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Cancer Care

Diagnosis and Treatment in LMIC

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October 4, 2017
Global Health Workshop Pre-Conference
Houston, TX

Disclosures

- None

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Learning Objectives

- Understand the **epidemiology** of the most common cancers in low and middle income countries (LMIC)
- Learn about **typical presentations**
- Plan a **treatment strategy** for a resource limited setting

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Best Buys in Chronic Disease Prevention

Risk factor / disease	Interventions
Tobacco use	• Tax increases • Smoke-free indoor workplaces and public places • Health information and warnings • Bans on tobacco advertising, promotion and sponsorship
Harmful alcohol use	• Tax increases • Restricted access to retailed alcohol • Bans on alcohol advertising
Unhealthy diet and physical inactivity	• Reduced salt intake in food • Replacement of trans fat with polyunsaturated fat • Public awareness through mass media on diet and physical activity
Cardiovascular disease (CVD) and diabetes	• Counselling and multi-drug therapy for people with a high risk of developing heart attacks and strokes (including those with established CVD) • Treatment of heart attacks with aspirin
Cancer	• Hepatitis B immunization to prevent liver cancer (already scaled up) • Screening and treatment of pre-cancerous lesions to prevent cervical cancer

WHO and World Economic Forum, “From Burden to ‘Best Buys’”, 2009

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Cost-Effectiveness Analysis

- WHO-Choice ((**CHO**osing **I**nterventions that are **C**ost-**E**ffective): http://www.who.int/choice/cost-effectiveness/en/
  - program in the World Health Organization that helps countries decide health system priorities based on considerations of costs and impacts.
- One Health Tool – software – released 2012 http://www.who.int/choice/onehealthtool/en/
  - software tool designed to inform national strategic health planning in low- and middle-income countries

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Cost-Effectiveness Analysis

- Economic evaluation: http://www.who.int/choice/documents/economic_evaluation/en/

  publications seeking to analyze cost: benefit for a variety of diseases and syndromes

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Cancer Screening and Care

- I can't (or shouldn't) practice "there" just like I practice here.
- Someone knows what is being and should be screened, diagnosed and treated (the WHO policy wonks and hopefully the MOH)
- I should integrate with national practice standards.
- http://www.who.int/cancer/country-profiles/en/
- National treatment guidelines http://apps.who.int/medicinedocs/en/cl/CL9.1/clmd,50.html

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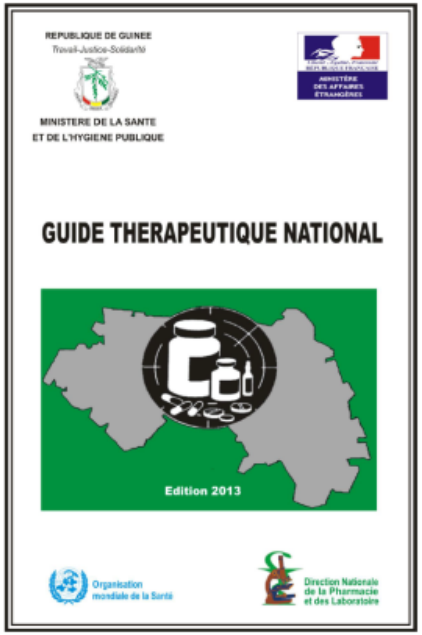
So, how should I decide who to screen / treat?

- National treatment guidelines http://apps.who.int/medicinedocs/en/cl/CL9.1/clmd,50.html
- Ask your national colleague (and accept their approach as best)
- Mental math – estimate ratio of benefit to cost/harm in light of resources



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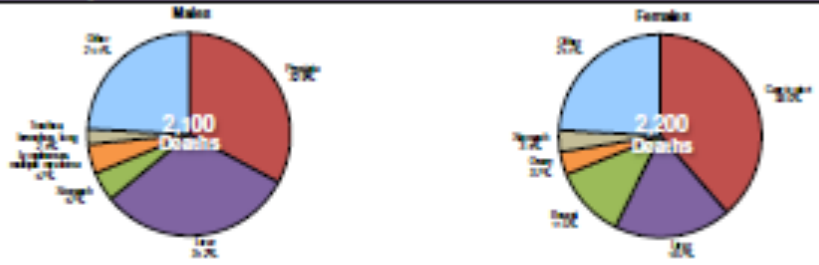
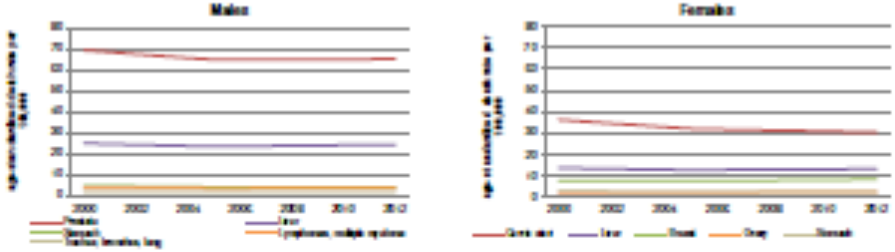
Guinea

Total population: 11,481,000
Income group: Low
Total deaths: 119,000
Life expectancy at birth: Total [illegible] Females [illegible]

