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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Webappendix:

Essential medicines for Universal Health Coverage

Contents

Appendix 1.1: Medicine list (in alphabetical order), and sources of quantity estimation data for Scenarios 1-4

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
339	Abacavir	Oral solution	20mg/mL	Forecast*	Forecast*	Forecast*	Forecast*
340	Abacavir	tablet	300mg	Forecast	Forecast	Forecast	Forecast
341	Abacavir	tablet	60mg	Forecast*	Forecast*	Forecast*	Forecast*
349	Abacavir/lamivudine	tablet	600/300	Forecast	Forecast	Forecast	Forecast
476	Abacavir/Lamivudine	Tablet	60 mg / 30 mg	Forecast	Forecast	Forecast	Forecast
477	Abacavir/Lamivudine	Tablet	120mg / 60mg	Forecast*	Forecast*	Forecast*	Forecast*
463	Acetazolamide	tablet	250mg	Denmark	KZN	Denmark	KZN
462	Acetylcholine	Eye drop	10mg/mL	Prevalence	Prevalence	Prevalence	Prevalence
325	Aciclovir	Oral solution	40 mg/mL	Prevalence	Prevalence	Prevalence	Prevalence
326	Aciclovir	tablet	200mg	Prevalence	Prevalence	Prevalence	Prevalence
327	Aciclovir	tablet	400mg	Prevalence	Prevalence	Prevalence	Prevalence
328	Aciclovir	Vial	250mg	Prevalence	Prevalence	Prevalence	Prevalence
199	Acitretin	Capsule	10mg	Denmark	Denmark	Denmark	Denmark
437	Albendazole	suspension	20 mg/mL	KZN	KZN	KZN	KZN
438	Albendazole	tablet	400mg	KZN	KZN	KZN	KZN
365	Allopurinol	tablet	100mg	Prevalence	Prevalence	Prevalence	Prevalence
366	Allopurinol	tablet	300mg	Prevalence	Prevalence	Prevalence	Prevalence
297	Amikacin	vial	250mg	Forecast	KZN	IMS	IMS
160	Amiodarone	tablet	200mg	Denmark	Denmark	Denmark	Denmark
419	Amitriptyline	tablet	10mg	Prevalence	KZN	Prevalence	KZN
420	Amitriptyline	tablet	25mg	Prevalence	KZN	Prevalence	KZN
421	Amitriptyline	tablet	50mg	Prevalence	KZN*	Prevalence	KZN*
179	Amlodipine	tablet	10mg	Denmark	KZN	IMS	IMS
180	Amlodipine	tablet	5mg	Denmark	KZN	IMS	IMS
251	Amoxicillin	tablet	250mg	KZN	KZN	IMS	IMS
252	Amoxicillin	tablet	500mg	KZN	KZN	IMS	IMS

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
253	Amoxycillin	suspension	125mg/5mL	KZN	KZN	IMS	IMS
254	Amoxycillin	suspension	250mg/5mL	KZN	KZN	IMS	IMS
264	Amoxycillin/clavulanic acid	suspension	125/31.25mg/5mL	KZN	KZN	IMS	IMS
265	Amoxycillin/clavulanic acid	suspension	250/62.5mg/5mL	KZN	KZN	IMS	IMS
266	Amoxycillin/clavulanic acid	tablet	250/125mg	KZN	KZN	IMS	IMS
248	Ampicillin	tablet	500mg	KZN*	KZN*	IMS	IMS
249	Ampicillin	vial	500mg/vial	KZN	KZN	IMS	IMS
250	Ampicillin (as sodium)	vial	250mg	KZN*	KZN*	IMS	IMS
432	Artemether/lumefantrine	tablet	20/120mg	Forecast	Forecast	Forecast	Forecast
141	Aspirin	tablet	100mg	Denmark	KZN	Denmark	KZN
378	Aspirin	tablet	300mg	Denmark	KZN	Denmark	KZN
332	Atazanavir	capsules	150mg	Forecast	Forecast	Forecast	Forecast
177	Atenolol	tablet	100mg	Denmark	KZN	IMS	IMS
178	Atenolol	tablet	50mg	Denmark	KZN	IMS	IMS
192	Atorvastatin	tablet	10mg	Denmark	KZN	IMS	IMS
110	Atropine	ampoule	0.5mg/mL	Denmark	KZN	Denmark	KZN
111	Atropine	ampoule	1mg/mL	Denmark	KZN*	Denmark	KZN
464	Atropine	eye drops	1%	KZN	KZN	KZN	KZN
361	Azathioprine	tablet	50mg	Denmark	KZN	Denmark	KZN
289	Azithromycin	tablet	250mg	KZN	KZN	IMS	IMS
290	Azithromycin	tablet	500mg	KZN	KZN	IMS	IMS
291	Azithromycin	powder for infusion	250mg	KZN	KZN	IMS	IMS
446	Beclomethasone	inhaler	50 mcg	Prevalence	KZN	Prevalence	KZN
447	Beclomethasone	inhaler	250mcg/dose	Prevalence	KZN*	Prevalence	KZN*
448	Beclomethasone	inhaler	100 mcg	Prevalence	KZN	Prevalence	KZN
261	Benzathine penicllin G	vial	0.72mg (1.2 MU)	KZN	KZN	KZN	KZN
262	Benzathine penicllin G	vial	1.44mg (2.4 MU)	KZN	KZN	KZN	KZN

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
213	Benzoyl peroxide	gel	5%	Denmark	KZN	Denmark	KZN
441	Benzyl benzoate	emulsion	25%	KZN*	KZN*	KZN*	KZN*
255	Benzylpenicillin	vial	3000mg	KZN	KZN	KZN	KZN
256	Benzylpenicillin	vial	600mg	KZN	KZN	KZN	KZN
234	Betamethasone	ampoule	4mg/mL	Denmark	KZN	Denmark	KZN
398	Biperiden	tablet	2mg	Prevalence	Prevalence	Prevalence	Prevalence
359	Bleomycin	vial	15IU/vial	KZN*	KZN*	KZN*	KZN*
442	Budesonide	nasal spray	100mcg	Denmark	KZN	Denmark	KZN
449	Budesonide	inhaler	100mcg	Prevalence	KZN	Prevalence	KZN
450	Budesonide	inhaler	200mcg	Prevalence	KZN	Prevalence	KZN
451	Budesonide	inhaler + spacer	100mcg	Prevalence*	KZN*	Prevalence*	KZN*
452	Budesonide	inhaler + spacer	200mcg	Prevalence*	KZN*	Prevalence*	KZN*
112	Butylscopolamine	syrup	5mg/5mL	Denmark*	KZN	Denmark	KZN
113	Butylscopolamine	tablet	10mg	Denmark	KZN	Denmark	KZN
100	Calamine BP	lotion	15%	KZN	KZN	KZN	KZN
133	Calcium carbonate	tablet	420/180mg	Denmark	KZN	Denmark	KZN
134	Calcium carbonate	tablet	500mg	Denmark*	KZN	Denmark*	KZN
131	Calcium gluconate	ampoule	100mg/mL	Denmark*	KZN	Denmark*	KZN
132	Calcium gluconate	tablet	300mg	Denmark	KZN*	Denmark	KZN*
312	Capreomycin	vial	1000mg	Forecast	Forecast	Forecast	Forecast
391	Carbamazepine	tablet	200mg	Prevalence	KZN	IMS	IMS
392	Carbamazepine	tablet (controlled release)	200mg	Prevalence	KZN	IMS	IMS
393	Carbamazepine	tablet (controlled release)	400mg	Prevalence	KZN	IMS	IMS
267	Cefalexin	capsules	250mg	KZN	KZN	IMS	IMS
268	Cefalexin	capsules	500mg	KZN	KZN	IMS	IMS
269	Cefalexin	suspension	125mg/5mL	KZN	KZN	IMS	IMS
270	Cefalexin	suspension	250mg/5mL	KZN	KZN	IMS	IMS

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
276	Cefixime	suspension	100mg/5ml	KZN*	KZN*	IMS	IMS
277	Cefixime	tablet	200mg	KZN*	KZN*	IMS	IMS
278	Cefixime	tablet	400mg	KZN	KZN	IMS	IMS
271	Cefotaxime	vial	1g	KZN	KZN	IMS	IMS
272	Cefoxatime	vial	500mg/vial	KZN	KZN	IMS	IMS
273	Ceftriaxone	vial	1g	KZN	KZN	IMS	IMS
274	Ceftriaxone	vial	250mg/vial	KZN	KZN	IMS	IMS
275	Ceftriaxone	vial	500mg/vial	KZN	KZN	IMS	IMS
245	Chloramphenicol	capsules	250mg	KZN	KZN	IMS	IMS
246	Chloramphenicol	suspension	30mg/mL	KZN*	KZN*	IMS	IMS
247	Chloramphenicol	injection	1g	KZN*	KZN*	IMS	IMS
465	Chloramphenicol	eye ointment	1%	KZN	KZN	KZN	KZN
204	Chlorhexidine	solution (scrub)	4%	KZN	KZN	KZN	KZN
205	Chlorhexidine	solution (scrub)	4%	KZN	KZN	KZN	KZN
206	Chlorhexidine/alcohol	solution (topical)	0.50%	KZN	KZN	KZN	KZN
207	Chlorhexidine/alcohol	solution (topical)	0.5/70%	KZN	KZN	KZN	KZN
427	Chloroquine	syrup	50mg/5mL	Forecast*	Forecast*	Forecast*	Forecast*
428	Chloroquine	tablet	150mg	Forecast	Forecast	Forecast	Forecast
457	Chlorphenamine	syrup	2mg/5mL	Denmark	KZN	Denmark	KZN
400	Chlorpromazine	injection	25MG/mL	Prevalence	KZN	Prevalence	KZN
401	Chlorpromazine	tablet	100mg	Prevalence	KZN	Prevalence	KZN
402	Chlorpromazine	tablet	25mg	Prevalence	KZN	Prevalence	KZN
403	Chlorpromazine	tablet	50mg	Prevalence	KZN	Prevalence	KZN
300	Ciprofloxacin	suspension	250mg/5mL	KZN	KZN	IMS	IMS
301	Ciprofloxacin	tablet	250mg	KZN	KZN	IMS	IMS
302	Ciprofloxacin	tablet	500mg	KZN	KZN	IMS	IMS
460	Ciprofloxacin	eye drops	0.30%	Denmark	KZN	Denmark	KZN

