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Title: Methodology and results for systematic search, cost and cost-effectiveness analysis, Cancer Volume

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Abstract:

This working paper provides more detailed information on the search strategy and results obtained from the systematic review of the cost and cost-effectiveness of cancer covered in the Cancer Volume of DCP-3. The search was conducted in Pubmed and was limited to journal articles published in English language from 2000 onward. The cost-effectiveness results on screening, diagnosis and treatment of six types of cancer are summarized and presented.

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Annex 16A/DCP3 Working Paper# XX

Methodology and results for systematic search, cost and cost-effectiveness analysis

Cancer Volume

Susan Horton

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This working paper describes in more detail the methods employed for the systematic search undertaken for cost and cost-effectiveness data, summarized in the DCP-3 volume on Cancer (Gelband and others 2015). It also provides supplementary more detailed tables.

The economic analysis was based on systematic searches undertaken for the project. For cancer, the search terms used are listed in Table 1. The literature search undertaken in June 2013 was limited to English language from 2000 onward in PubMed and restricted to published journal articles. The focus was on low and middle-income countries unless specified otherwise.

For specific topics, additional searches were undertaken to augment the database if there were insufficient results obtained. For breast and colorectal cancer, additional searches included searching for studies from selected high-income Asian economies (Hong Kong region of China, Republic of Korea, Singapore, Taiwan province of China). Research from these countries may serve as guidance to middle-income countries in Asia in particular.

These articles were analyzed to extract cost-effectiveness information summarized in the volume. All articles chosen for analysis were read by two readers and any discrepancies in cost-effectiveness data extracted were resolved by discussion. All costs were standardized to US dollars of 2012 as follows. First, costs were converted back into the currency of the original study country using exchange rates from the World Development Indicators (World Bank, 2013). The same source was used to obtain a consumer price index which was used to update prices to the year 2012, and costs and cost-effectiveness numbers were converted then back to US dollars using the market exchange rate. Where the original study used international dollars for a regional grouping (primarily some WHO-CHOICE studies), the conversion to US dollars of 2012 was not undertaken, since published data on consumer price indices and exchange rates are not available on a regional basis.

For interventions involving vaccinations (in this case primarily Hepatitis B (protective against liver cancer) and Human Papillomavirus (HPV: protective against cervical cancer), the cost per vaccine dose (or the cost per "fully vaccinated girl") is given. Vaccine price is a crucial determinant of cost-effectiveness, and vaccine studies are generally done using a range of prices (prior to the final price being known). In Tables 2 and 3, not all the results available in the original sources are summarized. Instead, the Gavi (Global Alliance for Vaccines and Immunization) prices are used for Gavi-eligible countries, and a relevant price used for countries no longer eligible for Gavi funding.

All articles used for cost-effectiveness were graded for quality, using the Drummond and others (2005) checklist, as used by Chao and others (2014), to provide a quality score for each article out of 10. Table 2 contains the cost-effectiveness results and the quality score for five cancers (breast, colorectal, liver, oral and pediatric): note that no studies met the criteria for pediatric cancer. Table 3 contains the results for cervical cancer.