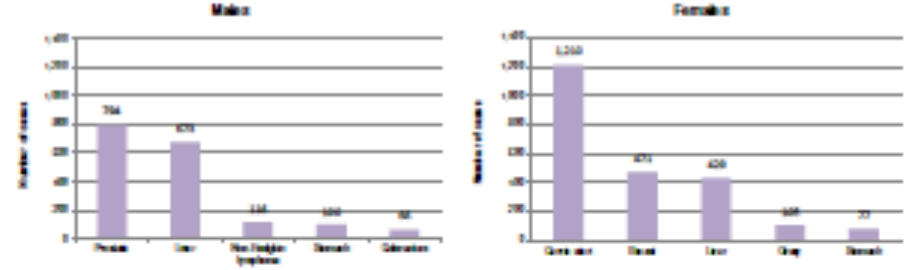
Cancer Mortality Profile*



Age-Standardized Cancer Mortality Trends*



Cancer Incidence



Adult Risk Factors

	Males	Females	Total
Current tobacco smoking (2011)	23%	2.2%	12.6%
Total alcohol per capita consumption, in litres of pure alcohol (2010)	1.4	0.1	0.7
Physical inactivity (2010)	6.4%	11.0%	8.2%
Obesity (2014)	2.8%	8.8%	5.8%
Insufficient fruit and vegetable intake (2012)	-	-	86.2%

World Health Organization - Cancer Country Profiles, 2014.

Cancer Plans, Monitoring and Surveillance

Has an operational cancer policy/plan/action plan	Yes
Has a cancer registry	Yes
Scope	Hospital-based
Coverage	Incidence
Last year of data	2005

Cancer Primary Prevention Policies

Tobacco control

Has an operational policy, strategy or action plan to reduce the burden of tobacco use	Yes
Smoke-free legislation	There is no public place completely smoke-free
Tobacco dependence treatment	NRT and/or some cessation services (neither used/unused)
Warning labels	Medium size warnings missing some appropriate characteristics (25% large warnings, missing many appropriate characteristics
Bans on advertising, promotion and sponsorship	Ban on all forms of direct and indirect advertising*
Tobacco taxes	26-50% of retail price is tax

Overweight and obesity prevention and control

Has an operational policy, strategy or action plan for reducing overweight/obesity	Yes

Physical inactivity prevention and control

Has an operational policy, strategy or action plan to reduce physical inactivity and/or promote physical activity	Yes

Harmful use of alcohol prevention and control

Has an operational policy, strategy or action plan to reduce the harmful use of alcohol	Yes

National immunization

Human papillomavirus vaccination schedule	...
Hepatitis B vaccination schedule	...
Hepatitis B vaccination coverage, infants	0%

Cancer Screening and Early Detection

Cervical cancer

Cervical cytology (PAP)	Not generally available in the public primary health care level
Acetic acid visualization (VIA)	Not generally available in the public primary health care level

Breast cancer

Breast palpation / clinical breast exam (CBE)	Not generally available in the public primary health care level
Mammogram	Not generally available in the public primary health care level

Colorectal cancer

Fecal occult blood test or fecal immunological test	Not generally available in the public primary health care level
Bowel cancer screening by exam or colonoscopy	Not generally available in the public primary health care level

Cancer Treatments and Palliative Care

Radiotherapy	Not generally available in the public health system
Total high energy (teletherapy units) / million inhabitants	0.0
Number of radiotherapy centres	...
Number of radiation oncologists	...
Chemotherapy (medicines not specified)	Not generally available in the public health system
Oral morphine (formulation not specified)	Not generally available in the public health system
Non-metabolic morphine equivalent consumption per cancer death (mg)	...
Community home care for people with advanced stage cancer and other needs	Not generally available

* No country data available. Figures were based on national estimates, estimates and modelled methods.
** Indicates highest possible level of achievement.
... = No data available

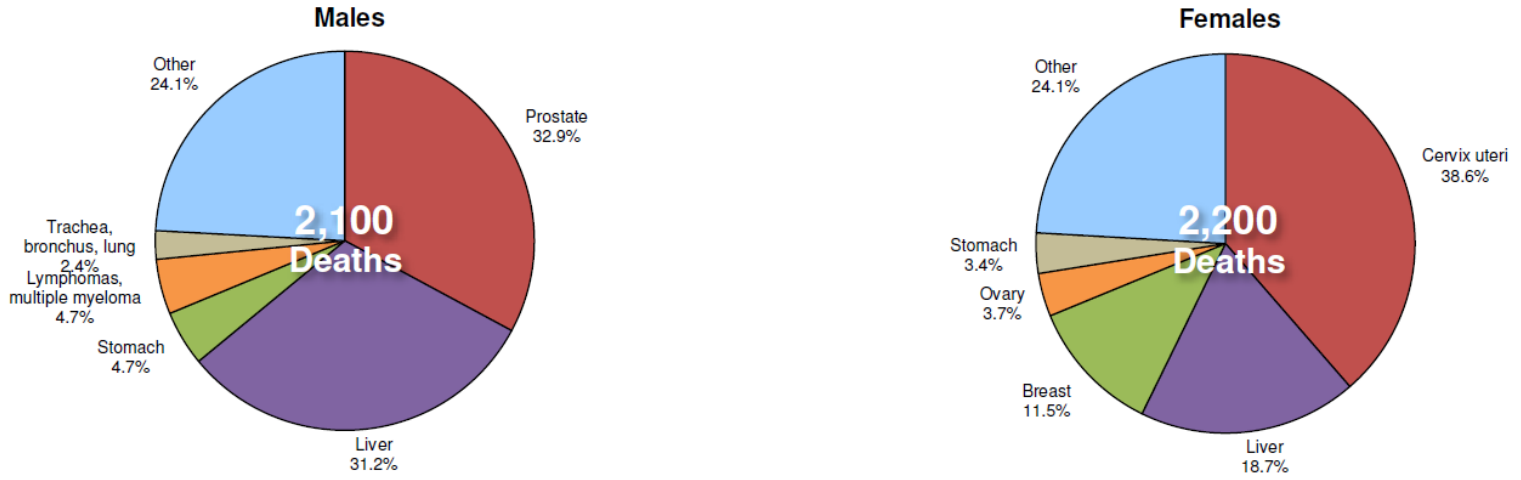
World Health Organization - Cancer Country Profiles, 2014.