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
292	Clindamycin	ampoule	300mg/2mL	KZN	KZN	IMS	IMS
293	Clindamycin	capsules	150mg	KZN	KZN	IMS	IMS
101	Clobetasol	topical ointment	0.50%	Denmark	Denmark	Denmark	Denmark
322	Clofazimine	capsule	100mg	Prevalence	Prevalence	Prevalence	Prevalence
323	Clofazimine	capsule	50mg	Prevalence*	Prevalence*	Prevalence*	Prevalence*
418	Clomipramine	tablet	10mg	Prevalence	KZN	Prevalence	KZN
390	Clonazepam	tablet	2mg	Prevalence	KZN	IMS	IMS
280	Clotrimazole	cream	10mg/g	KZN	KZN	KZN	KZN
281	Clotrimazole	cream (vaginal)	1%	KZN	KZN	KZN	KZN
282	Clotrimazole	vaginal tablet	500mg	KZN	KZN	KZN	KZN
263	Cloxacillin	tablet	500mg	KZN	KZN	IMS	IMS
407	Clozapine	tablet	100mg	Prevalence	Prevalence	Prevalence	Prevalence
377	Codeine	tablet	30mg	KZN	KZN	KZN	KZN
283	Co-trimoxazole	suspension	240mg/5mL	KZN	KZN	IMS	IMS
284	Co-trimoxazole	suspension	240mg/5mL	KZN	KZN	IMS	IMS
285	Co-trimoxazole	tablet	480mg	KZN	KZN	IMS	IMS
357	Cyclophosphamide	tablet	50mg	KZN*	KZN*	KZN*	KZN*
358	Cyclophosphamide	vial	1g/vial	KZN*	KZN*	KZN*	KZN*
324	Dapsone	tablet	100mg	Prevalence	Prevalence	Prevalence	Prevalence
467	Deferoxamine	vial	500mg/vial	Denmark	Denmark	Denmark	Denmark
235	Dexamethasone	ampoule	4mg/mL	KZN	KZN	KZN	KZN
150	Dextrose (Carbohydrates)	ampoule	50%	Denmark	KZN	Denmark	KZN
151	Dextrose (Carbohydrates)	ampoule	50%	Denmark*	KZN	Denmark*	KZN
412	Diazepam	ampoule	5mg/mL	Denmark	KZN	Denmark	KZN
413	Diazepam	tablet	10mg	Denmark*	KZN	Denmark*	KZN
414	Diazepam	tablet	2mg	Denmark	KZN*	Denmark	KZN
415	Diazepam	tablet	5mg	Denmark	KZN	Denmark	KZN

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
159	Digoxin	tablet	0.25mg	Denmark	KZN	Denmark	KZN
243	Doxycycline	capsules	100mg	KZN	KZN	IMS	IMS
345	Efavirenz	capsules	200mg	Forecast*	Forecast*	Forecast*	Forecast*
346	Efavirenz	capsules	50mg	Forecast*	Forecast*	Forecast*	Forecast*
347	Efavirenz	capsules	600mg	Forecast	Forecast	Forecast	Forecast
469	Efavirenz	Tablet	200 mg	Forecast	Forecast	Forecast	Forecast
351	Emtricitabine / Tenofovir / Efavirenz	tablet	200/300/600mg	Forecast	Forecast	Forecast	Forecast
186	Enalapril	tablet	10mg	Denmark	KZN	IMS	IMS
187	Enalapril	tablet	20mg	Denmark	KZN	IMS	IMS
188	Enalapril	tablet	5mg	Denmark	KZN	IMS	IMS
139	Enoxaparin	syringe	40 mg	Denmark*	KZN	Denmark*	KZN
140	Enoxaparin	syringe	80mg	Denmark	KZN	Denmark	KZN
161	Epinephrine	injection	1mg/ml	Denmark	KZN	Denmark	KZN
214	Ergometrine	ampoule	0.5mg/mL	KZN	KZN	KZN	KZN
286	Erythromycin	suspension	125mg/5mL	KZN	KZN	IMS	IMS
287	Erythromycin	suspension	250mg/5mL	KZN	KZN	IMS	IMS
288	Erythromycin	tablet	400mg	KZN*	KZN*	IMS	IMS
317	Ethambutol	tablet	400mg	Forecast	Forecast	Forecast	Forecast
315	Ethionamide	tablet	250mg	Forecast	Forecast	Forecast	Forecast
144	Ferrous sulfate	oral drops	125mg/mL	Prevalence	Prevalence	Prevalence	Prevalence
145	Ferrous sulfate	syrup	200mg/5mL	Prevalence*	Prevalence*	Prevalence*	Prevalence*
146	Ferrous sulfate	tablet	50mg	Prevalence*	Prevalence*	Prevalence*	Prevalence*
147	Ferrous sulfate	tablet	170mg	Prevalence	Prevalence	Prevalence	Prevalence
306	Fluconazole	capsules	200mg	KZN	KZN	KZN	KZN
307	Fluconazole	capsules	50mg	KZN	KZN	KZN	KZN
308	Fluconazole	injection	2mg/mL	KZN	KZN	KZN	KZN
422	Fluoxetine	capsules	20mg	Prevalence	KZN	Prevalence	KZN

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
404	Fluphenazine	ampoule	25 mg/mL	Prevalence	Prevalence	Prevalence	Prevalence
148	Folic acid	tablet	1mg	Denmark	KZN*	Denmark	KZN*
149	Folic acid	tablet	5mg	Denmark	KZN	Denmark	KZN
329	Ganciclovir	powder for injection	500mg/10mL	KZN	KZN	KZN	KZN
295	Gentamicin	ampoule	40mg/mL	KZN	KZN	IMS	IMS
296	Gentamicin	eye drops	3mg/ml	KZN	KZN	KZN	KZN
128	Glibenclamide	tablet	5mg	Prevalence	Prevalence	Prevalence	Prevalence
129	Gliclazide	tablet	80mg	Prevalence	Prevalence	Prevalence	Prevalence
162	Glyceryl trinitrate	sublingual capsule	0.4mg	Denmark	KZN	Denmark	KZN
163	Glyceryl trinitrate	tablet	6.4mg	Denmark*	KZN	Denmark*	KZN
164	Glyceryl trinitrate	tablet SR	2.6mg	Denmark	KZN*	Denmark	KZN*
405	Haloperidol	capsules	0.5mg	Prevalence	Prevalence	Prevalence	Prevalence
406	Haloperidol	tablet	1.5mg	Prevalence	Prevalence	Prevalence	Prevalence
169	Hydralazine	tablet	25mg	KZN	KZN	IMS	IMS
170	Hydrochlorothiazide	tablet	12.5mg	Denmark	KZN	IMS	IMS
171	Hydrochlorothiazide	tablet	25mg	Denmark	KZN	IMS	IMS
203	Hydrocortisone	cream	1%	KZN	KZN	KZN	KZN
239	Hydrocortisone	tablet	10mg	Denmark	KZN	Denmark	KZN
240	Hydrocortisone	injection	100mg/8ml	Denmark	KZN	Denmark	KZN
362	Ibuprofen	suspension	100mg/5mL	Denmark*	KZN	IMS	IMS
363	Ibuprofen	tablet	200mg	Denmark	KZN	IMS	IMS
364	Ibuprofen	tablet	400mg	Denmark	KZN	IMS	IMS
279	Imipenem plus cilastatin	vial (powder for injection)	500mg/500mg	KZN	KZN	IMS	IMS
355	Immunoglobulin, Anti-D rhesus	ampoule	100mcg	Denmark	Denmark	Denmark	Denmark
125	Insulin combined	prefilled syringe	100IU/mL	Prevalence	Prevalence	Prevalence	Prevalence
126	Insulin combined	vial	100IU/mL	Prevalence	Prevalence	Prevalence	Prevalence
123	Insulin isophane (intermediate acting)	prefilled syringe	100IU/mL	Prevalence	Prevalence	Prevalence	Prevalence

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
124	Insulin isophane (intermediate acting)	vial	100IU/mL	Prevalence	Prevalence	Prevalence	Prevalence
121	Insulin, soluble (fast acting)	prefilled syringe	100IU/mL	Prevalence	Prevalence	Prevalence	Prevalence
122	Insulin, soluble (fast acting)	vial	100IU/mL	Prevalence	Prevalence	Prevalence	Prevalence
453	Ipratropium	inhaler	40mcg/dose	Prevalence	KZN	Prevalence	KZN
454	Ipratropium	vial, inhalation solution	0.5mg/2mL	Prevalence	KZN	Prevalence	KZN
367	Isoflurane USP	liquid for vaporization	0.999	Denmark*	KZN*	Denmark*	KZN*
368	Isoflurane USP	liquid for vaporization	0.999	Denmark	KZN	Denmark	KZN
313	Isoniazid	tablet	100mg	Forecast	Forecast	Forecast	Forecast
314	Isoniazid	tablet	300mg	Forecast	Forecast	Forecast	Forecast
165	Isosorbide dinitrate	tablet	10mg	Denmark*	KZN	IMS	IMS
166	Isosorbide dinitrate	tablet	5mg	Denmark	KZN*	IMS	IMS
167	Isosorbide dinitrate	tablet SR	40mg	Denmark	KZN*	IMS	IMS
117	Lactulose	syrup	3.3g/5mL	Denmark	KZN	Denmark	KZN
336	Lamivudine	oral solution	10mg/mL	Forecast*	Forecast*	Forecast*	Forecast*
337	Lamivudine	tablet	150mg	Forecast*	Forecast*	Forecast*	Forecast*
338	Lamivudine	tablet	300mg	Forecast	Forecast	Forecast	Forecast
354	Lamivudine, Tenofovir disoproxil, Efavirenz	tablet	300/300/600mg	Forecast	Forecast	Forecast	Forecast
348	Lamivudine/zidovudine HCl	tablet	300/150mg	Forecast	Forecast	Forecast	Forecast
439	Levamisole	tablet	50mg	KZN*	KZN*	KZN*	KZN*
399	Levodopa/carbidopa	tablet	100/25mg	Prevalence	Prevalence	Prevalence	Prevalence
217	Levonoregestrel/ethinyl oestradiol, Triphasic	tablet	0.05/0.03, 0.075/0.04 and 0.125/0.03mg	KZN	KZN	KZN	KZN
220	Levonorgestrel	implant	75mg/implant	KZN	KZN	KZN	KZN
221	Levonorgestrel	tablet	0.03mg	KZN	KZN	KZN	KZN
223	Levonorgestrel	tablet	1.5mg	KZN	KZN	KZN	KZN
216	Levonorgestrel/ethinyl oestradiol	tablet	0.15/0.03mg	KZN	KZN	KZN	KZN
241	Levothyroxine	tablet	0.05mg	Prevalence	Prevalence	Prevalence	Prevalence
242	Levothyroxine	tablet	0.1mg	Prevalence	Prevalence	Prevalence	Prevalence