Table 1. Search Terms and Strategy for Literature Reviews Used, Cancer Volume

Cancer type	Country Group	Terms
Breast	HICs	Publication dates 01/01/2006 through to 05/08/2013. Breast neoplasms, breast cancer
	LMICs	2003 through 2013. Breast neoplasms, breast cancer
	All countries (primarily HICs)	Tufts Medical Center Cost-Effectiveness Registry results (http://www.cearegistry.org) as published in Greenberg and others 2010; search through 2007; restricted to English language, cost per QALY
Cervical	LMICs	Cervical cancer; human papillomavirus (HPV); HPV vaccination: cervical cancer prevention: cervical cancer prevention
Colorectal	LMICs	2003 through 2013. Colorectal neoplasms, colonic neoplasms, rectal neoplasms, colorectal cancer, colon cancer, rectal cancer, colonoscopy, sigmoidoscopy
	HICs	Tufts Medical Center Cost-Effectiveness Registry results (http://www.cearegistry.org) as published in Greenberg et al (2010); search through 2007; restricted to English language, cost per QALY
Liver	LMIC	• Hepatitis B vaccination; hepatitis B, HBV, and vaccination, vaccine; hepatitis B screening • Hepatitis C, HCV • Hepatocellular screening; Hepatocellular carcinoma, HCC • Aflatoxin control; screening for liver flukes (Opisthorchis) • Cholangiocarcinoma, bile duct cancer • Treatment with praziquantel for liver flukes
Oral	LMICs	head and neck neoplasms; mouth neoplasms; thyroid neoplasms; esophageal neoplasms; head cancer; neck cancer; oral cancer; esophageal cancer; thyroid cancer
Pediatric	LMICs	pediatric cancer; acute lymphoblastic leukemia; B- and T-Cell acute lymphoblastic leukemia; Burkitt's lymphoma; Burkitt's tumor; Burkitt's leukemia; Wilms' tumor; nephroblastoma; retinal glioblastomas; retinal neuroblastoma; eye cancer; Hodgkin's disease; Hodgkin's lymphoma; Hodgkins lymphoma; Hodgkin lymphoma; childhood Hodgkin lymphoma; childhood Hodgkins lymphoma; childhood Hodgkin's lymphoma; children; infants
Cost terms		cost-effectiveness*; cost-utility*; economics; cost-benefit analysis; costs and cost analysis; cost savings; cost of treatment; cost of disease treatment; economic analysis; cost benefit analysis; QALY; quality adjusted life year*

Source: Authors

Note:
HBV = Hepatitis B vaccination

HCC = Hepatocellular carcinoma
HCV = Hepatitis C vaccination
QALY = quality-adjusted life-year
Geographic terms and individual country names were used to capture country income groups.

Table 2. Results of systematic survey of LMIC literature, cost-effectiveness, breast, colorectal, liver, oral and pediatric cancer

Source	Year	Study Grade	Condition/ Intervention	Country	Cost per outcome	Unit of outcome	Currency	Cost per outcome US $ of 2012[1]
Breast Cancer								
Wong and others (multiple cohort model)	2007	10	Biennial mammography + treat, women 40-69 (vs no screening)	Hong Kong SAR, China	$63,400	QALY	US $ of 2005	$78,759
			Biennial mammography + treat, women 40-79 (vs no screening)	Hong Kong SAR, China	$100,900	QALY	US $ of 2005	$124,964
Okwonko and others (model) (MISCAN model)	2008		Biennial clinical breast exam + treat, women 40-60 (vs no screening)[1]	India	$1341	LY	Int $ of 2001	$257
			Biennial mammography + treat, women 40-60 (vs no screening)	India	$3468	LY	Int $ of 2001	$664
Fonseca and others (model)	2009	10	Anastrazole (vs tamoxifen) for treatment early stage cancer	Brazil	$11,225	LY	US $ of 2005	$21,124
Lee and others[1] (model)	2009		Triennial mammography + treat, women 45-69	Korea, Rep	$100,007	Case found	US $ of 2009	$127,465
			Triennial mammography + treat, women 40-69	Korea, Rep	$154,502	Case found	US $ of 2009	$196,922
Yang and others (observational study)	2010		Treat with adjuvant tamoxifen, ER+, stage 1 or 2 (vs surgery only)	Korea, Rep	$739	LY	US $ of 2005	$852
			As above, either ER+ or PR+ but not both	Korea, Rep	$1217	LY	US $ of 2005	$1403
			As above, ER- and PR-	Korea, Rep	dominated	LY		
			Treat with adjuvant tamoxifen, stage 3, irrespective of ER or PR status (vs surgery only)	Korea, Rep	$393	LY	US $ of 2005	$453
Ginsberg and others (WHO-	2012	10	Treat cancer (all 4 stages) plus annual mammogram			DALY	Int $ of 2005	n/a