Guinea

Total population: 11,451,000
Income group: Low

Total deaths: 119,000
Life expectancy at birth: Total:58 Males:57 Females:59

Cancer Mortality Profile*



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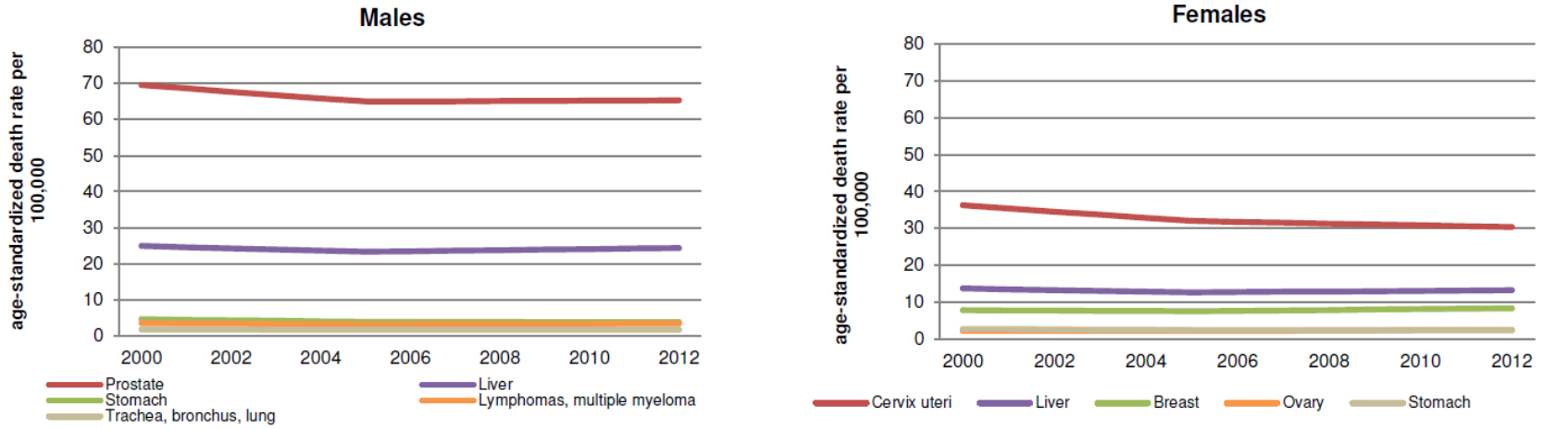

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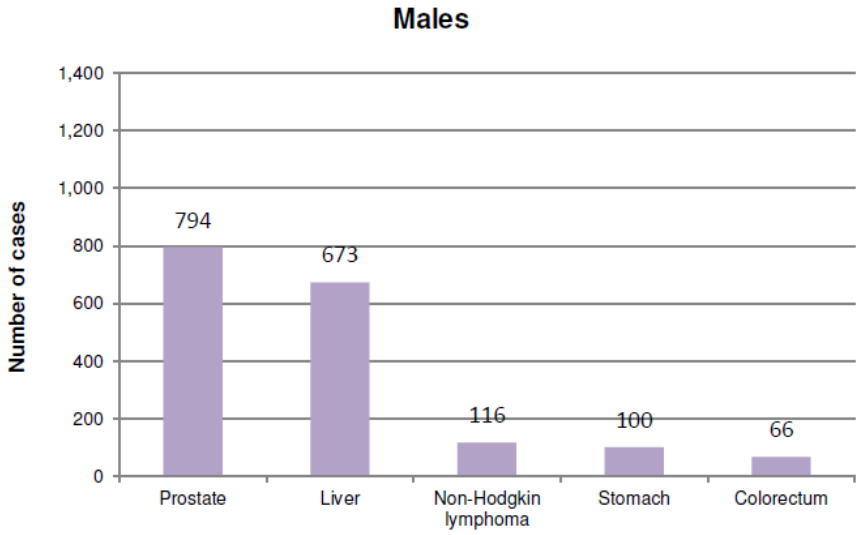
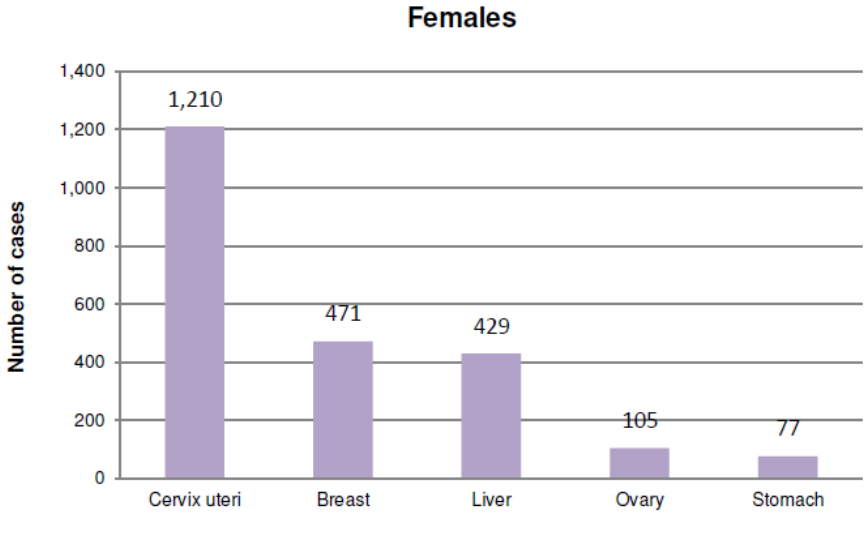
Cancer Incidence