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
197	Lidocaine	gel	2%	Denmark	KZN	Denmark	KZN
370	Lidocaine	vial	1%	Denmark*	KZN	Denmark*	KZN
371	Lidocaine	injection	2%	Denmark	KZN	Denmark	KZN
372	Lidocaine/adrenaline	dental cartridge	2%	Denmark	KZN	Denmark	KZN
408	Lithium carbonate	tablet	250mg	Prevalence	Prevalence	Prevalence	Prevalence
409	Lithium carbonate	tablet	400mg	Prevalence	Prevalence	Prevalence	Prevalence
119	Loperamide	tablet	2mg	Denmark	KZN	Denmark	KZN
352	Lopinavir/ritonavir	tablet	100/25mg	Forecast*	Forecast*	Forecast*	Forecast*
353	Lopinavir/ritonavir	tablet	200/50mg	Forecast	Forecast	Forecast	Forecast
472	Lopinavir/ritonavir	Tablet	100 mg / 25mg	Forecast	Forecast	Forecast	Forecast
473	Lopinavir/ritonavir	Oral liquid	80 mg / 20 mg/ml	Forecast	Forecast	Forecast	Forecast
416	Lorazepam	tablet	1mg	Denmark	KZN	Denmark	KZN
417	Lorazepam	tablet	2mg	Denmark*	KZN	Denmark*	KZN
189	Losartan	tablet	50mg	Denmark	KZN	IMS	IMS
158	Magnesium sulphate	ampoule	50%	KZN	KZN	KZN	KZN
434	Mebendazole	suspension	100mg/5mL	KZN	KZN	KZN	KZN
435	Mebendazole	tablet	100mg	KZN*	KZN*	KZN*	KZN*
436	Mebendazole	tablet	500mg	KZN	KZN	KZN	KZN
222	Medroxyprogesterone	vial	150mg/mL	KZN	KZN	KZN	KZN
228	Medroxyprogesterone	tablet	10mg	Denmark	KZN*	Denmark	KZN*
229	Medroxyprogesterone	tablet	5mg	Denmark*	KZN	Denmark*	KZN
360	Medroxyprogesterone	tablet	100mg	Denmark	Denmark	Denmark	Denmark
127	Metformin	tablet	500mg	Prevalence	Prevalence	Prevalence	Prevalence
102	Methyl salicylate	ointment	10%, 25g	KZN	KZN	KZN	KZN
168	Methyldopa	tablet	250mg	KZN	KZN	IMS	IMS
236	Methylprednisolone	injection	40mg/ml	Denmark	KZN	Denmark	KZN
114	Metoclopramide	ampoule	5mg/mL	Denmark	KZN	IMS	IMS

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
115	Metoclopramide	syrup	5mg/5mL	Denmark*	KZN	IMS	IMS
116	Metoclopramide	tablet	10mg	Denmark	KZN	IMS	IMS
423	Metronidazole	suspension	200mg/5mL	KZN	KZN	IMS	IMS
424	Metronidazole	tablet	200mg	KZN*	KZN*	IMS	IMS
425	Metronidazole	tablet	400mg	KZN	KZN	IMS	IMS
426	Metronidazole	oral suspension	125mg/5ml	KZN*	KZN*	IMS	IMS
231	Mifepristone	tablet	200mg	KZN	KZN	KZN	KZN
215	Misoprostol	tablet	200mcg	KZN	KZN	KZN	KZN
373	Morphine	ampoule	10mg	Forecast	Forecast	Forecast	Forecast
374	Morphine	tablet	100mg	Forecast	Forecast	Forecast	Forecast
375	Morphine	oral solution	2 mg/ml	Forecast	Forecast	Forecast	Forecast
376	Morphine	oral solution	2 mg/ml	Forecast*	Forecast*	Forecast*	Forecast*
201	Mupirocin	topical ointment	2%	Denmark	KZN	Denmark	KZN
466	Naloxone	ampoule	0.4mg/mL	Denmark	KZN	Denmark	KZN
343	Nevirapine	suspension	50mg/5mL	Forecast*	Forecast*	Forecast*	Forecast*
344	Nevirapine	tablet	200mg	Forecast	Forecast	Forecast	Forecast
470	Nevirapine	Tablet	50 mg	Forecast	Forecast	Forecast	Forecast
471	Nevirapine	Oral liquid	50 mg / 5mL, 100ml	Forecast	Forecast	Forecast	Forecast
440	Niclosamide	chewable tablet	500mg	KZN	KZN	KZN	KZN
130	Nicotinamide	tablet	100mg	KZN	KZN	KZN	KZN
193	Nicotinic acid (Niacin)	tablet	100mg	Denmark*	Denmark*	IMS	IMS
194	Nicotinic acid (Niacin)	tablet	25mg	Denmark*	Denmark*	IMS	IMS
195	Nicotinic acid (Niacin)	tablet	500mg	Denmark*	Denmark*	IMS	IMS
181	Nifedipine	capsules	10mg	Denmark	KZN	IMS	IMS
182	Nifedipine	capsules	5mg	Denmark*	KZN	IMS	IMS
183	Nifedipine XL	tablet	30mg	Denmark	KZN	IMS	IMS
184	Nifedipine XL	tablet	60mg	Denmark	KZN*	IMS	IMS

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
305	Nitrofurantoin	suspension	25mg/5ml	KZN	KZN	KZN	KZN
218	Norethisterone	ampoule	200mg/mL	KZN	KZN	KZN	KZN
219	Norethisterone	tablet	5mg	Denmark	KZN	Denmark	KZN
196	Nystatin	suspension	0.1MU/mL	KZN	KZN	KZN	KZN
224	Oestradiol	tablet	2mg	Denmark	KZN*	Denmark	KZN*
227	Oestradiol/norethisterone	tablet	1/0.5mg	KZN	KZN	KZN	KZN
225	Oestrogens (conjugated)	tablet	0.3mg	KZN	KZN	KZN	KZN
226	Oestrogens (conjugated)	tablet	1.25mg	KZN	KZN	KZN	KZN
298	Ofloxacin	tablet	200mg	KZN*	KZN*	IMS	IMS
299	Ofloxacin	tablet	400mg	Forecast	KZN	IMS	IMS
108	Omeprazole	capsules	20mg	Prevalence	KZN	Prevalence	KZN
109	Omeprazole	tablet	10mg	Prevalence	KZN	Prevalence	KZN
118	Oral rehydration	satchet	20g/L	KZN	KZN	KZN	KZN
232	Oxytocin	ampoule	10IU/mL	KZN	KZN	KZN	KZN
233	Oxytocin	ampoule	5IU/mL	KZN	KZN	KZN	KZN
379	Paracetamol	suppositories	125mg	Denmark	KZN	Denmark	KZN
380	Paracetamol	syrup	120mg/5mL	Denmark	KZN	Denmark	KZN
381	Paracetamol	tablet	500mg	Denmark	KZN	Denmark	KZN
382	Paracetamol	mL	120mg/5mL	Denmark*	KZN	Denmark*	KZN
383	Phenobarbital	tablet	100mg	Prevalence	KZN*	IMS	IMS
384	Phenobarbital	tablet	15mg	Prevalence	KZN*	IMS	IMS
385	Phenobarbital	tablet	30mg	Prevalence	KZN	IMS	IMS
386	Phenobarbital/vit B Co	syrup	16mg/5mL	Prevalence*	KZN*	IMS	IMS
257	Phenoxymethylpenicillin	tablet	500mg	KZN*	KZN*	IMS	IMS
258	Phenoxymethylpenicillin	suspension	125mg/5mL	KZN	KZN	IMS	IMS
259	Phenoxymethylpenicillin	suspension	250mg/5mL	KZN*	KZN*	IMS	IMS
260	Phenoxymethylpenicillin	tablet	250mg	KZN	KZN	IMS	IMS

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
387	Phenytoin	capsules	100mg	Prevalence	KZN	IMS	IMS
388	Phenytoin	oral suspension	125mg/5mL	Prevalence*	KZN	IMS	IMS
389	Phenytoin sodium	injection	250mg/5mL	Prevalence*	KZN	IMS	IMS
461	Pilocarpine HCl	eye drops	1%	Prevalence	Prevalence	Prevalence	Prevalence
135	Potassium chloride	tablet	600mg	KZN	KZN	KZN	KZN
208	Povidone iodine	cream	5%	KZN	KZN	KZN	KZN
209	Povidone iodine	cream	5%	KZN	KZN	KZN	KZN
210	Povidone iodine	ointment	10%	KZN	KZN	KZN	KZN
211	Povidone iodine	solution	0.75%	KZN	KZN	KZN	KZN
212	Povidone iodine	solution	10mg/mL	KZN*	KZN*	KZN*	KZN*
433	Praziquantel	tablet	600mg	Forecast*	Forecast*	Forecast*	Forecast*
237	Prednisolone forte	tablet	50mg	Denmark	KZN*	Denmark	KZN*
238	Prednisone	tablet	5mg	Denmark	KZN	Denmark	KZN
429	Primaquine phosphate	tablet	15mg	Forecast	Forecast	Forecast	Forecast
230	Progesterone	injection	50mg/ml	Denmark	KZN*	Denmark	KZN*
458	Promethazine	tablet	10mg	Denmark*	KZN	Denmark*	KZN
459	Promethazine	tablet	25mg	Denmark	KZN	Denmark	KZN
174	Propranolol	tablet	10mg	Denmark	KZN	IMS	IMS
175	Propranolol	tablet	20mg	Denmark*	KZN*	IMS	IMS
176	Propranolol	tablet	40mg	Denmark	KZN	IMS	IMS
316	Pyrazinamide	tablet	500mg	Forecast	Forecast	Forecast	Forecast
430	Quinine	ampoule	300mg/ml	Forecast	Forecast	Forecast	Forecast
431	Quinine	tablet	300mg	Forecast*	Forecast*	Forecast*	Forecast*
106	Ranitidine	tablet	150mg	Prevalence	KZN	Prevalence	KZN
107	Ranitidine HCl	ampule	25mg/ml	Prevalence	KZN	Prevalence	KZN
309	Rifampicin	capsules	150mg	Forecast	Forecast	Forecast	Forecast
310	Rifampicin	capsules	600mg	Forecast	Forecast	Forecast	Forecast