CHOICE model)			- 50% coverage - 80% coverage - 95% coverage - 50% coverage - 80% coverage - 95% coverage	AFR-E SEAR-D	$2248 $2253 $2323 $4338 $4362 $4399			
Salomon and others (WHO-CHOICE model)	2012	10	Treat (vs not treat) stage 1/2/3/4	Mexico	$898/1486/ 4526/8271	DALY	Int $ of 2005	$143/237 721/1318
			Treat (vs not treat) cancer, any stage	Mexico	$1411	DALY	Int $ of 2005	$225
			Mammography and treat (vs neither)	Mexico	$11,501	DALY	Int $ of 2005	$1833
			Mammography and treat (vs treat only)	Mexico	$18,358	DALY	Int $ of 2005	$2926
Zelle and others (WHO-CHOICE model)[2,3]	2012		Treat (vs not treat) cancer stages 1/2/3/4	Ghana	$14,173/5012/ 5547/16,824	DALY	US $ of 2009	$17,422/6161/ 6818/20,681
			Treat (vs not treat) all stages cancer	Ghana	$3219	DALY	US $ of 2009	$3956
			Basic/media awareness raising and treat all (vs not)	Ghana	$2298/1364	DALY	US $ of 2009	$2825/1677
			Biennial CBE 40-69 + treat all (vs not)	Ghana	$1299	DALY	US $ of 2009	$1597
			Biennial mammography 40-69 + treat all (vs not)	Ghana	$2907	DALY	US $ of 2009	$3573
Nguyen and others (model)[1,2]	2013	10	Annual CBE 40-55 + treat (vs no screening)	Vietnam	$995	LY	US $ of 2008	$1447
Colorectal cancer								
Wong and others	2004		Screening with: Fecal occult blood	Singapore	 $96	LY	US $ of 2004	 $166

			Fecal Immunochemical Flexible Sigmoidoscopy Double-contrast barium enema Colonoscopy		$218 $201 $125 $238			$378 $248 $216 $411
Park and others	2005	10	Colonoscopy every 3 years	Korea, Rep	$157	LY	US $ of 2005	$181
Wu and others[4]	2006	10	DNA test every 3 yrs DNA test every 5 yrs DNA test every 10 yrs Fecal occult blood every year Sigmoidoscopy every 5 years Colonoscopy every 10 year		$9,794 $9,335 $7,717 Cost-saving $2,087 Cost-saving	LY	US $ of 2004	$16,566 $16,171 $13,368 Cost-saving $3615 Cost-saving
Tsoi and others	2008	10	Fecal occult blood Flexible sigmoidoscopy Colonoscopy	Taiwan, China	$15,547.00 $15,980.00 $12,703.00	LY	US $ of 2008	$20,112 $20,672 $16,438
Ginsberg and others	2010	10	0. Current strategy (very limited treatment) 1.Treat all cases found 2. Colonoscopy at age 50 + treat 3. Colonoscopy every 10 years + treat 0. Current strategy (limited treatment) 1. Treat all cases found 2. Sigmoidoscopy age 50 + treat	AFR-E EUR-C (Eastern Europe/Russia)	$4206 $1666 $2643 $3162 $2596 $2891	DALY	I $ of 2000	n/a