Adult Risk Factors

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Current tobacco smoking (2011)	23%	2.2%	12.6%
Total alcohol per capita consumption, in litres of pure alcohol (2010)	1.4	0.1	0.7
Physical inactivity (2010)	5.4%	11.0%	8.2%
Obesity (2014)	2.8%	8.9%	5.9%
Household solid fuel use (2012)	-	-	96.0%

World Health Organization - Cancer Country Profiles, 2014.

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Cancer Plans, Monitoring and Surveillance

Has an operational cancer policy/strategy/action plan	Yes
Has a cancer registry	Yes
Scope	Hospital-based
Coverage	Subnational
Last year of data	2006

Cancer Primary Prevention Policies

Tobacco control

Has an operational policy, strategy or action plan to reduce the burden of tobacco use	Yes
Smoke-free legislation	Three to five public places completely smoke-free
Tobacco dependence treatment	NRT and/or some cessation services (neither cost-covered)
Warning labels	Medium size warnings missing some appropriate characteristics OR large warnings missing many appropriate characteristics
Bans on advertising, promotion and sponsorship	Ban on all forms of direct and indirect advertising**
Tobacco taxes	26–50% of retail price is tax

Overweight and obesity prevention and control

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National immunization

Human Papillomavirus vaccination schedule	. . .
Hepatitis B vaccination schedule	. . .
Hepatitis B vaccination coverage, infants	63%

Cancer Screening and Early Detection

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Oral morphine (formulation not specified)	Not generally available in the public health system
Non-methadone morphine equivalent consumption per cancer death (mg)	. . .
Community/home care for people with advanced stage cancer and other NCDs	Not generally available

* No mortality data available. Figures are based on national incidence estimates and modelled survival.
** Indicates highest possible level of achievement

... = No data available

World Health Organization - Cancer Country Profiles, 2014.

Cancer Screening Recs for Thailand (*MIC*) 2014: based on country income

	Strategy	Intervention	Comparator	Incremental cost-effectiveness ratio (Baht per quality-adjusted life-year)	Budget effect (million Baht per year)	Inclusion in universal health-care coverage benefit package
Hepatocellular carcinoma	Prevention	Population-based HBsAg screening for people age 31–40 years	No screening	Cost saving	NA	Yes
Hepatocellular carcinoma	Prevention	Lamivudine in HBsAg-positive individuals, and administration of tenofovir after development of lamivudine resistance	Do nothing	Cost saving	NA	Yes
Alcohol-associated malignant disease	Prevention	Screening for an alcohol-use disorder with the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST), followed by brief intervention in people age 15–59 years	No screening	Cost saving	NA	Under consideration
Smoking-associated malignant disease	Prevention	Application of a community pharmacist-based smoking cessation programme	Usual care	Cost saving	NA	Under consideration
Cervical cancer	Screening	Visual inspection with acetic acid every 5 years for women aged 30–45 years, followed by Papanicolaou smear every 5 years for women aged 50–60 years	No screening	Cost saving	NA	Yes
Chronic myeloid leukaemia resistant to standard-dose imatinib	Treatment	Dasatinib	High-dose imatinib (800 mg/day)	Cost saving	NA	Under consideration
Chronic myeloid leukaemia resistant to standard-dose imatinib	Treatment	Nilotinib	High-dose imatinib (800 mg/day)	72 908	..	Under consideration
Cervical cancer	Prevention	HPV vaccine for girls aged 15 years	Papanicolaou smear for women aged 35–60 years, every 5 years	181 000	6000	No
Breast cancer	Screening	Once-in-a-lifetime population-based mammographic screening for women aged 40–49 years	No screening	1 847 481	2086	No
Breast cancer	Screening	Once-in-a-lifetime population-based mammographic screening for women aged 50–59 years	No screening	1 368 764	1579	No
Advanced-stage gastrointestinal stromal tumour	Treatment	Imatinib 400 mg/day, followed by sunitinib 50 mg/day if disease cannot be controlled	Imatinib 400 mg/day, followed by palliative care if disease cannot be controlled	2 273 414	695	No
Advanced-stage clear-cell renal-cell carcinoma	Treatment	Interferon α, followed by palliative care	Palliative care	478 486	19	No
Advanced-stage clear-cell renal-cell carcinoma	Treatment	Sunitinib, followed by palliative care	Palliative care	1 887 373	131	No
Advanced-stage clear-cell renal-cell carcinoma	Treatment	Bevacizumab plus interferon α, followed by palliative care	Palliative care	3 825 307	216	No
Cancer patients with anaemia induced by chemotherapy	Palliative	Recombinant human erythropoietin	Blood transfusion	3 700 000	NA	No

Data obtained from the Health Intervention and Technology Assessment Program (HITAP), 2013.

Table 3: Cost-effectiveness league table on cancer prevention and control in Thailand

Chalkidou, K., P. Marquez, et al. (2014). "Evidence-informed frameworks for cost-effective cancer care and prevention in low, middle, and high-income countries." The Lancet. Oncology **15**(3): e119-131.