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
318	Rifampicin/isoniazid	tablet	150/75mg	Forecast*	Forecast*	Forecast*	Forecast*
319	Rifampicin/isoniazid	tablet	300/150mg	Forecast	Forecast	Forecast	Forecast
320	Rifampicin/isoniazid	tablet	60/60mg	Forecast	Forecast	Forecast	Forecast
321	Rifampicin/isoniazid/pyrizinamide/ethambutol	tablet	150/75/400/275mg	Forecast*	Forecast*	Forecast*	Forecast*
311	Rifampin (Rifampicin)	capsule	300mg	Forecast*	Forecast*	Forecast*	Forecast*
410	Risperidone	tablet	0.5mg	Prevalence	KZN	Prevalence	KZN
411	Risperidone	tablet	1mg	Prevalence	KZN	Prevalence	KZN
330	Ritonavir	capsules	100mg	Forecast	Forecast	Forecast	Forecast
331	Ritonavir	oral solution	80mg/mL	Forecast*	Forecast*	Forecast*	Forecast*
443	Salbutamol	inhaler	100mcg/dose	Prevalence	KZN	Prevalence	KZN
444	Salbutamol	inhaler	100mcg/dose	Prevalence*	KZN*	Prevalence*	KZN*
445	Salbutamol	solution for inhalation	0.50%	Prevalence	KZN	Prevalence	KZN
455	Salbutamol	ampoule	1mg/mL	Prevalence	KZN	Prevalence	KZN
456	Salbutamol sulfate	syrup	2mg/5ml	Prevalence	KZN	Prevalence	KZN
202	Silver Sulfadiazine	topical cream	10mg/g	Denmark	KZN	Denmark	KZN
190	Simvastatin	tablet	10mg	Denmark	KZN	IMS	IMS
191	Simvastatin	tablet	20mg	Denmark	KZN	IMS	IMS
152	Sodium chloride	ampoule	0.90%	Denmark*	KZN	Denmark*	KZN
153	Sodium chloride	ampoule	0.90%	Denmark*	KZN*	Denmark*	KZN*
154	Sodium chloride	solution	0.90%	Denmark*	KZN*	Denmark*	KZN*
155	Sodium chloride	solution	0.90%	Denmark	KZN	Denmark	KZN
156	Sodium chloride	solution	0.90%	Denmark*	KZN	Denmark*	KZN
157	Sodium chloride	solution	0.90%	Denmark*	KZN	Denmark*	KZN
394	Sodium valproate	CR tablet	200mg	Prevalence	KZN	IMS	IMS
395	Sodium valproate	tablet	100mg	Prevalence	KZN*	IMS	IMS
396	Sodium valproate	oral solution	200mg/5mL	Prevalence	KZN	IMS	IMS
397	Sodium valproate SR	SR tablet	500mg	Prevalence	KZN	IMS	IMS

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
172	Spironolactone	tablet	100mg	Denmark	KZN	Denmark	KZN
173	Spironolactone	tablet	25mg	Denmark	KZN	Denmark	KZN
294	Streptomycin sulfate	injection	1g	Forecast*	Forecast*	Forecast*	Forecast*
120	Sulfasalazine	tablet	500mg	Denmark	KZN	Denmark	KZN
468	Tamoxifen	tablet	20mg	Prevalence	Prevalence	Prevalence	Prevalence
342	Tenofovir	tablet	300mg	Forecast*	Forecast*	Forecast*	Forecast*
350	Tenofovir/emtricitabine	tablet	300/200mg	Forecast*	Forecast*	Forecast*	Forecast*
356	Tetanus Immune Globulin	injection	250IU	KZN	KZN	KZN	KZN
369	Tetracaine HCl	eye drops	0.50%	KZN	KZN	KZN	KZN
198	Tetracaine/arnica/salvia/aluminium	oral ointment	0.5/10%	KZN	KZN	KZN	KZN
200	Tetracycline HCl	topical ointment	3%	Denmark*	Denmark*	Denmark*	Denmark*
244	Tetracycline HCl	capsule	250mg	Denmark	KZN*	IMS	IMS
142	Tranexamic acid	ampule	100mg/mL	Denmark	KZN	Denmark	KZN
143	Tranexamic acid	tablet	500mg	Denmark	KZN	Denmark	KZN
303	Vancomycin	vial	500mg/10ml	KZN	KZN	IMS	IMS
304	Vancomycin	vial	1000mg	KZN	KZN	IMS	IMS
185	Verapamil	tablet	40mg	Denmark	KZN	IMS	IMS
138	Warfarin	tablet	5mg	Denmark	KZN	Denmark	KZN
103	Water for injection	ampoule		KZN	KZN	KZN	KZN
104	Water for injection	ampoule		KZN	KZN	KZN	KZN
105	Water for injection	ampoule		KZN	KZN	KZN	KZN
333	Zidovudine	syrup	50mg/5mL	Forecast*	Forecast*	Forecast*	Forecast*
334	Zidovudine	tablet	100mg	Forecast*	Forecast*	Forecast*	Forecast*
335	Zidovudine	tablet	300mg	Forecast	Forecast	Forecast	Forecast
474	Zidovudine/Lamivudine	Tablet	60 mg / 30 mg	Forecast	Forecast	Forecast	Forecast
475	Zidovudine/Lamivudine/Nevirapine	Tablet	60 mg / 30 mg / 50 mg	Forecast	Forecast	Forecast	Forecast
136	Zinc	syrup	10mg/5mL	KZN	KZN	KZN	KZN

Item ID	Compound	Formulation	Strength	Scenario 1 source	Scenario 2 source	Scenario 3 source	Scenario 4 source
137	Zinc	tablet	20mg	KZN	KZN	KZN	KZN

* indicates that this method of estimation resulted in zero consumption for this drug in the given scenario

Appendix 1.2: Detailed methods for costing exercise

1. Creating the list of medicines

A critical question to address before starting this exercise was its scope. We sought to conform to the principle of essential medicines by including the most efficacious, safe and cost-effective treatments for priority disease conditions in low- and middle-income countries (LMICs). This analysis focused on medicines that can be administered in relatively low-resource health systems, without specialized care.

From the most recent core WHO Model List of Essential Medicines (WHO EML), we included all medicines categorized for use at the primary care level, and excluded those that are used only in tertiary care settings; secondary care medicines for priority or high-burden diseases in LMICs were included. Priority was defined based on current and estimated future public health relevance, and potential for safe and cost-effective treatment. The WHO core EML includes some products that were not modelled here due to data limitations, for example, some medicines for cancer, advanced cardiovascular care and hepatitis. For many of these conditions, global burden of disease data cannot be used to estimate demand for medicines as there is a complex progression through therapy options, based on an individual's pathology. Additionally, since some of the products are new, there are limited past-use data from LMICs. Furthermore the prices for some of these products are likely to change significantly in the future as the markets are nascent and evolving. In addition, a few additional primary care medicines were included based on national medicines lists from Iran and South Africa. We also removed all duplicates and standardized spellings (including across brand and generic names).

Using the WHO EML, we specified dosage forms and strength for these medicines (including multiple forms and strengths for some medicines). If the WHO EML did not include this information, we referred to procurement data from KwaZulu-Natal and, when still unclear, to the South African National Department of Heath master procurement database. We omitted information on pack size, because various lists and formularies include different pack sizes; and a brief analysis revealed no consistent relationship between pack size and unit price (for the smallest dosing unit, e.g. tablet, capsule or ml in case of liquids). As a result, each unique medicine was included only with an associated dosage form and strength.

We matched each unique medicine on the list to an ATC (Anatomical Therapeutic Chemical) classification based on its active ingredient and indication, and a DDD (defined daily dose) based on the dosage form (http://www.whocc.no/atc_ddd_index/). For combination medicines, the DDD for each component was used and then summed during analysis. For medicines without a DDD, we defined a dosing unit based on the functional unit; for example, a 5 milligram suppository was assumed to have a dose of 5 milligrams per day. However, when data from IMS Health were incorporated in the analysis (see below), the IMS Standard Unit was used: the functional unit as described above for oral solids, suppositories and vials; for liquids, a quantity of 5 millilitres (thus a 100 millilitre bottle of suspension would include 20 doses of a medicine).

2. Estimating quantities

We applied an overall decision rule to estimate quantity required per medicine. First, for medicines with pre-existing demand scenario data (i.e., HIV, TB, malaria, and schistosomiasis), we used those numbers. Second, for medicines with a single indication, we used prevalence data to estimate the number of people requiring treatment in LMICs. Lastly, for all other medicines (i.e., those with multiple indications or for symptom relief), we used data on previous consumption.

Demand data

External groups such as Clinton Health Access Initiative,[1] AIDS Medicines and Diagnostics Service,[2] UNITAID's ACT forecasting project,[3] the Reproductive Health Supplies Coalition,[4] and the Stop TB Partnership[5] create global demand forecasts for many of the products on our list (refs to be added. Such forecasts are typically constrained-need projections based on funding availability, disbursement timing and other scale-up constraints. In broad terms, these demand forecasts project the epidemiological need for a given disease in all LMICs, then estimate the number of people on treatment, and adjust for program target, case detection and other constraints that could not be overcome even with unlimited funding. This patient volume is translated into product demand (i.e., number of pills, tablets, capsules, vials) per country based on a standard treatment protocol; and these national-level estimates are aggregated to a global estimate.

These forecasts rely on several assumptions, which are detailed in Appendix 1.3. For example, all assume complete adherence to WHO or other normative guidelines on medicine use and duration. Clinically inferior products are therefore assumed to be discontinued if there is strong WHO recommendation against their use. This assumption would be violated in real-world situations of continued use of inferior products (e.g., stavudine for HIV/AIDS or chloroquine for malaria).[6] The global forecasts capture underlying need and translate it into a demand forecast based on funding availability, scale-up plans and other health system related constraints. The analysis presented here attempts to capture demand in an ideal scenario with low barriers to access to care and full funding. Whenever available, we therefore utilized the unconstrained scenarios of these forecasts; but in many cases, we readjusted the forecasts to reflect the unconstrained needs estimate required for the purposes of this study.

Consumption data

There were three sources of data for calculating previous consumption, and these estimates were applied to different analysis scenarios (see Analysis Scenarios section).

- First, we used a combined dataset of all depot purchases and direct deliveries to public sector health facilities in KwaZulu-Natal province, South Africa, between 1 December 2014 and 30 November 2015. This dataset thus captures all public sector medicine purchases in this province for a 12-month period. The KwaZulu-Natal (KZN) data are reported as quantity procured per item (an item is defined as a medicine with a defined strength and dosage form). These were converted into milligrams (based on strength, pack size and quantity procured), and divided by the WHO DDD for this item (to calculate the DDD procured per year) and then by the midyear KZN population size (to calculate the DDD per person per year).
- Second, we used data from the Denmark Medstat database (http://medstat.dk/en), which includes data from the Register of Medicinal Product Statistics and the Danish State Serum Institute about all medicines sold to individuals (via pharmacies and non-pharmacy outlets), as well as to primary health facilities and hospitals. We used the most recent data available (2014). Most Denmark data were reported as DDD per 1000 people per day, so these were arithmetically scaled to the DDD per person per year; for those reported as packs, items, or quantity (litres or millilitres) per 1000 people per day, these were converted as appropriate to the unit in which price was available for this item.
- Lastly, IMS data were used from four LMICs: Hungary, South Africa, Thailand and Turkey. Data for 2014 were used. In these countries IMS collects data from ambulatory and hospital channels. Supplies to military hospitals and prisons are excluded except in Thailand where military hospitals are included in the sampling frame. Data are generally collected on a sample basis and projected based on geography and supply chain characteristics (for example type of specialty or size of a hospital). South Africa hospital and Turkish hospital data are not projected. South African hospital data reflects sales information from 5 of the 8 largest provinces, in Turkey coverage is estimated at 94% and 97% respectively. Information on the accuracy of the audits, and the methods used to validate the data can be found at http://www.imshealth.com/en/acts. IMS data are collected

as packs but the weight of each molecule within the pack is added as part of the referencing system. This information, together with the calculation of Standard Units, as described above, was used to calculate DDDs per person per year. Data from the 7 countries are used to calculate a median, and an upper and lower limit.

