World Health Organization

Technical briefing for Appendix 3 of the Global Action Plan for Non-Communicable Diseases

Cardiovascular disease interventions

List of interventions

Number	Interventions
CV1	Pharmacological treatment of hypertension in adults using any of the following: thiazide and thiazide-like agents; angiotensin-converting enzyme inhibitors (ACE-Is)/angiotensin-receptor blocker (ARBs); calcium channel blockers (CCBs).
CV2a	Drug therapy (treatment with an antihypertensive and a statin) to control CVD risk using a total risk approach and counselling to individuals who have had a heart attack or stroke and to persons with high risk (≥ 20%) of a fatal and non-fatal cardiovascular event in the next 10 years using the updated WHO CVD risk charts
CV2b	Drug therapy (treatment with an antihypertensive) to control CVD risk using a total risk approach and counselling to individuals who have had a heart attack or stroke and to persons with high risk (≥ 10%) of a fatal and non-fatal cardiovascular event in the next 10 years using the updated WHO CVD risk charts
CV3	Treatment of new cases of acute myocardial infarction with either: acetylsalicylic acid , or acetylsalicylic acid and thrombolysis, or acetylsalicylic acid, thrombolysis and clopidogrel, or primary percutaneous coronary interventions (PCI) initially treated in a hospital setting with follow up carried out through primary health care facilities at a 95% coverage rate
CV4a	Treatment of acute ischaemic stroke with intravenous thrombolytic therapy
CV4b	Treatment of acute ischemic stroke with mechanical thrombectomy within an experienced facility
CV5a	Primary prevention of rheumatic fever and rheumatic heart diseases by increasing appropriate treatment of streptococcal pharyngitis at the primary care level
CV5b	Secondary prevention of rheumatic fever and rheumatic heart disease by developing a register of patients who receive regular prophylactic penicillin

CV6	Low-dose acetylsalicylic acid within 24 to 48 hours for secondary prevention of ischaemic stroke
CV7	Comprehensive* care of acute stroke patients in stroke units *Comprehensive care includes strategies such as staffing by a specialist stroke multidisciplinary team, access to equipment for monitoring and rehabilitation.

Identification of interventions

The interventions considered for analysis are drawn from the Package of Essential Non-Communicable Disease Interventions in low and middle income settings [1], as well as the previous update of the Appendix 3 interventions with WHO-CHOICE analysis [2] and new WHO guidelines [9,28]

Methodological assumptions

- The impact of interventions was estimated with the OneHealth Tool [3]
- Epidemiology data: prevalence, incidence and mortality data for Ischaemic Heart Disease and Stroke come from the Global Burden of Disease 2019 study at the country-level [4]
- The distribution of the population by CVD risk come from the WHO CVD Risk Charts 2019 and it is estimated for 21 Global Regions [5]
- Country-specific risk factor prevalence data required for the risk prediction equations is sourced from the WHO Global Health Observatory [6] and the NCD Risc group database [7]
- Regional estimates for Acute Rheumatic Fever (ARF) were derived from [8]
- Disability weights for each health condition were drawn from the Global Burden of Disease 2019 disability weight study. [4]

Table 1: Impact sizes used in WHO-CHOICE analysis

	Population (P), effect size of interventions (E) and outcomes (O)	**Comments on evidence and main changes to 2017 analysis**
CV1	**P:** Adults with blood pressure above 140mmHg **E:** Reduction of IHD (RR 0.75) and reduction of stroke (RR 0.74) [9] **O**: Reduction on CVD events, IHD and stroke	New intervention The RRs are coming from the systematic review supporting the WHO guidance and classified as high quality [10]. Additional supporting evidence was obtained through desktop review and cross-checked to verify impact.

CV2a	**P:** Adults with CVD risk ≥ 20% based on WHO risk charts (excluding people with diabetes) **E:** -1.05 mmol/L change in cholesterol [11] and 5.9mmHg reduction in systolic blood pressure [12] **O**: reduction on CVD events and mortality through the absolute reduction of SBP and CHOL	Pre-existing intervention with: -Updated WHO CVD risk charts used -New risk threshold used -Exclusion of diabetic patients (as those are captured in the diabetes intervention D5) Intervention impact is mediated via the risk prediction equation and excluding diabetic patients who are included in the diabetes intervention D5 Risk approach and charts available at [5]
CV2b	**P**: Adults with CVD risk ≥ 10% based on WHO risk charts (excluding people with diabetes) **E:** 5.9mmHg reduction in systolic blood pressure [12] **O:** reduction on CVD events and mortality through the absolute reduction of SBP	Pre-existing intervention with: -Updated WHO CVD risk charts used -New risk threshold used leading to the use of only BP lowering drugs and not statins for this group of patients -Exclusion of diabetic patients (as those are captured in the diabetes intervention D5) Intervention impact is mediated via the risk prediction equation and excluding diabetic patients who are included in the diabetes intervention D5 Risk approach and charts available at [5]
CV3	**P:** 30% of AMI patients for interventions a), b) and c) and 10% of AMI patients for intervention d) E: a) Acetylsalicylic acid – reduction in CVD mortality: -25% [13] b) Acetylsalicylic acid and thrombolysis – reduction in CVD mortality: -43% [14] c) Thrombolysis, acetylsalicylic acid and clopidogrel – reduction in CVD mortality: - 52% [15] d) Primary percutaneous coronary interventions (PCI), acetylsalicylic acid and clopidogrel: - 74% [16] **O**: reduction of deaths from stroke	Pre-existing interventions, the split of the population has been revised based on expert consultation and up-to-date evidence has been used for the effect sizes Impact sizes were drawn from RCTs and meta-analyses.