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Cervical Cancer Screening

- India, Kenya, Peru, South Africa, and Thailand computer modeling study
- Cost effective in LMIC
- “Once at age 35 years
- …visual inspection of the cervix with acetic acid (or DNA testing for HPV in cervical cell samples)
- reduced the lifetime risk of cancer by …25 to 36 percent, and cost less than $500 per year of life saved.”

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Goldie, NEJM, 2005

Cervical Cancer Screening

- 2 screenings with visual inspection/cryo if + (at 35 and 40 years of age) reduce lifetime cancer risk by 40 percent
- Resulted in a cost per year of life saved that was less than each country's per capita gross domestic product: $91 in India & $319 in Kenya
- If you add DNA testing costs $310 per year of life saved in Thailand, $453 in Peru, and $1,093 in South Africa.

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Goldie, NEJM, 2005

VIA vs VILI

- Visual inspection under Lugol's iodine (VILI)
  - VILI 95% sensitive vs 82% for VIA
  - Equal specificity to VIA
  - 7% more sensitive and 13% more specific than HPV testing
  - Color changes by iodine more easily seen than acetowhite changes.
  - VILI is better if
    - eye (vs colposcopy)
    - poor lighting & time gap (lasts longer)

Fokom-Domgue, BMJ, 2015

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Other Cancer *Screening*?

- Not colon (cost effective in US but not LMIC)
  - Maybe hemocult if family hx or risk
- Not breast (hardly cost effective in US)
  - But if VHW and nurses aware of disease -> refer early!
- Not prostate (questionable even in US)
  - Orchiectomy if treatment needed
- Not liver
  - Need to prevent with Hep B vaccine and treatment of Hep B/C.

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Other Cancer *Screening*?

- Not stomach – EGD like in Japan?
  - But, treatment of PUD with antibiotics for H. pylori
- Not melanoma – skin checks
  - But, referral of patients with growing pigmented skin lesions
- Not bladder – urinalysis for smokers ever
  - But, referral to hospital of patients with hematuria (except in S. haematobium endemic areas)

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Figure 9. Sample organization of cancer interventions by care level

Community engagement and empowerment	Primary care level	Secondary care level	Tertiary care level
Key functions • Cancer awareness • Community leaders and cancer advocates engagement • Addressing cancer stigma • Facilitating health-seeking behaviour • Identification of barriers to accessing care	**Diagnosis** • Recognition of cancer signs and symptoms • Appropriate clinical evaluation • Early referral of suspicious cases **Treatment** • Basic procedures (e.g. cryotherapy) • Patient education and rehabilitation **Additional functions** • Health education, counselling • Coordination of services across facilities • Supportive, palliative and survivorship care	**Diagnosis** • Cytology, biopsy, routine histopathology • X-ray, ultrasound, endoscopy **Treatment** • Moderately complex surgery • Outpatient chemotherapy **Additional functions** • Coordinating with primary and tertiary care levels • Supportive, palliative and survivorship care	**Diagnosis** • Cytology, biopsy, histopathology, prognostic markers, immunochemistry • X-ray, ultrasound, endoscopy, computerized tomography **Treatment** • Radiotherapy • Complex surgery • Chemotherapy • Rehabilitation **Additional functions** • Communication with primary and secondary care levels, counter-referrals • Supportive palliative and survivorship care

Note: Organization of cancer interventions depends on local capacity.

Source: Adapted from WHO 2008 *(44)*.

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Guide to Cancer Early Diagnosis, WHO, 2017

Table 3. Common symptoms and signs that may be due to cancer[a]

Site of cancer	Common symptoms
Breast	Lump in the breast, asymmetry, skin retraction, recent nipple retraction, blood stained nipple discharge, eczematous changes in areola
Cervix	Post-coital bleeding, excessive vaginal discharge
Colon and rectum	Change in bowel habits, unexplained weight loss, anaemia, blood in the stool (rectal cancer)
Oral cavity	White lesions (leukoplakia) or red lesions (erythroplakia), growth or ulceration in mouth
Naso-pharynx	Nosebleed, permanent blocked nose, deafness, nodes in upper part of the neck
Larynx	Persistent hoarseness of voice
Stomach	Upper abdominal pain, recent onset of indigestion, weight loss
Skin melanoma	Brown lesion that is growing with irregular borders or areas of patchy colouration that may itch or bleed
Other skin cancers	Lesion or sore on skin that does not heal
Urinary bladder	Pain, frequent and uneasy urination, blood in urine
Prostate	Difficulty (long time) in urination, frequent nocturnal urination
Retinoblastoma	White spot in the pupil, convergent strabismus (in a child)
Testis	Swelling of one testicle (asymmetry)

[a] These common symptoms may be due to cancer or due to a different medical condition. People with these symptoms should seek medical attention without delay.

Source: Adapted from WHO 2007 *(5)*.

