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DEFINING DISEASE TYPES I, II AND III

The CEWG was tasked with framing its analysis around disease Types that were first introduced by the Commission on Macroeconomics and Health and elaborated in the report of the Commission on Intellectual Property Rights, Innovation and Public Health. The definition of diseases into Types mixes a number of concepts together including the wealth of a country between rich and poor; the state of its development between developed and developing and most importantly a measure of the burden of diseases by the incidence of the disease within the population. The definitions themselves are combined such that:

Type I diseases: are incident in both rich and poor countries, with large numbers of vulnerable populations in each.

Type II diseases: are incident in both rich and poor countries, but with a substantial proportion of the cases in poor countries.

Type III diseases: are those that are overwhelmingly or exclusively incident in developing countries.

In addition the CEWG analysis for Type I diseases was to focus on the R&D needs specific to developing countries.

While often quoted these disease Type definitions have never been mapped against a full range of diseases, instead examples in each Type have been highlighted. For example cancer is a typical Type I disease, TB and AIDs being typical of Type II with Type III diseases broadly corresponding to the infectious tropical diseases such as leishmaniasis or malaria.

However, if greater efforts are to be made to map resource flows for R&D against these disease Types then an approach for classifying them needs to be developed and agreed. As a starting point the WHO Global Burden of Diseases report, last published in 2004 and due to be updated with data up to 2010, provides an accepted list of disease causes that can be used at a global level for this type of analysis. The next category within the original definition is wealth and/or the stage of development of a country. While in common usage there is no agreed UN convention that defines all countries between developed and developing. Therefore, an objective alternative is to use the income categories calculated by the World Bank. Finally measuring disease incidence is only one element of disease burden whereas the Disability Adjusted Life Years (DALYs) seeks to bring together a range of measures that, when combined with population size, can be used to give an estimate of the disease burden at a national, regional or even global level.

In order to inform discussion at the Open Ended Member States meeting 26th-28th November a working list of diseases was generated using a combination of the measures cited above.

The approach involved using the conditions/diseases presented in the 2004 Global Burden of Diseases report. The DALYs for each disease per 100,000 population was aggregated and a total for each disease cause was obtained for low and middle income countries combined to enable a comparison with the total DALYs per 100,000 population per disease for high income countries. A ratio was then calculated comparing the DALY figure between the low/middle income countries with the high income countries. These ratios were then ranked high to low where a ratio of 1.0 means the disease is found in equal measure in all countries which is analogous to the concept of a Type I disease. Looking at this ranking table diseases were then subjectively categorised using the following range of ratio figures where this created recognisable groups that aligned with an understanding of what the disease Types were aiming to represent where (Table 1):

- Type I: 0.0 - < 3.0 i.e. the disease burden is approximately the same and no more than 3 times higher in low/middle income countries than high income countries.

- Type II: > 3.0 < 35.0 the disease burden is at a rate that is between 3.0–35.0 times higher in low/middle income countries than in a high income country.

- Type III: > 35.0 the disease burden is at a rate that is at least 35.0 times and up to more than a 1000 times higher than is recorded in high income countries.

It is to be stressed this approach is ***not*** intended to be prescriptive but enables a categorization of diseases to be generated in a transparent manner that can then form the basis for discussion and further analysis. So, for example, the exact boundary between the disease Types is not an exact figure and only suggested here.

There is no simple metric that combines the socio-economic and public health data inherent in the original Commission definitions and it is recognised that there are a number of limitations in this approach. For example the figures used are crude aggregates and not age-weighted for population size so, for example, colon cancer will have a higher measure of prevalence in high income countries due to the older age of those populations. The DALYs measure itself is often an estimate where accurate disease figures (incidence, mortality etc.) are not available, which is often a challenge for low income countries.

The advantages or this approach are that it is a relatively simple method that can be developed using publically available data to produce a categorization of disease Types to inform debates on the scope of any R&D monitoring activities. The method is offered here as a tool that can be adapted or discarded to suit one's needs. It is also a dynamic measure that can change over time and can be adapted for use at a national, sub-national or regional level. For example the diseases in the Type categories will vary greatly between individual countries and over time; a concept that was envisioned by the Commission in the original definition.

