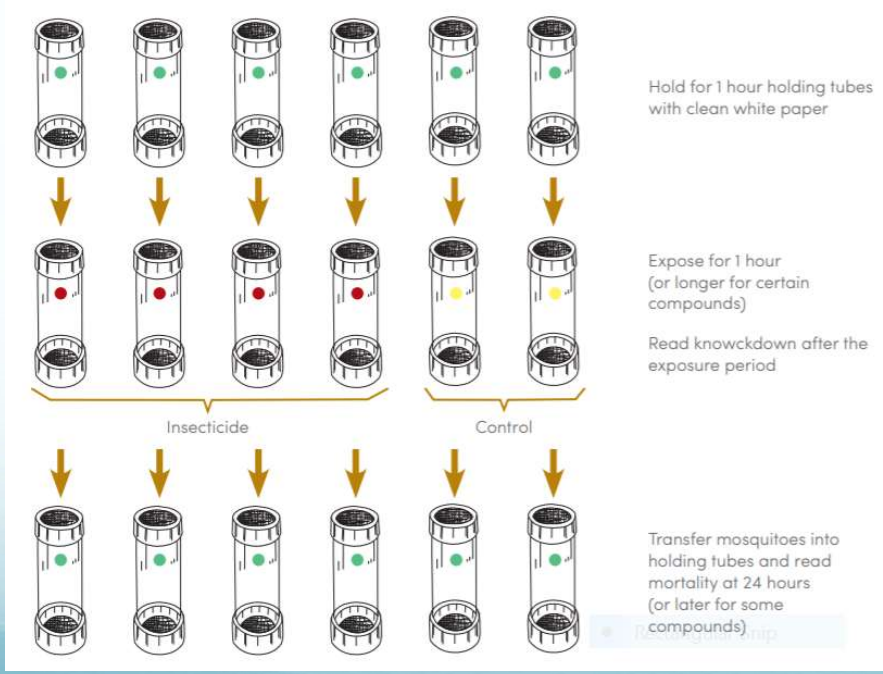
WHO Insecticide Susceptibility Test – a direct response-to-exposure test

- Test steps:
  1. Detect the presence of insecticide resistance phenotypes using a DC
  2. Assess the strength of phenotypic resistance by intensity bioassays at 5X and 10X of DC
  3. Determine the involvement of metabolic resistance by exposure to 4% PBO papers
- Test species: wild-caught versus 3–5d old F1 progeny females
- Test conditions: 25 °C ± 2 °C and 80% ± 10% relative humidity (no test > 30 °C)
- Sample size: 120–150 female mosquitoes (insecticide = 25x4; control: 25x2)
- Use of a paper: no more than 6 times
- Store papers at 4–8 °C; acclimatize at room temperature before opening the packet and use.

WHO (2012). *GPIRM* (http://apps.who.int/iris/bitstream/10665/44846/1/9789241564472_eng.pdf).

Test procedure and scheme

- Mosquitoes are exposed to an insecticide discriminating concentration (DC) on filter papers
- Exposure: a fixed time period of 1h



Recording test results

Number of knocked down mosquitoes after exposure for 60 minutes (120 minutes for fenitrothion)

	Replicate 1		Replicate 2		Replicate 3		Replicate 4		Control 1		Control 2	
	Time	No.	Time	No.	Time	No.	Time	No.	Time	No.	Time	No.
Start												
60'												

Number of dead and number of alive mosquitoes* at the end of holding period (24 hours)

	Replicate 1	Replicate 2	Replicate 3	Replicate 4	Control 1	Control 2
No. dead						
No. alive						

* These counts need to be by species, once dead and alive mosquitoes have been examined for taxonomic determination.

- Recording mortality:
  - Knock down at 60 min
  - at 24h, i.e. 1 hr exposure + 24h holding/recovery period
  - or longer up to 72h for slow-acting compounds

WHO mortality criteria

- Criteria for measuring phenotypic resistance (WHO, 2012)
  - Susceptible (S) = 98–100% mortality;
  - Suspected resistance (SR) = 90–97% mortality;
  - Resistant (R) = < 90% mortality.

Pre-emptive actions against malaria vector resistance

Geographical areas with:	IRM pre-emptive actions
1. Unknown resistance levels	Conduct susceptibility tests; monitor & map IR and resistance mechanisms.
2. IRS alone (as the main vector control intervention)	Rotate use of insecticides with unrelated modes of actions; use mixtures/rotations with new chemistries; ***– current options are***: pyrethroids – malathion – pirimiphos-methyl – clothianidin
3. LLINs alone as the main VC intervention	Use combination or PBO ITNs: ***– near future options are***: pyr.+PBO ITN; pyr+chlorfenapyr ITN; pyr+pyriproxyfen ITN.
4. Combination of IRS+LLINs	Stop IRS with pyrethroids, no change in LLIN strategy
5. Selection for alternative insecticides	Consider: cross-resistance, efficacy of new insecticide and costs