			3. Colonoscopy age 50 + treat		$2978 $3056			
Ginsberg and others[5]	2012	10	Treat cancer Colonoscopy@50+treat Colonoscopy every 10 years + treat Annual FOBT+ sigmoidoscopy + treat Treat cancer Sigmoidoscopy@50+treat Colonoscopy@50+treat Colonoscopy every 10 years + treat Annual FOBT+ sigmoidoscopy + treat	AFR-E (95% coverage) SEAR-D (95% coverage)	$336 $585 $766 $952 $362 $574 $794 $1124 $1735	DALY	US $ of 2010	$430 $749 $981 $1219 $425 $673 $931 $1318 $2035
Liver								
Prakash	2003	9	3 doses Hepatitis B vaccine @$0.75/dose	India	$58	DALY	US $ of 2010	$61
Griffiths and others	2005	10	3 doses Hep B@$0.29 3 doses Hep B @$1.08	Mozambique	$23-29 $55-72	DALY	US $ of 2010	$24-31 $58-76
Kim and others	2007	10	3 doses Hep B @$0.32	Gambia	$34-58	DALY	US $ of 2010	$36-61
Klingler and others	2012	10	Add birth dose @$0.71 to existing 3-dose series	Mozambique	$250.95	DALY	US $ of 2008	$282
Reid	2012	7.5	Auto-disable syringes to prevent reuse	India	$46	DALY	US $ of 2012	$46
Oral								
Subramanian and others	2009	10	Screen all population Screen tobacco & alcohol users	India	$165	LY	US $ of 2004	$259

Notes: [1] Costs of biennial and annual mammography, and extending range either to start at age 35 or end at age 75, are correspondingly higher.

[2] Clinical effectiveness of CBE has not yet been established – trials are ongoing; hence cost-effectiveness is speculative.
[3] Study also provides estimates of 6 other combinations including palliative care not included here – DALY measures for palliation are quite speculative; also provide results for mammography ages 50-69 with treatment.
[4] DNA test is not yet considered a practical option in any country for colorectal cancer screening.
[5] Study also considers sigmoidoscopy every 5 years and treat, versus colonoscopy at age 50; and sigmoidoscopy every 5 years plus annual/biannual fecal occult blood tests plus treat, versus sigmoidoscopy every 5 years plus treat.

Table 3. Results of systematic survey of LMIC literature, cost-effectiveness, cervical cancer

Source	Year	Study Grade	Condition/ Intervention	Country	Cost per outcome	Unit of outcome	Currency	Cost per outcome US $2012
Screening - Cytology								
Kim and others	2008	10	Cytology every 5 years, South Vietnam, I$50 cost per vaccinated girl	Vietnam	$470	LY	US $ of 2000	Negative
Screening - Pap test								
Ezat and others	2010	8.5	Pap smear 70% coverage (vs status quo – 40%)	Malaysia	987	QALY	Malaysia Ringgit 2010	$335
Praditsitthikorn and others	2011	10	Pap smear every 5 years (age 30-60)	Thailand	-60,000	QALY	Thailand 2007	-$2229
Screening - DNA test								
Levin and others	2010	10	Rapid HPV-DNA test, two visits and one screen per lifetime, county level (vs hybrid capture 2 test with three visits and one screen per lifetime, national level)	China	$50	LY	US $ of 2005	$81
			Rapid HPV-DNA test, two visits and three screens per lifetime, county level	China	$150	LY	US $ of 2005	$243
			Rapid HPV-DNA test, two visits and two screens per lifetime, county level (vs rapid HPV-DNA test with three visits and three screens per lifetime, township level)	China	$80	LY	US $ of 2005	$130
Campos and	2012	9	HPV-DNA test or VIA, women	Kenya	$450 -	LY	US $ of	$904-

others			over 30		$1400		2005	12,811
Screening - Visual Inspection with Acetic Acid (VIA)								
Praditsitthikorn and others	2011	10	VIA every 5 years (age 30-45)	Thailand	-72,000	QALY	Thai Bhat of 2007	-$2675
			VIA every 5 years (age 30-45) and pap smear every 5 years (50-60)	Thailand	-69,000	QALY	Thai Bhat of 2007	-$2564
Vaccination								
		9.5	Vaccination of 12 year old females and males and 12-24-year-old temporary catch-up for females and males (vs both sex vaccination and female catch-up); current screening levels	Mexico	$16702	QALY	US $ of 2005	$18483
			Vaccination of 12 year old females and males and 12-24-year-old temporary catch-up vaccination of females (vs only female vaccination); current screening levels	Mexico	$16663	QALY	US $ of 2005	$18440
			Vaccination of 12 year old girls (vs none); current screening levels	Mexico	$2719	QALY	US $ of 2005	$3009
Insinga and others	2007		Vaccination of 12 year old girls and 12-24 year old temporary female catch-up vaccination (vs vaccination of 12 year old girls); current screening levels	Mexico	$3048	QALY	US $ of 2005	$3373
Goldie and	2007	10	Vaccination (girls receive 3 doses	Brazil	Negative	LY	US $ of	Negative