At this high level the classification of Type II and III diseases are relatively uncontested, even if the boundary between them might be raised up or down, and this method supports the general consensus. However, while Type I diseases can be identified, as having a ratio near to 1.0 comparing all countries, the specific R&D requirement - particularly the R&D needs for 'developing' countries for Type I diseases requires a significantly different approach.

In fact for all the disease Types defining what the specific R&D needs are for developing or low income countries is a more complex decision based on a wide range of technical, business and intellectual property considerations. For example HIV is a global disease with the majority of the burden in the low/middle income countries and therefore is considered a typical Type II disease. However, the R&D landscape is mixed and in different circumstances it could be considered as being Type I, II or III. There are drugs available to treat adults and so affordable access is more of an issue for low and middle income

countries rather than R&D for new product development - unless R&D is considered necessary for the development of quality affordable generics. In contrast there is very limited work on formulations to treat HIV in children and infants where the majority of the disease burden is in low income countries and there is no market incentives for commercial research. Therefore in this instance paediatric formulations to treat HIV appears as a Type III disease.

While there is no simple answer to identifying priorities numerous working groups and conferences have established R&D roadmaps in many disease areas. A review undertaken in 2010 revealed that 230 documents were deposited in the WHO Library Database since 2005 that referred to priority setting in various disease areas.[1, 2] Therefore, a lot of the information to set an R&D agenda exists but is found to be of varying quality and dispersed across many sources. This information needs to be organized and accessible in a more standard form perhaps through the development of methods similar to those devised by the Cochrane Collaboration in undertaking systematic reviews or utilized by the WHO in developing its Guidelines where the quality of evidence – and therefore its reliability - is graded. A standard reporting system for research priority setting exercises, similar to the systems developed in the reporting for clinical trials would be beneficial.[3] This is a further example of the standards and good practice approaches that could be developed to facilitate the harmonization of global health R&D efforts.

In conclusion using these disease Types as a proxy to identify the burden of disease as it relates to the income of the population it affects is an important element to enable the monitoring of resource flows. However, much more additional work is required to decide and agree on the specific priority areas for the R&D agenda.

[1] WHO library databases http://www.who.int/library/databases/en/

[2] Viergever RF, Terry R, Matsoso MP: Health research prioritization at WHO: an overview of methodology and high level analysis of WHO led health research priority setting exercises Geneva: World Health Organization; 2010 http://www.who.int/rpc/publications/en/

[3] Consolidated Standards of Reporting Trials (CONSORT) statement http://www.consort-statement.org/