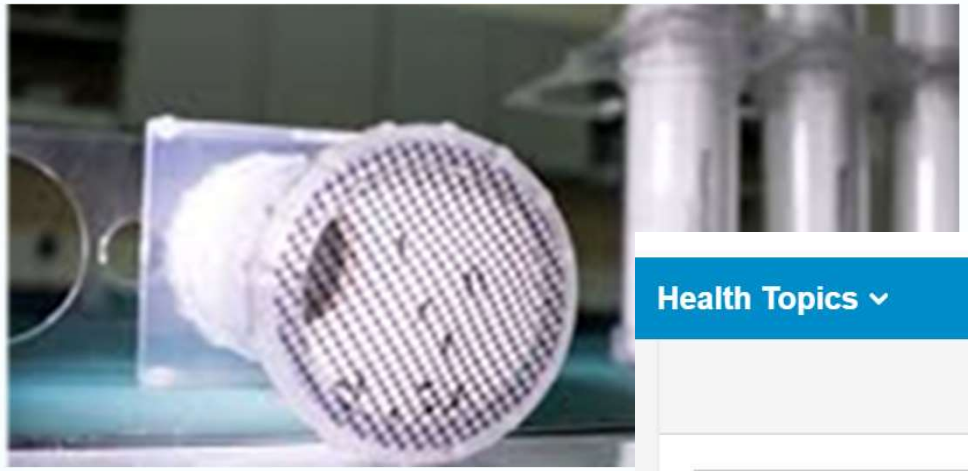
Strategies to delay resistance

- Action must be pre-emptive, right from the outset
- Don't wait for building high resistance levels, or proof of control failure
  - because methods for delaying resistance become less effective as resistance intensity increases
- IVM approach
  - judicious use & informed decision-making
  - sound pesticide management to reduce selection pressure
  - situation-specific use of alternative VC methods

Key country actions and way a foreward

1. Development of country IRM plan
   - Situation analysis
   - Entomological surveillance
   - Resistance monitoring and data management
2. Coordination with research institutions
   - Fill knowledge gaps on R–mechanisms
   - Assess impact of current management approaches
   - Develop/test innovative VC tools/novel approaches
3. Develop capacity: NVBDCP, sentinel institutions/Universities
4. Advocacy for adequate resources
5. Coordination, networking, data/information exchange
6. Supply of test kits

WHO test kits for IR testing



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Insecticide resistance

Order test kits and supplies

– Catalogue for test kits
– Order form (updated 23 September 2019)

Discriminating concentrations

– Discriminating concentrations of insecticides for adult mosquitoes

Test guidelines

Resistance monitoring should be an integral part of vector/public health pest control programmes. Knowledge of vector/pest susceptibility to pesticides, changing trends of resistance and their operational implications are basic

https://www.who.int/neglected_diseases/vector_ecology/resistance/en/

WHO data collation and management

National databases

dhis2

Scientific publications

Unpublished reports

WHO regional database

GMP-IR database

Research results


HEALTH IN THE SDG ERA
3 GOOD HEALTH AND WELL-BEING
ENSURE HEALTHY LIVES AND PROMOTE WELL-BEING FOR ALL AT ALL AGES
1 NO POVERTY
PRIORITIZING THE HEALTH NEEDS OF THE POOR
2 ZERO HUNGER
ADDRESSING THE CAUSES AND CONSEQUENCES OF ALL FORMS OF MALNUTRITION
4 QUALITY EDUCATION
SUPPORTING HIGH-QUALITY EDUCATION FOR ALL TO IMPROVE HEALTH AND HEALTH EQUITY
5 GENDER EQUALITY
FIGHTING GENDER INEQUITIES, INCLUDING VIOLENCE AGAINST WOMEN
6 CLEAN WATER AND SANITATION
PREVENTING DISEASE THROUGH SAFE WATER AND SANITATION FOR ALL
7 AFFORDABLE AND CLEAN ENERGY
PROMOTING SUSTAINABLE ENERGY FOR HEALTHY HOMES AND LIVES
8 DECENT WORK AND ECONOMIC GROWTH
PROMOTING HEALTH EMPLOYMENT AS A DRIVER OF INCLUSIVE ECONOMIC GROWTH
9 INDUSTRY, INNOVATION AND INFRASTRUCTURE
PROMOTING NATIONAL R&D CAPACITY AND MANUFACTURING OF AFFORDABLE ESSENTIAL MEDICAL PRODUCTS
10 REDUCED INEQUALITIES
ENSURING EQUITABLE ACCESS TO HEALTH SERVICES THROUGH UNIVERSAL HEALTH COVERAGE BASED ON STRONGER PRIMARY CARE
11 SUSTAINABLE CITIES AND COMMUNITIES
FOSTERING HEALTHIER CITIES THROUGH URBAN PLANNING FOR CLEANER AIR AND SAFER AND MORE ACTIVE LIVING
12 RESPONSIBLE CONSUMPTION AND PRODUCTION
PROMOTING RESPONSIBLE CONSUMPTION OF MEDICINES TO COMBAT ANTIBIOTIC RESISTANCE
13 CLIMATE ACTION
PROTECTING HEALTH FROM CLIMATE RISKS, AND PROMOTING HEALTH THROUGH LOW-CARBON DEVELOPMENT
14 LIFE BELOW WATER
SUPPORTING THE RESTORATION OF FISH STOCKS TO IMPROVE SAFE AND DIVERSIFIED HEALTHY DIETS
15 LIFE ON LAND
PROMOTING HEALTH AND PREVENTING DISEASE THROUGH HEALTHY NATURAL ENVIRONMENTS
16 PEACE AND JUSTICE
EMPOWERING STRONG LOCAL INSTITUTIONS TO DEVELOP, IMPLEMENT, MONITOR AND ACCOUNT FOR AMBITIOUS NATIONAL SDG RESPONSES
17 PARTNERSHIPS FOR THE GOALS
MOBILIZING PARTNERS TO MONITOR AND ATTAIN THE HEALTH-RELATED SDGs
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Thank you