CV4a	**P**: The population receiving thrombolytic therapy is 35% of total ischemic stroke patients. Based on evidence on eligible population from [17] **E**: Treatment of acute ischaemic stroke with intravenous thrombolytic therapy - Reduction in stroke mortality of 34% and reduction in stroke disability weight of 50% [18] **O:** reduction of deaths from stroke and improvement on quality of life	Pre-existing intervention, new expert consultations and evidence have updated the impact and costs of this intervention. Impact size was drawn from a Cochrane review of RCTs
CV4b	**P:** The population receiving thrombectomy is 15% of total ischemic stroke patients. Based on evidence on eligible population from [19] **E**: Treatment of acute ischaemic stroke with mechanical thrombectomy within an experienced facility -Reduction in stroke mortality of 15% and reduction in stroke disability weight of 50% [20] **O:** reduction of deaths from stroke and improvement on quality of life	New intervention Impact size was drawn from a Cochrane review of RCTs
CV5a	**P:** Population receiving the intervention is 100% of children between 5-14 years **E:** Reduction in incidence of primary Acute Rheumatic Fever (ARF) episodes: -80% [21] **O**: Reduction of deaths from RHD through reduction in ARF	Updated epidemiological data and modelling approach. All countries with RHD prevalence >25th percentile are included in the analysis Impact size was drawn from a meta-analysis
CV5b	**P:** Population receiving the intervention is children between 5-14 years who have ARF **E:** Reduction in incidence of secondary ARF episodes: -55% [22] **O:** Reduction of deaths from RHD through reduction in ARF	Updated epidemiological data and modelling approach. All countries with RHD prevalence >25th percentile are included in the analysis Impact size was drawn from a Cochrane review of Randomised and quasi-randomised studies
CV6	**P:** Interventions applied to all ischaemic stroke patients **E:** Reduction in stroke mortality of -5% [23] **O:** reduction of deaths from stroke	New intervention Impact size was drawn from a Cochrane review of RCTs

CV7	**P:** Interventions applied to all ischaemic stroke patients **E:** Reduction in stroke mortality of -20% [24] **O:** reduction of deaths from stroke	New intervention This intervention is relevant for all stroke patients, but only the impact on ischaemic stroke patients has been modelled Impact size was drawn from a Cochrane review of RCTs

Table 2: Costing assumptions used in WHO-CHOICE analysis

	Major costing assumptions	**Comments**
CV1	Visits: • 4 outpatient visits/year (100% receiving) Drugs: • A combination of Amlodipine 10mg and Losartan 50mg (100% receiving, 1/day, 365 days/year)	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26] Drugs were chosen as per the guideline protocol. Losartan has been used instead of Telmisartan due to data availability
CV2a	Visits: • 6 outpatient visits (100% receiving) Drugs and supplies required per patient: • Losartan 50mg (100% receiving, 1/day, 365 days/year) • Amlodipine 10 mg (100% receiving, 1/day, 365 days/year) • Simvastatin 20 mg (100% receiving, 1/day, 365 days/year) Laboratory tests per patient • Blood glucose level test (100% receiving, 1/year) • Cholesterol test (100% receiving, 1/year) • Urine test (100% receiving, 1/year) Equipment: • Computer (for the CVD Chart) • Scale • Stadiometer	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26] Data on laboratory tests and equipment from UNICEF product catalogue [27] and WHO-CHOICE price database [25]