Table 1 Global Burden of diseases		DALYs by World Bank Income Groups 2012 per 100,000 population					DALYS Ratio low + middle income/ high income per 100,000 of population	Suggested disease Type I, II or III
GBoD No.	GBoD cause name*	Low	Lower-middle	Upper-middle	Low + middle income	High		
23	Chagas disease	0.00	3.85	14.32	7.94	0.00	1869.12	
31	Trachoma	68.76	18.06	17.91	24.80	0.02	1358.34	
22	Trypanosomiasis	158.93	22.79	0.17	31.12	0.04	867.12	
26	Lymphatic filariasis	282.28	169.92	0.84	110.61	0.19	569.48	
14	Diphtheria	8.04	4.89	0.16	3.23	0.01	390.20	
56	Vitamin A deficiency	57.68	8.76	0.52	11.71	0.03	338.60	
15	Measles	389.48	518.38	7.46	276.22	1.03	266.90	
16	Tetanus	235.88	145.59	10.50	98.27	0.37	264.13	
20	Malaria	2537.27	674.78	8.13	631.60	3.41	185.06	
27	Onchocerciasis	11.31	13.32	0.06	7.21	0.05	152.11	
25	Leishmaniasis	42.79	69.63	2.99	36.70	0.30	122.67	TYPE III
28	Leprosy	4.75	5.98	0.95	3.60	0.03	118.17	DALYs Ratio
43	Maternal haemorrhage	242.03	107.99	9.00	82.43	0.72	114.74	> 35.0
5	Syphilis	161.49	64.90	7.93	52.80	0.68	78.02	
45	Hypertensive disorders of pregnancy	77.92	50.71	6.67	34.98	0.58	60.13	
30	Japanese Encephalitis	12.90	19.52	5.91	12.64	0.22	58.61	
33	Ascariasis	67.80	46.97	11.86	34.32	0.62	54.96	
47	Abortion	325.01	193.03	26.50	137.47	3.32	41.46	
55	Iodine deficiency	159.20	66.99	35.17	65.37	1.65	39.60	
24	Schistosomiasis	115.67	31.32	6.25	31.62	0.81	38.85	
12	Pertussis	361.00	301.87	13.73	183.01	4.89	37.39	
46	Obstructed labour	92.03	83.55	12.21	53.29	1.54	34.65	
34	Trichuriasis	33.69	22.45	10.56	18.73	0.56	33.36	
3	Tuberculosis	1263.97	771.42	306.48	632.98	20.03	31.60	
10	Diarrhoeal diseases	3893.35	1609.69	313.16	1345.90	45.66	29.48	
54	Protein-energy malnutrition	882.15	386.36	89.14	322.17	13.32	24.19	TYPE II
29	Dengue	22.33	17.78	4.05	12.35	0.61	20.34	DALYs Ratio
17	Meningitis	574.63	259.51	52.00	210.52	11.42	18.43	>3.0 < 35.0
35	Hookworm disease	38.80	19.64	14.84	20.10	1.10	18.20	
9	HIV/AIDS	3759.08	745.15	578.03	1076.48	63.00	17.09	
51	Birth asphyxia and birth trauma	1605.14	967.32	314.41	765.68	49.65	15.42	
39	Lower respiratory infections	5185.63	2072.82	352.81	1734.05	128.12	13.53	
50	Low birth weight	1399.47	1120.39	328.56	809.42	76.35	10.60	

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44	Maternal sepsis	256.75	152.00	44.58	118.80	14.22	8.35	
100	Cataracts	411.32	354.22	261.82	321.23	45.34	7.09	TYPE II
105	Rheumatic heart disease	90.76	129.23	60.82	93.96	13.29	7.07	DALYs Ratio
40	Upper respiratory infections	87.26	26.64	20.71	32.18	5.57	5.78	>3.0 < 35.0
18	Hepatitis B	67.65	42.24	22.37	36.91	8.01	4.61	
57	Iron-deficiency anaemia	443.40	356.03	173.57	287.47	65.95	4.36	
116	Peptic ulcer disease	102.67	114.76	57.85	88.09	21.97	4.01	
41	Otitis media	38.79	28.63	18.86	25.70	10.08	2.55	
85	Epilepsy	203.67	147.39	102.40	135.15	55.34	2.44	
121	Nephritis and nephrosis	205.14	188.05	109.43	155.75	65.04	2.39	
99	Glaucoma	97.61	79.76	75.19	80.15	39.56	2.03	
118	Appendicitis	9.55	7.26	6.13	7.07	3.60	1.96	TYPE I
84	Schizophrenia	268.96	294.75	269.56	280.20	161.76	1.73	DALYs Ratio
70	Cervix uteri cancer	80.45	74.12	44.62	61.99	36.97	1.68	0.0 - < 3.0
101	Refractive errors	321.35	456.20	510.14	461.82	279.31	1.65	
62	Oesophagus cancer	61.76	42.71	119.40	79.02	49.97	1.58	
106	Hypertensive heart disease	167.82	114.87	138.10	132.21	85.85	1.54	
108	Cerebrovascular disease	617.87	595.36	977.12	766.39	514.96	1.49	
83	Bipolar affective disorder	247.43	238.47	232.62	237.10	159.58	1.49	
122	Benign prostatic hypertrophy	34.49	42.93	46.81	43.50	30.87	1.41	
113	Asthma	356.88	283.57	221.16	265.95	191.53	1.39	
93	Panic disorder	117.09	118.61	108.36	113.90	82.60	1.38	
129	Low back pain	39.86	39.54	38.66	39.20	28.57	1.37	
112	Chronic obstructive pulmonary disease	271.72	465.98	580.95	490.48	366.26	1.34	
92	Obsessive-compulsive disorder	100.36	79.26	79.87	82.36	63.97	1.29	
65	Liver cancer	87.24	42.16	178.97	108.42	84.48	1.28	
109	Inflammatory heart disease	126.55	100.31	92.88	100.57	78.97	1.27	
61	Mouth and oropharynx cancers	64.60	81.48	40.38	61.12	48.13	1.27	
128	Gout	32.56	55.16	62.51	55.36	45.35	1.22	
117	Cirrhosis of the liver	157.93	253.99	201.68	218.06	182.92	1.19	
107	Ischaemic heart disease	791.16	1249.88	818.29	998.33	849.43	1.18	