others			before age 12, 70% coverage), I$35 per vaccinated woman				2000	
			Vaccination (girls receive 3 doses before age 12, 70% coverage), I$50 per vaccinated woman	Brazil	$300	LY	US $ of 2000	$601
		10	Increasing HPV vaccine coverage from 25% to 50% for girls only	Brazil	$30	LY	US $ of 2000	$60
			Increasing HPV vaccine coverage to 75% for girls only	Brazil	$130	LY	US $ of 2000	$260
Kim and others	2007		Increasing HPV vaccine coverage to 90% for girls only	Brazil	$300	LY	US $ of 2000	$601
		10	Vaccination alone, I$10 per vaccinated girl	India	Negative	LY	US $ of 2005	Negative
Diaz and others	2008		Vaccination and two-visit HPV DNA screening three times per lifetime at 35, 40, and 45, I$10 per vaccinated girl	India	$82540	LY	US $ of 2005	$123133
Reynales-Shigematsu and others	2009	10	HPV vaccination (age 12); $45 per vaccinated woman	Mexico	$68	LY	US $ of 2004	$81
Canfell and others	2011	10	Vaccination only, $50 per vaccinated girl	China	$2644	LY	US $ of 2010	$3069
Praditsitthikorn and others	2011	10	HPV vaccination at age 15; $465 per immunized woman	Thailand	147000	QALY	Thai Bhat of 2007	$5462
Sharma and	2011	10	3-Visit HPV Vaccination alone	Thailand	$350 -	LY	US $ of	$560 -

others			(no cytology) I$10-I$100 per vaccinated girl		$2400		2005	$13,837
Campos and others	2012	9	HPV 16/18 vaccination in pre-adolescent girls; I$10-I$50 per vaccinated girl	Kenya	$20 - $1440	LY	US $ of 2005	$40 - $12,891
Kawai and others	2012	10	Vaccination of 12 year old females with a school-based program (vs no vaccination); $45 per vaccinated girl	Brazil	$219	QALY	US $ of 2011	$198
			Vaccination of 12 year old females with a school-based program and a catch-up program for women aged 12-26 (vs without catch-up); $45 per vaccinated girl	Brazil	$450	QALY	US $ of 2011	$406
Termrungruang lert and others	2012	10	HPV vaccination at age 12, 100% compliance; $177 per vaccinated woman	Thailand	160650	QALY	Thai Bhat of 2012	$5168
Vanni and others	2012	10	HPV vaccine of young girls, 70% vaccine coverage, US$60 per vaccinated girl	Brazil	$232	LY	US $ of 2008	$270
				Brazil	$255	QALY	US $ of 2008	$296
Tracy and others	2014	10	Bivalent HPV vaccination of girls age 10-14, 90% coverage, rural, I$5/dose	Mali	$1059	LY	US $ of 2011	$1032
			Bivalent HPV vaccination of girls	Mali	$1528	LY	US $ of	$1489