Consumption of a specific medicine in a given context may depend on treatment protocols, prescribing preferences, and available substitutes. So we identified all possible therapeutic substitutes for medicines with the same indication on our list based on the second or third level (therapeutic subgroup) WHO ATC and dosage form; additionally, where IMS data were used, comparison with the EphMRA list of medicines falling into the same ATC class. We made the assumption that, in a hypothetical clinical scenario wherein only the listed item was available, its consumption would be equal to the summed consumption of all these substitute medicines. Using this comprehensive substitution matrix, we identified the consumption of all substitutes, converted these to DDDs as described above, and added these together to estimate the total consumption for each medicine on our list in DDDs. We assumed that the reported data covered all drug procurement mechanisms for these populations, so could calculate population-based consumption directly from the reported data.

For items with multiple dosage forms and/or strengths on our list, we allocated total consumption across the forms and strengths based on the Denmark and KZN data. We estimated the proportion of consumption per dosage form, and then per strength, within each medicine – and split the DDD per person per year for that compound accordingly. In cases where Denmark data were used to calculate the DDD, these items had their proportional allocation also determined from the Denmark data; likewise, other medicines had KZN data used for both DDD calculation and proportional allocation.

The resulting DDD per person per year for each unique item on our list was then multiplied by the population in low- and middle-income countries to calculate how much consumption would occur in these countries (assuming the same underlying degree and pattern of consumption as in the underlying dataset(s)). This was then multiplied by the WHO DDD for this item to calculate the total milligrams consumed in low- and middle-income countries; and then divided by the milligrams per unit (e.g., tablet, or millilitres, etc.) for this item to obtain an estimated number of units needed in low- and middle-income countries per year.

Prevalence data

The Global Burden of Disease (GBD) project supplied information on the number of people with each disease/condition in LMICs. For medicines on our list that did not have epidemiologic data from GBD, we conducted extensive literature reviews to identify a prevalence point estimate.

We then applied an estimate of treatment coverage to capture how many of these people would use the medicine. Because this costing model is a normative exercise – aiming to estimate the cost of providing essential medicines to all those who need them in low- and middle-income countries – these estimates were based on the level of treatment coverage attained in higher-income settings. (See Appendix 1.4 for a list of treatment coverage estimates used in this analysis.) This estimate of treatment coverage was used to scale the number of people with each disease/condition to the number who would use the relevant medicine.

For medicines with multiple dosage forms and/or strengths on our list, we applied the same process as described above for dividing across these: proportional allocation based on Denmark data, or where these would be misrepresentative, KZN data. For indications with multiple medicines on our list (e.g. GERD, diabetes, epilepsy), standard treatment guidelines identify the first, second and third line treatment options – but they do not provide information on splitting a patient population across these first, second and third line treatments. We therefore searched the literature for information on the percentage of patients with each utilization pattern (Appendix 1.4 includes this information).

We then multiplied the number of people who would use each unique medicine by the WHO DDD for this item, to calculate the number of milligrams needed per year per unique item. All medicines on our list require ongoing treatment, so we could assume a full year of constant treatment, with exceptions. First, iron deficiency anaemia has variable treatment duration but we maintained the 1-year assumption for simplicity. Second, there is an 8-week treatment duration for GERD[7], so we assumed that each person using this medicine required exactly 56 days of the DDD. Third, antiviral medicines for herpes can be used as either suppressive or episodic treatment, with differing daily doses and durations; we assumed that 90% of patients would be on short episodic therapy and the rest would

use this suppressive therapy. The total milligrams per item were then divided by the strength of each item, to calculate the total number of units needed for each medicine on the list.

3. Estimating prices

Unit price data were obtained from the International Drug Price Indicator Guide (IDPIG). For each unique product, we used the supplier median price; if this was unavailable, we used the lowest buyer price from the IDPIG. If the IDPIG did not report a price for a given product, we calculated unit procurement price based first on KZN procurement data (2014) or else from Iran public sector procurement (2014). Average yearly exchanges reported by IRS were used to convert from National Currency Unit into US dollar 2014.

Prices for South Africa's FTC were assumed for lowest prices for 3TC. (Even though RSA does not currently purchase 3TC, in case they did they are likely to negotiate to obtain prices closer to their current FTC prices.) For some of the medicines in this study (particularly ARVs), the single innovative manufacturer engages in tiered pricing. The prices used in this estimation are the lowest tier prices. Admittedly, some countries on our list are not eligible for the lowest tier prices. Similarly, the lowest prices we use are based on the assumption of generic availability. IP may prevent some countries from availing the generic prices.

4. Analysis scenarios

There were two main scenarios of interest for this analysis. In both scenarios, demand- and prevalence-based quantity estimates (as described above) were kept constant. The only thing that changed was the source of consumption data for those items using this method of quantity estimation:

1. What if consumption of medicines in low- and middle-income countries looked like Denmark?
2. What if consumption of medicines in low- and middle-income countries looked like KwaZulu-Natal?

In Scenario 1, data from Denmark were used to estimate consumption per item (both DDD for each medicine, and the proportional allocation of this across dosage forms and strengths) – except for medicines that would be rarely used in Denmark (e.g., antihelminthics) or would be used very differently in many low- and/or middle-income settings (e.g., antifungals for which usage would be higher in settings with higher HIV prevalence). For these medicines, consumption data from KZN were used in Scenario 1. In addition, we explored two alternate scenarios (3 and 4) where consumption data were replaced by data from IMS Health from four LMICs. (See Appendix 1.1 for a list of all the medicines and their data sources for scenarios 1, 2, 3 and 4.)

5. Sensitivity analyses

Quantity estimates	Demand forecast data	Different scenarios as published from the base models
	Prevalence data	Confidence intervals around point estimates
	Treatment coverage data	Set 50% as lower bound (no higher bound because the base case used a "best" scenario – i.e., treatment coverage from a high-income setting)
Price estimates	Unit prices	Lowest and highest prices listed in IDPIG
	Mark-ups (quality assurance, supply chain)	Upper limit: mark-ups for supply chain costs (12%),[8] and for quality assurance (1.7%)[9]

Appendix 1.2 – Reference List

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Appendix 1.3: Assumptions

We made a number of assumptions for this modeling exercise:

- First, a major assumption (in using KZN and Denmark consumption data along with the substitution matrix) is that clinicians and patients consistently follow treatment guidelines; and those who do not would randomly distribute across possible medicines (within a therapeutic group), or dosage forms, or strengths. This assumption would be violated and would impact the results of this model if, in real clinical settings, clinicians are non-randomly inclined towards substitutes, and in particular those with particularly high or low prices – but we had no reason to believe this might be the case, so made this assumption so the model could be fully specified.
- Second, even when using prevalence data to estimate the number of individuals in need for treatment, it is unknown how many individuals require a first, second or subsequent treatment line. We assumed that split between different lines of treatment are similar across populations. Because this model was taking a normative costing approach, and assuming very low barriers to access to medicines and services, we felt more confident in making this assumption. We also conducted literature reviews to support our assumptions about treatment coverage and how patients divide across treatment lines, and we primarily incorporated data from higher-income settings where such barriers would likely be lowered.
- Third, there are many assumptions embedded in the demand forecasts used here – for example, whether constraints in diagnosis may in fact lead to under-estimates of the number of people with each disease; and that certain historic behaviors (such as countries' preferences for procurement of different triple fixed-dose combinations) would continue into the future.

Additionally, there were assumptions incorporated within the ARV demand forecasts:

- The total number of people on treatment was assumed to be 28.7 million adults and 2.3 million children. This is based on country targets and does not reflect funding commitment/availability, diagnostic and other scale up barriers that may be encountered. It is still lower than the 90-90-90 targets.
- Most adults on first line treatment were assumed to be on one of the two triple FDCs: TDF+3TC+EFV, TDF+FTC+EFV.
- Historical procurement split in LMICS between these two triple FDCs was used to project split between them.
- Global ARV forecasts made based on country projections as captured in WHO/CHAI/Avenir Health document were used to estimate the splits for second line treatment.
- In conformity with WHO recommendations it was assumed that there would be no use of d4T in the future.
- It was assumed that there would be no use of TDF individually and it will only be used in the FDC forms.
- Single 3TC use was restricted to the 150 mg strength only primarily for patients unable to take FDC and who need dose adjustments for renal impairment etc. 3TC 300 mg strength was assumed to have zero demand.

Another set of assumptions was used for the malaria medicine forecasts:

- Projections for number of Pf and Pv cases in 2016 were used from a forecast developed by the William Davidson Institute. These are based on a combination of historical WMR case estimates and API based projections.
- Treatment policy for uncomplicated Pf, Pv and severe malaria in each country was used from the World Malaria Report 2014. Full adherence to the treatment policy was assumed to estimate demand for SP, Primaquine, Quinine and CQ.
- ACT demand forecast was taken directly from the forecast developed by the William Davidson Institute. The ACT demand forecast included three demand scenarios: Low ACT demand, Moderate demand and high demand. These scenarios already included assumptions about greater use of RDTs.
- The total ACT demand was split into doses/strength based on past breakdown of doses/strength.
- Our essential list only had one ACT formulation so we there was no need to split total ACT demand into demand for individual formulations.
- Going with the assumption of normative estimates and adherence to treatment guidelines, the demand for oral quinine and chloroquine liquid suspension was assumed to be zero.