Guide to Cancer Early Diagnosis, WHO, 2017

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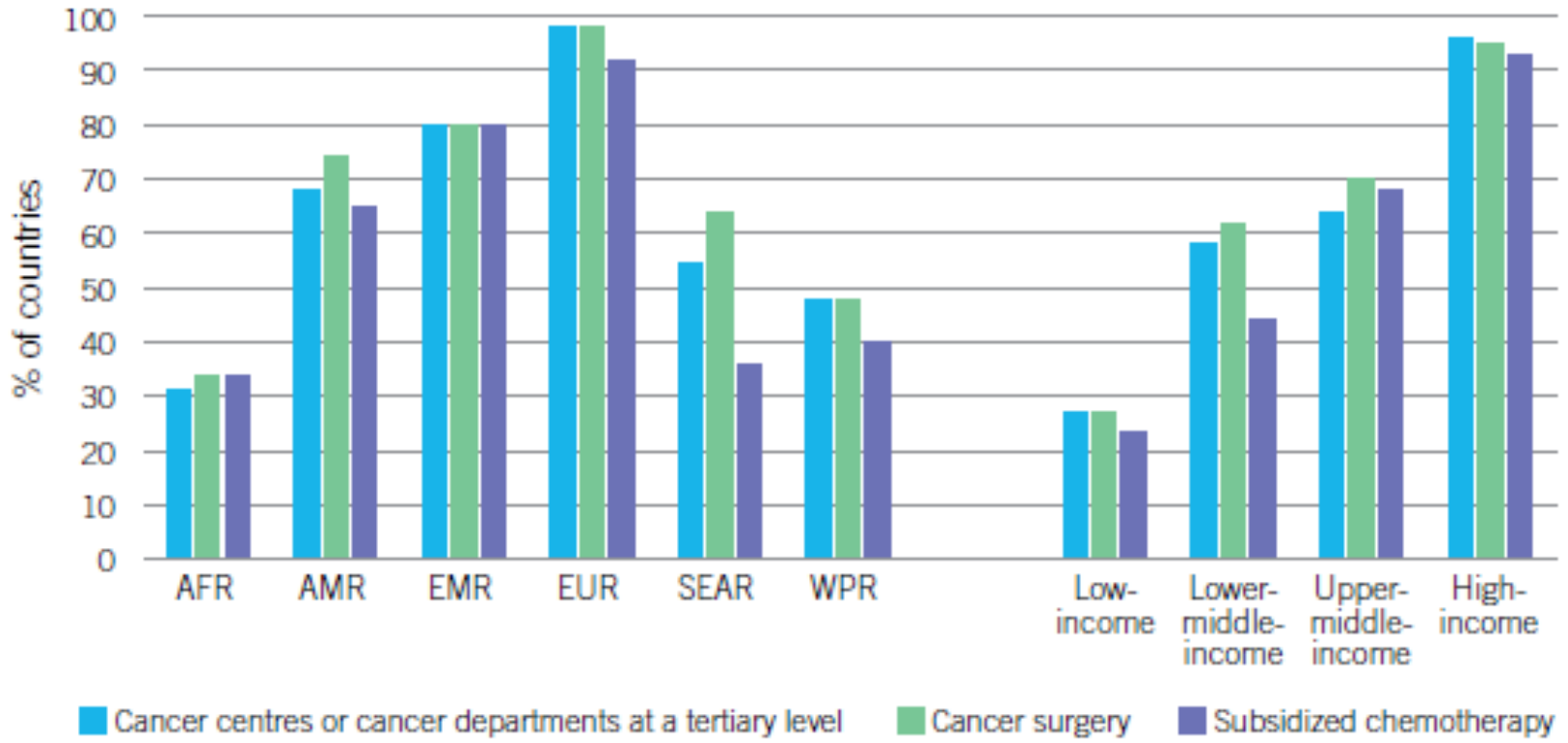
Figure 7. Percentage of countries with access to cancer treatment services in the public sector, by WHO region and World Bank income group



AFR, African Region; AMR, Region of the Americas; SEAR, South-East Asia Region; EUR, European Region; EMR, Eastern Mediterranean Region; WPR, Western Pacific Region

Note: The results are from 177 Member States that responded to the survey. "Don't know" responses were included in the subset of countries for which these services are not available.

Source: Data and graph based on 2015 WHO NCD Country Capacity Survey *(29)*.

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Guide to Cancer Early Diagnosis, WHO, 2017

Cervical Cancer

- Primary prevention
  - ABCs
  - Male circumcision
  - HPV vaccination in future
- Secondary prevention (preventing CIN changing to Ca)
  - VIA
  - Cryotherapy (vs LEEP/cold knife conization)

WHO, Comprehensive Cervical Cancer Control, 2nd ed., 2014

Other Cancer ***Screening***?

- Not colon (cost effective in US but not LMIC)
  - Maybe hemocult if family hx or risk
- Not breast (hardly cost effective in US)
  - But if VHW and nurses aware of disease -> refer early!
- Not prostate (questionable even in US)
  - Orchiectomy if treatment needed
- Not liver
  - Need to prevent with Hep B vaccine and treatment of Hep B/C.

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What Cancers Should I Treat?

- Burkitt's Lymphoma
  - 40% of childhood cancers in some areas Africa
  - Curable 50% +

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Burkitt's Lymphoma

- Most common malignancy in African children
- Mitogenic affect on B lymphocytes by EBV causing chromosomal translocation (moves growth-promoting c-myc gene from chromosome 8 to 14 or 2 or 22)
- Malarial co-factor (impairs immunity)
- Mean age 5 yo; boys 2:1 girls.
- Tumors in jaw or abdominal paired organs – kidney or ovaries.