			age 10-14, 90% coverage, urban and rural				2011	
Vaccination and screening								
Goldie and others	2007	10	Two-visit HPV DNA screening (age 35-45), I$100 per vaccinated woman	Brazil	$500	LY	US $ of 2000	$1002
			Vaccination (ages 9-12) and 2-visit HPV DNA screening (age 35-45), I$75 per vaccinated woman	Brazil	$1100	LY	US $ of 2000	$2204
			Vaccination (ages 9-12) and 3-visit cytology screening for women 35, 40, and 45, I$25 per vaccinated woman	Brazil	$200	LY	US $ of 2000	$401
Diaz and others	2008	10	Screening three times per lifetime at ages 35,40, and 45, I$20 per vaccinated girl	India	$60	LY	US $ of 2005	$90
			Vaccination and one-visit VIA screening three times per lifetime at ages 35,40, and 45, I$10 per vaccinated girl	India	$290	LY	US $ of 2005	$433
			Vaccination and one-visit VIA screening three times per lifetime at ages 35,40, and 45, I$20 per vaccinated girl	India	$340	LY	US $ of 2005	$507
			Vaccination and two-visit HPV DNA screening three times per lifetime at 35, 40, and 45, I$20	India	$82540	LY	US $ of 2005	$123134

			per vaccinated girl					
Kim and others	2008	10	Cytology (every 5 years), North Vietnam, I$50 per vaccinated girl	Vietnam	$560.00	LY	US $ of 2000	$1025
			Vaccination and cytology (every 5 years), North Vietnam, I$25 per vaccinated girl	Vietnam	$2180.00	LY	US $ of 2000	$3989
			Vaccination and cytology (three times), South Vietnam, I$25 per vaccinated girl	Vietnam	$270.00	LY	US $ of 2000	$494
Reynales-Shigematsu and others	2009	10	HPV vaccination (age 12) and pap smear every 3 years (age 25+); $45 US per vaccinated woman	Mexico	$17341	LY	US $ of 2004	$20666
			HPV vaccination (age 12) and pap smear every 5 years (age 25+)	Mexico	$15935	LY	US $ of 2004	$18991
Sinanovic and others	2009	10	Cervical cytology at ages 30, 40, and 50 and HPV vaccination at age 12; health service perspective, $480/vaccinated woman (vaccine cost only)	South Africa	$4495	LY	US $ of 2007	$5333
			Same as above	South Africa	$1460	QALY	US $ of 2007	$1732
			Cervical cytology at ages 30, 40, and 50 and HPV vaccination at age 12; societal perspective	South Africa	$3320	LY	US $ of 2007	$3939

			Same as above	South Africa	$1078	QALY	US $ of 2007	$1279
Ezat and others	2010	8.5	Vaccination (100 Ringgit/dose, i.e. $34) and pap smear	Malaysia	515	QALY	Malaysia Ringgit of 2010	$175
Canfell and others	2011	10	5-yearly screening and vaccination, $50 per vaccinated girl	China	$5963	LY	US $ of 2010	$6920
			5-yearly screening and vaccination, $87 per vaccinated girl	China	$5963	LY	US $ of 2010	$6920
			Once-lifetime screening and vaccination, $50 per vaccinated girl	China	$2746	LY	US $ of 2010	$3187
			Twice-lifetime screening and vaccination, $50 per vaccinated girl $50	China	$2919	LY	US $ of 2010	$3388
			Twice-lifetime screening and vaccination, $87 per vaccinated girl	China	$5907	LY	US $ of 2010	$6855
Praditsitthikorn and others	2011	10	HPV vaccination at age 15 and pap smear every 5 years (age 30-60); $465 per vaccinated woman	Thailand	141000	QALY	Thai Bhat of 2007	$5202
			HPV vaccination at age 15 and VIA every 5 years (age 30-45); $465 per vaccinated woman	Thailand	140000	QALY	Thai Bhat of 2007	$5165

Campos and others	2012	9	Pre-adolescent vaccination followed by screening at older ages I$10-I$50 per vaccinated girl	Kenya	$74 - $3580	LY	US $ of 2005	$1486 - $17,187

[1] Note that dose prices per vaccinated woman given are those used in the original year of study. When cost-effectiveness data were updated to US $ of 2012, not all studies provided sufficient information to maintain the original dose price, and instead dose costs were inflated along with other costs. Cost-effectiveness results are likely to be even better (lower cost per DALY/QALY/LY) if dose price were maintained at the level of the original study.

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