The TB medicine forecasts also included assumptions:

- All patients detected with pulmonary TB were assumed to be put on treatment.
- 95% of patients on first line treatment were assumed to be on standard patient kits.
- Full adherence to treatment guidelines was assumed.
- For MDR-TB, the split between demand for Group 2 medicines was based on historical split between these medicines from GDF & Global Fund procurement data.
- The only feasible regimens based on the medicines included in our list were the following:
    - 8 Amikacin/Ofx/Ethionamide/Ethambutol 12 Ofx/Ethionamide/Ethambutol
    - 8 Capreomycin/Ofx/Ethionamide/Pyrazanamide 12 Ofx/Ethionamide/Pyrazanamide
    - 8 Amikacin/Ofx/Ethionamide/Pyrazanamide 12 Ofx/Ethionamide/Pyrazanamide
    - 8 Capreomycin/Ofx/Ethionamide/Ethambutol 12 Ofx/Ethionamide/Ethambutol

Appendix 1.4: Treatment coverage assumptions

Table A1.4.1: Percentage of patients with each condition estimated to be on treatment, in high-income countries ("treatment coverage")

Indication	Treatment coverage
Antidepressant	29% (1)
Asthma	51% (1)
Bipolar disorder	29% (1)
Bronchospasm from COPD	83% (2)
Diabetes	94% (1)
Epilepsy	90% (3)
GERD	60% (1)
Gout	50%*
Herpes, varicella	50%*
Hypothyroidism	70%*
Iron supplement	100%
Obsessive Compulsive Disorder	30% [approximate, based on (1)]
Parkinson's	50%*
Schizophrenia	30%[approximate, based on (1)]
Breast cancer	60%*

* indicates an estimated value, and/or expert opinion

Table A1.4.2: Medicine coverage: percent of patients with a condition estimated on each listed drug

Compound and formulation	Medicine coverage
Ranitidine tablets	20%
Omeprazole capsules	80%
Insulin	15%
Metformin tablets	72%
Glibenclamide tablets	2%
Gliclazide tablets	88%
Ferrous sulfate tablets	100%
Levothyroxine tablets	100%
Clofazimine tablets	100%
Dapsone tablets	100%
Aciclovir vial	100%
Allopurinol tablets	100%
Phenobarbital tablets	12%
Phenytoin sodium injection	26%
Clonazepam tablets	5%
Carbamazepine tablets	22%
Sodium valproate tablets	49%
Biperiden tablets	8%
Levodopa/carbidopa 10 tablets	60%
Chlorpromazine tablets	6%
Fluphenazine decanoate	5%
Haloperidol tablets	12%
Clozapine tablets	4%
Lithium carbonate tablets	29%
Risperidone tablets	69%
Amitriptyline 25 mg 28 tablets	19%
Fluoxetine capsules	74%
Salbutamol inhaler	100%
Beclomethasone inhaler	2%
Budesonide inhaler	58%
Ipratropium inhaler	100%
Ipratropium inhalation solution	100%
Salbutamol ampoule	2%
Salbutamol solution	10%
Acetylcholine eye drops	17%
Tamoxifen tablets	100%

Data sources for values in Table A3-2: Diabetes (4); Psychiatric and mental health medicines (5-15); COPD (2, 16); GERD (17-19); Epilepsy (20-22); Parkinson (23); Asthma (24); Hypothyroidism (25)

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Appendix 1.5

Table: Total pharmaceutical expenditure as percentage of Gross Domestic Product (GDP), 2010

Countries Income group	N	Population (thousands)	Total pharmaceutical expenditure (% of GDP)				Public pharmaceutical expenditure (% of GDP)	Total health expenditure (% of GDP)	
			Mean (%)	Median (%)	Min (%)	Max (%)	Mean (%)	N	Mean (%)
High	49	1,091,925	1·4%	1·4%	0·2%	2·9%	0·8%	49	8·1%
Upper middle	53	2,457,274	1·4%	1·3%	0·3%	3·2%	0·6%	32	6·8%
Lower middle	48	2,428,619	1·6%	1·3%	0·2%	5·2%	0·5%	48	6·6%
Low	32	748,953	1·6%	1·5%	0·4%	3·6%	0·4%	53	6·9%
All countries	182	6,726,772	1·5%	1·4%	0·2%	5·2%	0·6%	182	7·1%

Source: Authors' own analysis of WHO National Health Accounts (NHA) data files for 2010.

Appendix 1.6

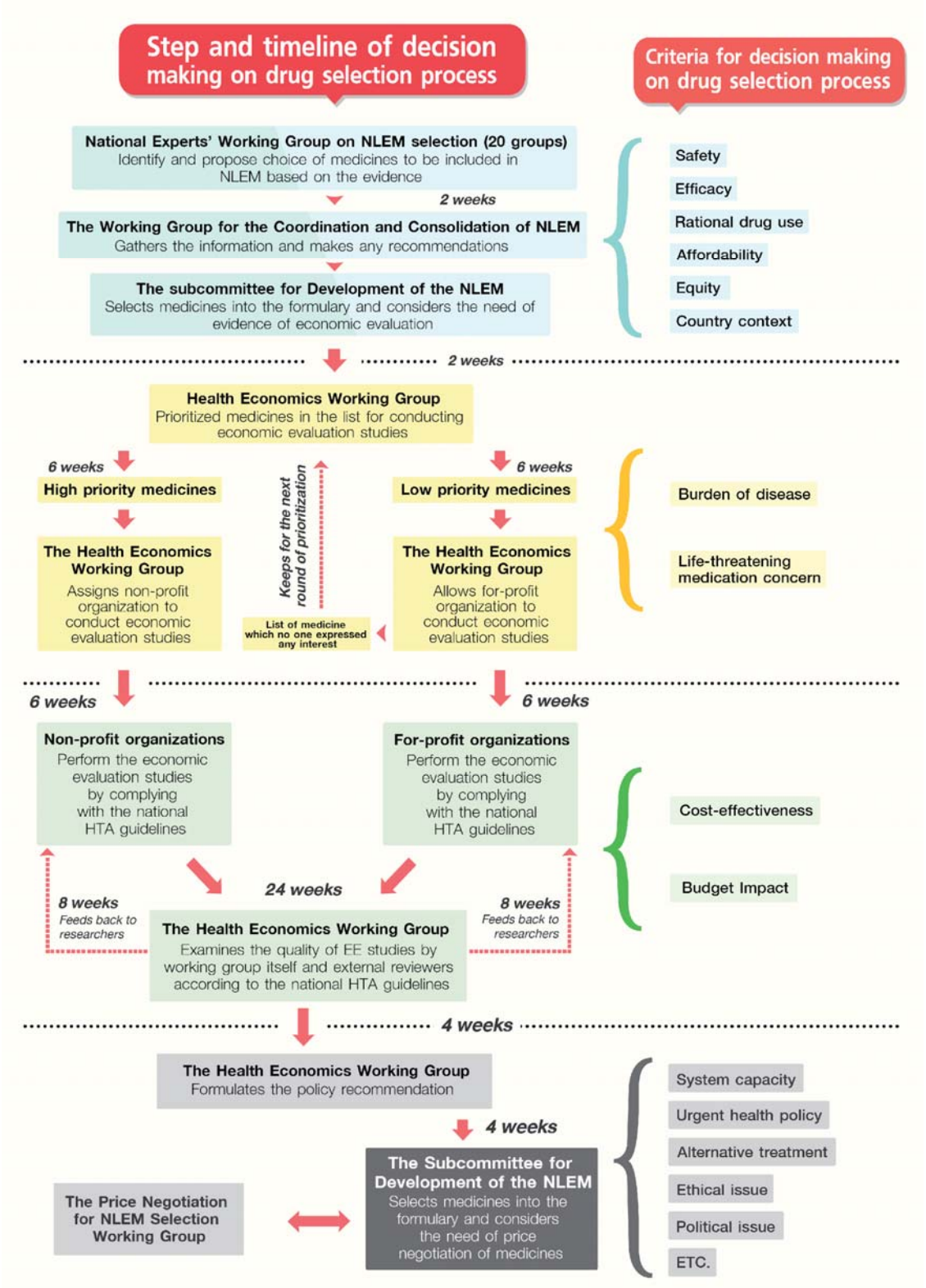
Panel: The Lancet Commission on Essential Medicines Policies

The Lancet Commission on Essential Medicines Policies was established in July 2014. The Commission's charge was to:

- synthesise lessons learned from the 30 years of development and implementation of essential medicines policies, after Nairobi;
- develop an agenda for the next 20 years of national and global policies on essential medicines;
- raise global awareness of the importance of essential medicines policies to broader global health and sustainable development goals, especially universal health coverage; and,
- define key questions for further operational research that will contribute to increasing the effective and efficient implementation of essential medicines policies.

The 21 Commissioners, from 12 countries, were invited in their personal capacity on the basis of their technical expertise. Three in-person meetings were held to define the focus of the work of the Commission and develop the content of the report. Between meetings, commissioners worked on aspects of the report in smaller groups, sometimes with additional research support.

Appendix 2.2: HITAP Assessment Process



Appendix 2.3

Figure 5 - Definition

Data: from 20 high income and 7 middle income countries

Biological: The definition used to create the list of biological molecules is as follows: (a) Structure: Biologic molecules are complex macromolecules, typically with some form of polymer structure. (b) Identifiable: Any 'molecule' where the molecule name is descriptive and the actual composition of the molecule is not identified (e.g. Vegetable Extract) is not classified as a biologic. (c) Use: Biologic molecules must be, or are intended to be, clearly defined active therapeutic ingredients in a product. (d) Regulatory: Biologic molecules must have undergone (or be undergoing) a regulatory human clinical trial programme under the auspices of a national or regional regulatory authority (e) Licensing: Products containing biologic molecules must have been classified by IMS at one time as an Original, Licensed or Unassigned brand. Original and licensed brands are branded products that is manufactured and/or marketed by the Originator of the active ingredient or under license from the Originator. This step excludes biological molecules such as vitamins. (f) Protection: Molecules must be protected from generic competition or are unassigned. Protection can include: molecule product patents, delivery device patents, composition patents, process patents, Method of Use (MOU) patents, Supplementary Protection Certificates (SPCs), Certificats Complementaire de Protection (CCPs), marketing exclusivity, data exclusivity, orphan drug exclusivity, paediatric indication extension and known ongoing litigation. In the event that a molecule was found in conflicting categories (2 instances) these were further investigated and then assigned.

Non-biological: This includes all molecules that were not classified as biological as above.

Protected: Product was protected from generic competition. Calculated on a per month basis, and by country.

No longer protected: Product was protected from generic competition in this country but was not in this period. Calculated on a per month basis, and by country.

Never protected: Product was never protected from generic competition. Calculated on a per month basis, and by country.

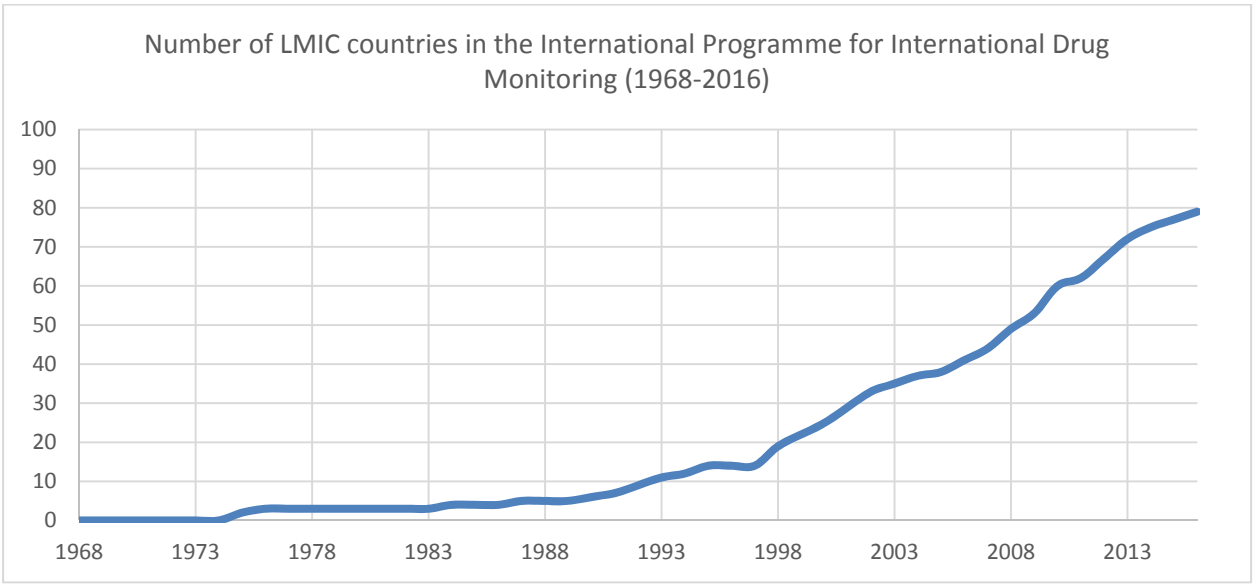
Appendix 3.1

Figure: Examples of falsified artemisinin-combination products found in Africa

The first product (left) is imitating a product containing artemether and lumefantrine, manufactured by IPCA, an Indian generic company. The second product (right) imitates Coartem, also claiming to contain artemether and lumefantrine, imitating a branded product produced by Novartis. Neither product contains any active pharmaceutical ingredient. In both cases the packaging is a close copy of the genuine product. These examples illustrate that both branded and generic products may be the target of falsification. When falsifications infringe on registered trademarks, they are also counterfeits.