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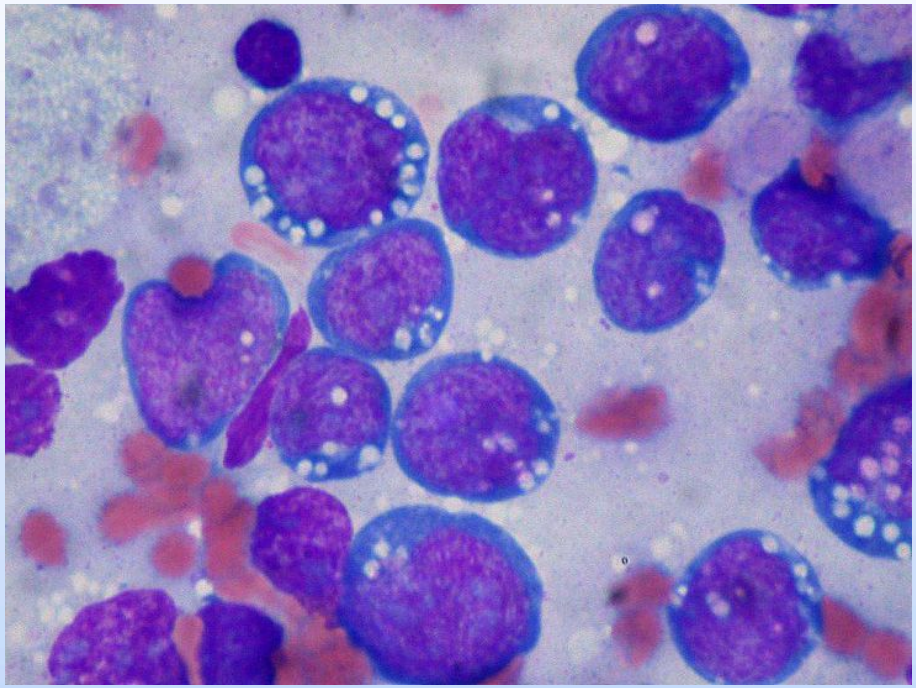
Burkitt's Lymphoma

- Doubling time 1 day
- Diagnose immediately:
  - FNA - 20 or 22 g, smear on slide. Wright Giemsa stain 400 x
  - Basophilic cytoplasm with vacuoles
  - Granular nucleus with many nucleoli



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Burkitt's Lymphoma Treatment

- Over 50% curable with simple chemotherapy:
  - Cyclophosphamide 1000 mg/m2 IV + Vincristine 1.4 mg/m2 IV + Methotrexate 15 mg/m2 oral or IV
  - Use Doxorubicin 60-75 mg/m2 IV over 30 min every 3 weeks for relapse
  - Repeat every 2-3 weeks for one course beyond complete remission
    - Expect WBC nadir of 1-2K at 10 days
  - Good hydration; if not may get tumor lysis syndrome (increased K, Phos, urate)
    - Allopurinol 200 mg three times daily

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What Cancers Should I Treat?

- Breast cancer
  - Modified radical mastectomy vs debulking/ palliation
  - LN dissection
  - Chemotherapy

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Primary Surgery

- Volume 1 – Non-trauma
- Volume 2 – Trauma
- WHO Global Initiative for Emergency and Essential Surgical Care (GIEESC)

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What Cancers Should I Treat?

- SCC
  - Albinos at high risk
  - Excision vs cryotherapy
- Melanoma
  - Unusual (except in depigmented areas - soles)
  - Early excision

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Hepatocellular Carcinoma

- 1 million deaths/year worldwide
- Most common cancer of men in sub-Saharan Africa
- Incidence 1/1000 in Mozambique
- Prevention!!!!!
- Chronic active Hep B/Hep C
- Aflatoxin B ingestion – peanuts, maize, millet
- Alcohol
- RUQ pain, weight loss, hepatomegaly, ascites (50%), hepatic bruit (50%), jaundice (25%), US+
- Palliate

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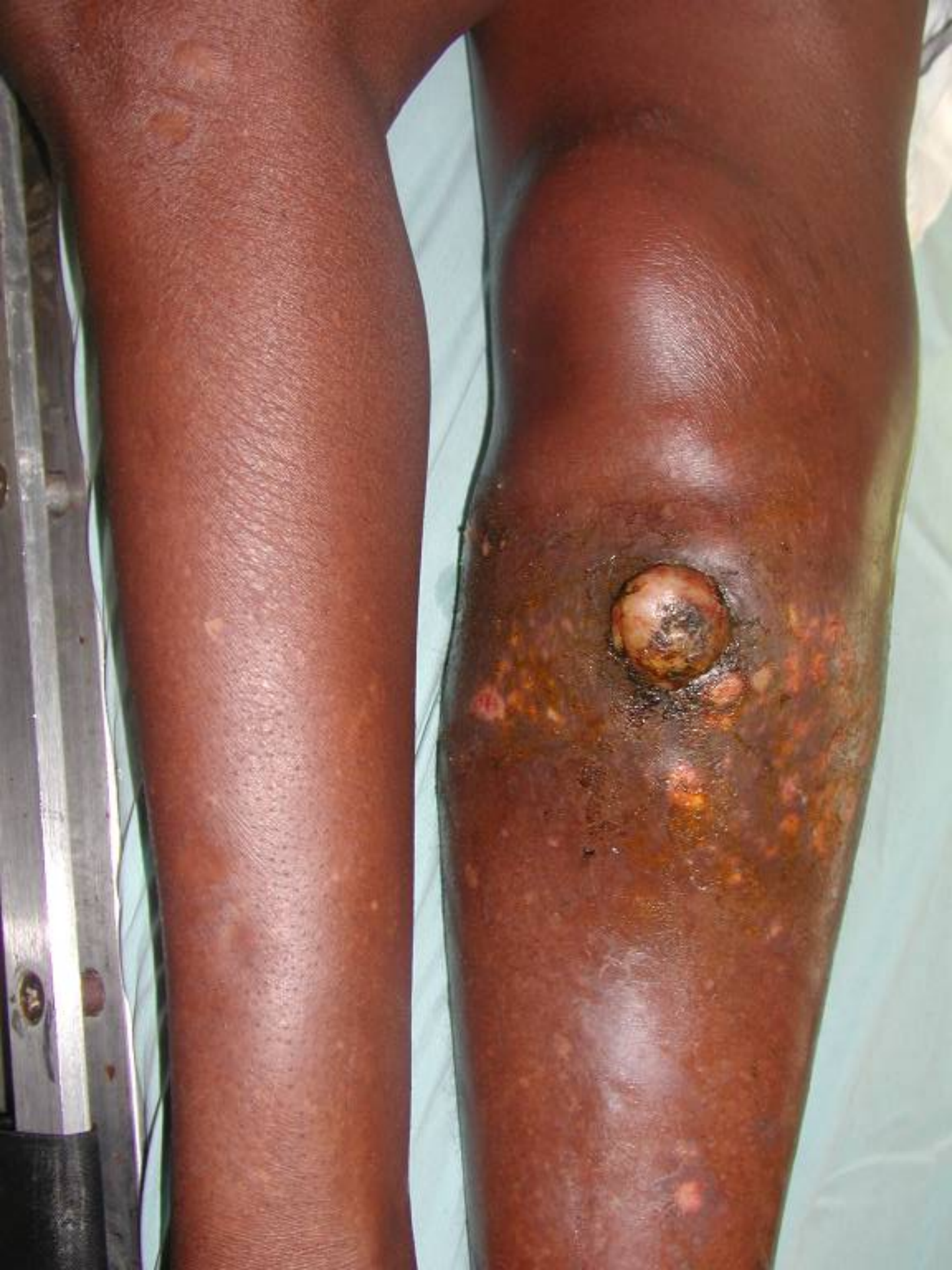