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63	Stomach cancer	61.93	47.37	204.26	118.37	107.90	1.10	
76	Leukaemia	48.27	75.38	89.65	78.02	71.38	1.09	
91	Post-traumatic stress disorder	50.67	55.35	54.26	54.24	52.61	1.03	
19	Hepatitis C	24.72	17.31	9.50	14.87	14.79	1.01	
82	Unipolar depressive disorders	858.90	1124.18	964.19	1018.14	1023.11	1.00	
102	Hearing loss, adult onset	362.68	486.80	384.59	425.15	429.11	0.99	
103	Macular degeneration and other sense disorders	116.43	157.58	136.63	142.83	153.98	0.93	
79	Diabetes mellitus	250.23	283.46	318.90	294.59	366.65	0.80	
86	Alcohol use disorders	111.63	234.67	547.27	355.71	442.97	0.80	
95	Migraine	100.51	120.55	116.74	116.18	144.72	0.80	
127	Osteoarthritis	183.96	200.04	278.78	232.53	293.95	0.79	
126	Rheumatoid arthritis	49.99	63.47	92.30	74.35	100.10	0.74	
94	Insomnia (primary)	49.10	55.79	49.63	52.18	77.93	0.67	
75	Lymphomas and multiple myeloma	77.93	71.02	47.69	61.68	92.13	0.67	
89	Multiple sclerosis	17.20	21.27	24.16	22.00	32.86	0.67	
90	Drug use disorders	100.65	125.93	117.46	118.81	188.03	0.63	
72	Ovary cancer	17.86	25.56	21.84	22.89	49.07	0.47	TYPE I
69	Breast cancer	59.24	84.21	96.32	86.18	190.51	0.45	DALYs Ratio
77	Other malignant neoplasms	111.02	110.29	125.63	117.14	269.23	0.44	0.0 - < 3.0
74	Bladder cancer	12.24	18.77	19.19	18.08	45.70	0.40	
67	Trachea, bronchus and lung cancers	67.23	79.99	230.74	144.62	381.30	0.38	
71	Corpus uteri cancer	3.62	6.80	11.67	8.52	27.21	0.31	
64	Colon and rectum cancers	28.18	51.42	92.56	66.41	219.64	0.30	
87	Alzheimer and other dementias	70.77	94.81	164.15	122.10	437.84	0.28	
73	Prostate cancer	18.87	19.03	21.68	20.17	72.60	0.28	
66	Pancreas cancer	12.08	15.65	35.57	23.93	88.95	0.27	
88	Parkinson disease	20.97	14.06	21.52	18.27	69.48	0.26	
68	Melanoma and other skin cancers	7.11	4.90	8.18	6.64	33.28	0.20	

***Notes:** Injuries were excluded from these classifications. So were residual categories ("other … ") and overarching categories (skin disorders, endocrine disorders and other neoplasms) and a small number of specific diseases for which uncertainties in the burden of disease estimates were large (chlamydia, gonorrhoea, neonatal infections, all congenital anomalies, all oral diseases and polio where new cases were eliminated from high income countries many years ago but death from late effects are still recorded - late effects are not estimated for low income countries.

Population figures 2004: Low income 721,185,675 ; Lower middle income 2,284,855,298 ; Upper middle income 2,362,577,894 ; High income 1,046,139,821 ; World 6,414,758,688