Appendix 3.2

Figure: Number of Low- and Middle-Income countries (LMIC) in the International Programme for International Drug Monitoring (1968-2015)



Data from World Health Organization. Accessed August 2016.

Appendix 3.3

Table: Essential Medicines Regulatory Functions

General regulatory functions for medicines	Minimum regulatory functions
• License the manufacture, importation, exportation, distribution, promotion and advertising of medicines • Issue marketing authorisations for products after thorough scientific assessment (medicines registration) • Inspect manufacturers, importers, wholesalers and dispensers of medicines • Control and monitor the quality and safety of medicines on the market; collect and analyse reports on adverse events • Control promotion and advertising of medicines • Provide independent information on medicines to professionals and the public	• Ensure that all premises and activities comply with Good Manufacturing Practice and other relevant standards • Before medicines are marketed, assess their safety, efficacy and quality through a transparent process which may involve various degree of reliance on other regulator's decisions • Control the manufacturing units and supply chain, including informal markets and e-commerce, to prevent illegal trade in medicines • Prevent harmful, substandard and falsified medicines from penetrating the supply chain or reaching the public by other means • Prevent misleading information from reaching the public and health professionals

Source: Adapted from WHO. Effective medicines regulation: ensuring safety, efficacy and quality. WHO Policy Perspective on Medicines. Geneva: WHO. No. 7, 2003.

Appendix 3.4

Panel: Fatal incident in Pakistan

A 2012 incident in Lahore, Pakistan, killed 230 patients and caused serious adverse reactions in more than 850 others. Some batches of a common generic cardiovascular medicine, isosorbide mononitrate, were tested for the active ingredient before the incident and met quality specifications. However, forensic testing of the implicated batches after the event revealed that, in addition to the active ingredient on the label, the product also contained pyrimethamine (an antimalarial medicine) in substantial overdose. The effects of this substance were consistent with the symptoms exhibited by the patients. A key reason for the contamination was the manufacturer's negligent disregard of Good Manufacturing Practice principles. Decentralisation of the medicines regulatory authority in Pakistan to provincial authorities made effective regulation challenging.

Appendix 4

Table A4.1: Evidence from high quality systematic reviews about effectiveness of interventions targeting health professionals *

Type of intervention	Description (Evidence Base)**	Selected results	Summary
Educational materials	Distribution of published or printed recommendations for clinical care, including clinical practice guidelines, audio-visual materials and electronic publications, either personally or through mass mailings. (16 quality reviews; 2 relevant)	Several previous reviews found educational materials alone to be ineffective[1] Current evidence suggests that educational materials may have small effects for improving drug choice[2]	Possible small effect
Educational meetings	Healthcare providers participate in conferences, lectures, workshops or traineeships. (19 quality reviews; 4 relevant)	Educational meetings have mixed effects for improving appropriate care,[3] although one found them to be generally effective[4] Educational meetings had mixed effects on improving antibiotic prescribing, but interactive educational meetings appeared to be more effective than didactic lectures[1] Combined with audit and feedback, educational meetings may be effective for improving appropriate care and prescribing[5]	Mixed depending on style
Educational outreach visits ("academic detailing")	Trained person meets with providers in their practice settings to give information with the intent of changing the provider's practice; information may include feedback on performance (8 quality reviews; 3 relevant)	Two reviews found educational outreach visits by physicians or pharmacists generally effective for improving appropriate care and prescribing[6,7] Results were mixed regarding the relative effectiveness of individual vs. group visits[6] One review indicated mixed effects for antibiotic prescribing[1]	Effective
Opinion leaders	Use of providers nominated by colleagues as Influential sources of clinical advice to promote specific changes in practice. (2 quality reviews; 1 relevant)	Use of local opinion leaders alone or combined with other interventions was generally effective for improving appropriate care outcomes[8]	Effective
Audit and feedback	Summary of clinical performance over specified period which may include recommendations for clinical action; information may be from medical records, computerized databases, or observations from patients. (11 quality reviews; 3 relevant)	Audit and feedback generally effective used alone or combined with other interventions for improving appropriate care outcomes[5,9] Generally effective for improving prescribing outcomes[5] No effect on improving patient-centered clinical consultations when combined with educational training[10]	Effective
Local consensus processes	Providers participate in discussion to ensure that they agree that the chosen clinical problem is important and the approach to managing the problem is appropriate. (0 quality reviews)	No high quality reviews have examined this approach	No evidence
Reminders - computer decision support for drug dosing	Patient or encounter-specific information provided on a computer screen targeting medication dosage. (9 quality reviews; 5 relevant)	Generally effective for improving dosing in hospitals[11,12] but mixed or no effects in outpatient care[13,14] Uncertain effects for improving drug safety[11,12,15] and ineffective for improving other physician or patient outcomes[11,12]	Mixed depending on setting and outcome
Reminders - computerized order entry	Patient or encounter specific information, provided on a computer screen to automate the ordering of medication. (3 quality reviews; 3 relevant)	Mixed effects on improving appropriate care behavior[13,16] No evidence about effects on prescribing or other clinician behaviors[13,15,16]	No evidence
Reminders – general	Patient or encounter-specific information, provided verbally, on paper or by computer, to prompt a health professional to recall information. (16 quality reviews; 2 relevant)	Generally effective for improving appropriate care behavior and some evidence of effectiveness in improving prescribing[17,18]	Generally effective

Type of intervention	Description (Evidence Base)**	Selected results	Summary
Financial incentives	Any change in reimbursement, incentive payment or penalty of healthcare professional, organization or patient. (6 quality reviews; 5 relevant)	Method of payment of primary care physicians appears to affect their behavior, but generalizability is unknown.[19] Provider drug budgets may be effective for improving appropriate use[20] Evidence about pay for performance is mixed and not convincing in many settings[21-23]	Limited evidence of mixed effects
Mass media	Use of communication that reached great numbers of people including television, radio, newspapers, posters, leaflets, and booklets, alone or in conjunction with other interventions; targeted at the population level. (2 quality reviews; 1 relevant)	Despite limited information about the interventions and poor quality research, it appears that mass media interventions may influence use of health care services[24] No direct evidence about use of medicines[24]	No evidence
Patient-mediated interventions	Clinical information not previously available collected from patients and given to providers e.g. depression scores. (5 quality reviews; 2 relevant)	Overall evidence base is limited Patient-mediated interventions appear to have mixed effects on improving appropriate care,[1,25] and little or no effect on improving antibiotic prescribing[1]	Limited evidence of small effects
Tailored interventions	Strategies tailored to address specific, identified barriers to change in professional performance. (2 quality reviews; 1 relevant)	Effective for improving appropriate care behavior and prescribing[26] No evidence about which aspects of tailoring improve effectiveness	Effective
Multifaceted interventions	Any combination of two or more professional, organizational, financial, structural or regulatory interventions designed to improve prescribing practices or other health provider behavior. (31 quality reviews; 8 relevant)	Most reviews have found multifaceted interventions to be generally effective to improve appropriate care and prescribing outcomes,[5,6,27-29] although some have reported mixed effects for antibiotic prescribing,[1,9] and for asthma and COPD care management[30]	Generally effective

* Evidence from Rx for Change database, http://www.cadth.ca/en/resources/rx-for-change, accessed January 22, 2016

** Number of high quality or key systematic reviews identified; number of these reviews with enough studies to draw conclusions about the outcomes most relevant to use of medicines

Table A4.2: Evidence from high quality systematic reviews about effectiveness of interventions to improve use of medicines by patients and consumers *

Type of intervention	Description (Evidence Base)	Selected results	Summary
Providing information or education	Strategies to provide information to consumers or promote health or treatment; can be provided to individuals or groups, in print or verbally, or face to face or remotely, simple or as part of a complex strategy (38 quality reviews; 14 relevant)	Information or education as a single strategy has few effects on adherence, use, or outcomes[31-39] Information or education in conjunction with self-management skills training or counselling more consistently improved medication use[32,39-44]	Ineffective alone, but effective in combination
Supporting behaviour change	Strategies focusing on adoption or promotion of health and treatment behaviours; may address underuse, overuse or misuse of medicines, and may include practical strategies to assist consumers in taking medicines correctly such as reminder devices, pre-packaging of multiple medicines, or simplified medicine formulations (45 quality reviews; 17 relevant)	Support, information, or education, alone or in multifaceted strategies, had inconsistent effects on adherence and outcomes across a range of conditions [35-39,41-43,45,46] Written or verbal information alone is only occasionally effective[33,34] Simplified dosing regimens improved adherence in half of studies,[35,37,38] while reminders had mixed effects[35,38, 41] Changing organization or delivery of care (e.g., pharmacist or nurse-led service delivery) had mixed effects on adherence and clinical outcomes[7,37,39,47,48]	Mixed depending on target behaviour and condition
Facilitating communication and decision making	Strategies to involve consumers in medicine decision making; to express their beliefs, values, or preferences about treatments and care; or to optimize communication with health professionals. (16 quality reviews; 2 relevant)	Decisions aids improved knowledge and decision making, but few changes in treatment, adherence, or clinical outcomes[49] Delayed prescribing decreased antibiotic use, but had mixed effects on clinical outcomes and decreased satisfaction[50]	Mixed depending on outcome
Improving care coordination or integration	Strategies to improve the coordination or integration of care; can involve interventions that aim to overcome system barriers to medicines use, including access and financial barriers (18 quality reviews; 7 relevant)	Less than half of strategies to improve care delivery and overcome system barriers improved adherence[45] Strategies to improve service quality or change the setting of care for specific conditions had mixed results[36,38,39,51] Reference pricing policies increased use of reference medicines, without affecting total use,[52,53] while patient cost sharing significantly decreased medicines expenditure and overall use[53]	Both effective and mixed
Interventions to prevent adverse events	Strategies to prevent or manage adverse events of treatment or complications of disease; can be for ongoing treatment or related to emergency events, at an individual or at a population level (24 quality reviews; 7 relevant)	Self-monitoring and self -management education decreased anticoagulation adverse events[54] but had mixed results for asthma [36,55,56] and epilepsy[39] Pharmacist-led medication quality reviews decreased adverse events[57] and pharmacy discharge planning reduced medication errors and improved adherence[58]	Both effective and mixed
Building skills and competencies	Strategies to assist consumers to develop a broad set of competencies around medicines use and health, such as medicines management or monitoring; or training consumers in the correct use of treatments or devices to deliver treatment (20 quality reviews; 9 relevant)	Self-monitoring and self-management skills for oral anticoagulation[54] and HAART[42] had positive effects on adherence and mixed effects on clinical outcomes Action plans or self-management education for diabetes,[37 40] cystic fibrosis,[43] asthma, or COPD[55,56,59,60] had mixed effects	Both effective and mixed
Support in care management	Strategies to assist and encourage consumers to cope with and manage their health and related medicines use; can target patients or carers, as individuals or in groups, and can be delivered face to face or remotely (16 quality reviews; 2 relevant)	Too little evidence to assess effectiveness of disease-specific counselling Simple interventions more effective for short-term and complex interventions more effective for long-term treatment[45] Contracts with support (e.g., counselling reinforcement) did not consistently improve adherence or treatment continuation[61]	Complex interventions more effective
Involving consumers in system decision making	Strategies to involve consumers in decision making on medicines use at a system level, such as in research planning, formulary and policy decisions; can involve different roles, such as planning, research, audit and quality reviews and governance (1 quality review; 1 relevant)	Involving consumers in developing patient information material results in material that is more relevant, readable and understandable to patients[62]	Limited information