HIV Associated Malignancy

- Kaposi sarcoma
  - Black nodules on black skin/purple on white
  - HHV8 (KSHV)
  - Treatment – ART. If > 25 lesions
    - Cryotherapy
    - Combination chemotherapy
      - Doxorubicin, vincristine, bleomycin
      - Radiation therapy

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HIV Associated Malignancy

- Non-Hodgkin's Lymphoma
  - 200-600 x more common in HIV
  - Ongoing infection with EBV
  - Fever, wasting, adenopathy, HS'megaly, CNS involvement
  - Biopsy
  - Treatment
    - ART
    - CHOP (cyclophosphamide, Adriamycin, vincristine, pred.)

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Cost-Effective Health Care

- Caring for people in resource limited setting
  - Less tests, technology, meds; just the essentials
  - Less specialists
  - Less physician driven – lifestyle/public health primary
  - Avoid futility
- Person centered, coordinated, comprehensive care by an accessible primary care provider

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Tribute to Barbara Starfield, MD

Cost-Effectiveness: Diagnosis

- Limited labs → Choose at most 1 or 2
- Limited imaging → Use rarely
- Careful exam → Yet efficient
- Rare specialists → Textbooks or Virtual Consults

Cost Effective Care

- Treatment
  - Lifestyle/public health
  - Essential meds
  - Efficient treatment of chronic disease
  - Task Shifting
  - Balance NNTB / NNTH
  - Avoid futility

Cost-Effective Care

- Treatment
  - Efficient treatment of chronic disease
    - Pills if treatment saves 1 year of disability adjusted life for < 3 x per capita household income

WHO Essential Medication List

- WHO Department of Essential Medicines and Health Products
- Find updated list here: http://www.who.int/medicines/en/
- Buy essential meds from IDA:
  - http://www.ida.nl/

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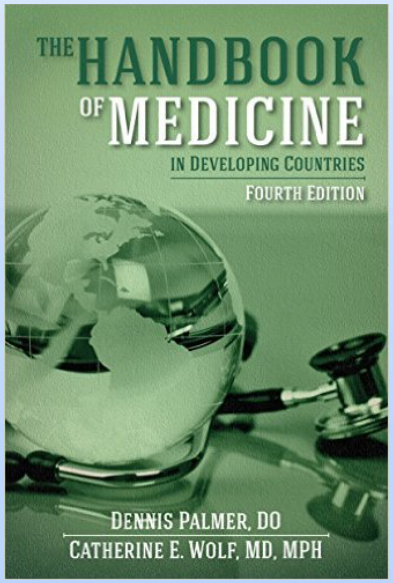
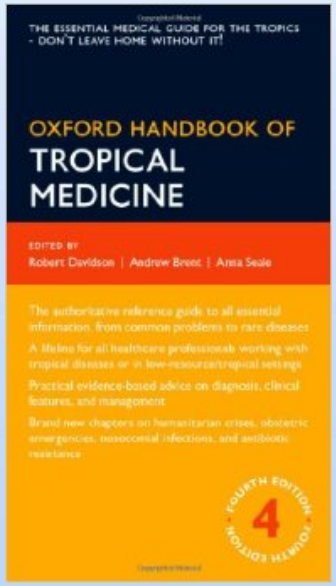
Cost-Effective Care

- Treatment
  - Task Sharing/Shifting - Increase access and lower costs
    - HIV/AIDS
    - Essential surgery
  - Avoid futility - intensive care of terminal patients
    - Helping patients/families face death
    - Dying with Hope – hospice, chaplains, pastors, community

So, how should I decide?

- Carry expert advice with you in your pocket!:
  - Oxford Handbook of TM
  - Handbook of Medicine in Developing Countries – Palmer and Wolf





Buy: www.talcuk.org

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Questions & Discussion

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