CV2b	Visits: • 6 outpatient visits (100% receiving) Drugs and supplies required per patient: • Losartan 50mg (100% receiving, 1/day, 365 days/year) • Amlodipine 10 mg (100% receiving, 1/day, 365 days/year) Laboratory tests per patient: • Blood glucose level test (100% receiving, 1/year) • Cholesterol test (100% receiving, 1/year) • Urine test (100% receiving, 1/year) Equipment: • Computer (for the CVD Chart) • Scale • Stadiometer	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26] Data on laboratory tests and equipment from UNICEF product catalogue [27] and WHO-CHOICE price database [25]
CV3	**CV3a)** Visits: • 2 inpatient bed-days (100% receiving) • 5 outpatient visits per year (100% receiving) Drugs: • Aspirin 75mg (100% receiving, 1/day, 365 days/year) **CV3b)** Visits: • 3 inpatient bed-days (100% receiving) • 5 outpatient visits per year (100% receiving) Drugs: • Aspirin 75mg (100% receiving, 1/day, 365 days/year) • Streptokinase (100% receiving, 1/year) **CV3c)** Visits: • 3 inpatient bed-days (100% receiving) • 5 outpatient visits per year (100% receiving) Drugs: • Aspirin 75mg (100% receiving, 1/day, 365 days/year) • Clopidogrel (100% receiving, 1/year)	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26] Data on laboratory tests and equipment from UNICEF product catalogue [27] and WHO-CHOICE price database [25] The quantity assumptions and % receiving refer to the population receiving each intervention as indicated in table 1

	• Streptokinase (100% receiving, 1/year) **CV3d)** Visits: • 4 inpatient bed-days (100% receiving) • 6 outpatient visits per year (100% receiving) Drugs: • Aspirin 75mg (100% receiving, 1/day, 365 days/year) • Clopidogrel (100% receiving, 1/year) Supplies (per patient): • PCI kit (100% receiving, 1/year) • Bare metal stent (100% receiving, 1/year)	
CV4a	Visits: • 7 inpatient bed-days (100% receiving) • 3 outpatient visits per year (100% receiving) Laboratory tests per patient: • Blood glucose level test (100% receiving, 1/year) Equipment: • CT scan (100% receiving, 2/year) Drugs: • Tissue plasminogen activator (100% receiving, 1/year)	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26] Data on laboratory tests, equipment and supplies from a variety of sources including the UNICEF product catalogue, the OneHealth tool and the literature
CV4b	Visits: • 7 inpatient bed-days (100% receiving) • 3 outpatient visits per year (100% receiving) Laboratory tests per patient: • Blood glucose level test (100% receiving, 1/year) • Complete blood count (100% receiving, 1/year) • Prothrombin time (100% receiving, 1/year) • Serum creatinine test (100% receiving, 1/year) Equipment and supplies: • CT scan (100% receiving, 2/year) • EDG (100% receiving, 1/year) • Suture set (100% receiving, 1/year) • MT device (100% receiving, 1/year)	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26] Data on laboratory tests, equipment and supplies from a variety of sources including the UNICEF product catalogue, the OneHealth tool and the literature

	• Oxygen (100% receiving, 1/year) Drugs: • Tissue plasminogen activator (100% receiving, 1/year)	
CV5a	Visits: • 5 outpatient visits/year (83% receiving) Drugs: • Benzathine Benzyl Penicillin 1.2 M IU (8% receiving, 1/day, 1/year) • Azithromycin 250 (0.4% receiving, 1/day, 5days/year) • Benzathine Benzyl Penicillin 2.4 M IU (3% receiving, 1/day, 1/year) • Azithromycin 500 (0.1% receiving, 1/day, 5days/year)	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26] % receiving refer to the proportion of children with sore throat
CV5b	Visits: • 14 outpatient visits/year (100% receiving) Drugs: • Benzathine Benzyl Penicillin 1.2 M IU (71.25% receiving, 1/day, 15days/year) • Azithromycin 250 (3% receiving, 1/day, 365 days/year) • Benzathine Benzyl Penicillin 2.4 M IU (23.75% receiving, 1/day, 15 days/year) • Azithromycin 500 (1% receiving, 1/day, 365 days/year)	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26]
CV6	Visits: • 1 inpatient visit/year (100% receiving) • 4 outpatient visits/year (100% receiving) Drugs: • Aspirin 75mg (100% receiving, 1/day, 365 days/year)	Data on outpatient visits sourced from WHO-CHOICE price database [25] Data on drug prices from MSH website (median seller price) [26]
CV7	Visits: • 7 inpatient bed-days (100% receiving) • 3 outpatient visits per year (100% receiving) Human resources per bed-day, per patient: • 1 Neurologist, 20 minutes per bed-day • 1 Stroke nurse, check-up of 10 minutes every 4 hours, for a total of 60 minutes per bed-day • Therapists (rehabilitation/speech/occupational), 30 minutes per bed-day	Data on inpatient and outpatient visits sourced from WHO-CHOICE [25] Data on staff salary from the WHO-CHOICE price database [25]

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