Type of intervention	Description (Evidence Base)	Selected results	Summary
* Evidence from Rx for Change database, http://www.cadth.ca/en/resources/rx-for-change, accessed September 18, 2015			

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Appendix 4.1

Table: World Health Assembly resolutions related to medicines use

Resolution Number	Year	Topic
WHA39·27	1986	Revised drug strategy
WHA41·16	1998	Rational drug use including counterfeit medicines and product quality
WHA43·20, WHA45·27	1992 1996	Ethical criteria for drug promotion*
WHA47·13	1994	Role of the pharmacist in support of the WHO revised drug strategy
WHA51·9	1998	Cross-border advertising, promotion and sale of medical products using the Internet
WHA57·14	2004	Scaling up treatment and care within a coordinated and comprehensive response to HIV/AIDS
WHA60·16	2007	Progress in the rational use of medicines
WHA67·22	2014	Access to essential medicines
WHA43·20 WHA45·27 WHA49·14 WHA52·19 WHA54·11	1992 1996 1996 1998 2001	WHO programs and medicines strategies

*see Panel 2: Better Regulatory Control of Pharmaceutical Promotion is Necessary

Appendix 4.2

Table 4: Seven dimensions and elements in routine data

Data dimension	Routine data elements (examples)
Pharmaceutical *(provides information about the medicinal products themselves)*	Molecule, therapeutic class, dosage form, strength, package size, manufacturer, distributor, product quality, product costs to payer (patient, insurer or government).
Longitudinal *(provides information on use of product over time)*	Time of event (diagnosis, prescribing, dispensing, outcome/death), time between events, unique patient identifier
Geographic *(provides information on location of use of product)*	National, regional, local, facility
Organizational *(provides information on setting for use of product)*	Facility type (public or private, formal or informal, primary care or specialty), provider type and characteristics
Socio-demographic *(provides information on characteristics of patients treated)*	Patient age, gender, religion, caste, deprivation
Clinical *(provides information on health status of patients and health outcomes)*	Diagnosis, diagnostic tests, organ function, concomitant diseases
Financial *(provides information on costs associated with use of product)*	Cost associated with using a product (e.g., costs of tests to identify appropriate patients, administration fees, cold chain distribution) and with monitoring its use (e.g., safety monitoring, medicines utilisation reviews); cost of care (increases and offsets) associated with use of a product.

Appendix 4.3

Instagram post by Kim Kardashian promoting a morning sickness medication

kimkardashian FOLLOWING

464k likes 1w

kimkardashian OMG. Have you heard about this? As you guys know my #morningsickness has been pretty bad. I tried changing things about my lifestyle, like my diet, but nothing helped, so I talked to my doctor. He prescribed me #Diclegis, I felt a lot better and most importantly, it's been studied and there was no increased risk to the baby. I'm so excited and happy with my results that I'm partnering with Duchesnay USA to raise awareness about treating morning sickness. If you have morning sickness, be safe and sure to ask your doctor about the pill with the pregnant woman on it and find out more www.diclegis.com; www.DiclegisImportantSafetyInfo.com

view all 10,983 comments

imoumaima @youssefchorfi

flawlessfashionstore Idk if shes getting paid for this and do not care. But it is safe for mom & baby. I called my doctor because i couldn't even keep water down.

Appendix 5

The patent-based innovation system has been globalized

The patent system is a social policy tool to encourage innovation for the benefit of society as a whole. Governments grant patents to innovators as a reward for an innovation when it is useful, new, non-obvious, and described in a manner that people of skill in the relevant field can understand. A patent holder can prevent others from using the innovation for a defined period, and thus recoup investments. Society can then benefit from the disclosure of the innovation and its wider application.

However, patents are often granted at a stage when little is known about the medical usefulness of a product, and patents are awarded irrespective of whether the innovation is important or trivial. Patents can also hamper innovation by excluding others from doing research on the patented subject matter or from accessing research tools.

With the creation of World Trade Organization (WTO) in 1994 and the accompanying Agreement on Trade Related Intellectual Property Right (TRIPS), the patent-based innovation system became globalised. TRIPS sets global minimum requirements for the creation and protection of intellectual property (IP), enforceable through WTO, thus introducing medicines patents in many countries that had not previously granted them. Since the adoption of TRIPS, regional and bilateral trade agreements have further expanded the reach of the IP-based system (see below).

A company that holds a patent has a *de facto* monopoly for a certain period of time because no-one else can bring the patented product to market, unless authorised by the patent holder or the government. The price of a patented product can be set by the patent holder and usually far exceeds the actual cost of production. For example, the cost of production of the 12-week hepatitis C treatment with sofosbuvir is estimated at between US$ 68 and US$ 136[1], while the company sells it in the US for up to US$ 84 000.[2] South Africa pays over US$ 3227 per patient per month for branded imatinib, while in India, where the product is not patented, the generic equivalent is priced at US$ 170 per patient per month.[3]

Flexibilities in patent law enabled by the TRIPS Agreement and the WTO Doha Declaration on TRIPS and Public Health of 2001 have been used by a number of countries to secure access to generic medicines. The most frequently deployed flexibilities are compulsory licensing of medicines, government use of patents, and the “LDC waiver“ which grants Least-Developed Countries (LDCs) the right to not grant or enforce medicines patents and test data protection until 2033.

Free trade agreements restrict access to generic medicines

The plethora of trade agreements containing TRIPS-plus provisions that have been concluded in the last decade, including after the adoption of the Doha Declaration on TRIPS and Public Health, are a serious threat to the policy space TRIPS flexibility provides. The US and the EU are systematically seeking higher levels of IP protection in agreements with countries, which affect access to medicines and seriously hamper the full implementation of the Doha Declaration. This is a failure of State parties to take into account their human rights obligations regarding the right to health when entering into bilateral or multilateral agreements with other states.[4]

The following “TRIPS-plus” provisions regularly feature in trade agreements and form part of the negotiating objectives of the US and/or the EU in trade talks. All of these TRIPS-plus features can delay the introductions of generic medicines and thereby affect access to medicines:

- *Patent linkage*: prohibits granting of marketing approval by national medicines regulatory authorities during the patent term without the consent of the patent holder, creating a new function for health authorities in the enforcement of patents on medicines;
- *Data exclusivity:* prohibits for a certain period of time the use of pharmaceutical test data for medicines regulatory purposes. This delays registration of generics and biosimilars regardless of the patent status of the product;
- *Extension of the patent term:* extending the patent term for pharmaceuticals beyond the 20 years required by the TRIPS Agreement;[5]
- *Extension of the scope of patent protection:* allowing patens on known substances for each “new use”;

- *Restrictions on the grounds for compulsory licensing:* contravening the Doha Declaration on TRIPS and Public Health which says that countries are free to determine the grounds for CL;
- *Restrictions to parallel importation:* importation without the consent of the patent holder is specifically allowed under WTO rules.

Some or all of these provisions appear in concluded agreements, such as the Central American Free Trade Agreement (CAFTA),[6] the US-Singapore Free Trade Agreement, the US-Chile Free Trade Agreement, the US-Morocco Free Trade Agreement, US-Peru Trade Promotion Agreement and other agreements that have already been signed such as NAFTA (US, Canada and Mexico). The TRIPS-plus provisions are also included in accession agreements with new WTO members, for example China and Cambodia. Many TRIPS-plus provisions can also be found in the recent Trans Pacific Partnership Agreement (TPPA), which is promoted as the new set of global trade rules. The TPPA's IP chapter is expected to become the template for future trade agreements.[7,8]

The drive for ever-higher levels of IP protection through trade agreements should be stemmed and will likely require intervention at the multilateral level. International access to medicines policies have always benefitted from more inclusive, multilateral negotiations where the needs of LMICs take a more central place. Examples include the Doha Declaration on TRIPS and Public Health and the special patent waivers for LDCs, both a result of talks at the WTO.

Appendix 5 – Reference List

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Appendix 6: Complementary Indicators

#	Indicator
2.e	Number of medicines for which children's-appropriate dosages forms have been included per total number of medicines for which dosage form is available on the national essential medicines/reimbursement list‡
2.f	Policy in place to manage conflict of interest issues for all members involved in medicines selection/reimbursement decision-making process (yes/no)
2.g	Patient OR civil society representation in the medicines selection/reimbursement decision-making process is specifically provided for (yes/no) ‡
2.h	Existence of national clinical trial register with requirement for timely publication of trial results (yes/no)
2.i	Provisions for the publication of summarised clinical trial data submitted to the NMRA (Yes/No) ‡
2.j	Provisions for the publication of summarised clinical trial data submitted to selection/reimbursement decision-makers (yes/no)
3.g	Number of domestic pharmaceutical manufacturers assessed as GMP compliant out of total number of domestic pharmaceutical manufacturers
3.h	Patient or civil society organization representation in the NMRA is specifically provided for (yes/no) ‡
4.f	Operational budget of the independent national medicines use programme/institute as a percentage of total public pharmaceutical expenditure‡
4.g	Policy in place to manage conflict of interest issues for all members involved in independent programme/institute (yes/no)
5.e	Percentage of public financial investment into the development of missing EM out of total public health research expenditure‡
5.f	Number of relevant products recently marketed for which effective access strategies have been established (per company)*

‡ New indicator that requires validation.

* Access strategies should include all LMICs.