CANCER INTERVENTIONS TECHNICAL BRIEFING

BREAST CANCER INTERVENTIONS FOR THE APPENDIX 3 OF THE GLOBAL ACTION PLAN FOR THE PREVENTION AND CONTROL OF NONCOMMUNICABLE DISEASES

IDENTIFICATION OF INTERVENTIONS

The interventions considered for breast cancer analysis are based on WHO guidance and emphasizes comprehensive cancer control including diagnosis, staging, multi-modality treatment, survivorship care and palliative care as well as the first Appendix 3 [1], [2], [3], [4].

METHODOLOGICAL ASSUMPTIONS

- Estimates of incidence of breast cancer and age of diagnosis are sourced from Globocan [5];
- Region-specific data on stage-distribution are based on [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17] when available;
- Disability weights for each health state were drawn from the Global Burden of Disease 2010 disability weight study [18];
- Modelled intervention effect changes in rates of diagnosis of invasive cancer (e.g. screening) and rates of mortality (e.g. surgery).

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Variable</th>
<th>Assumptions</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening with mammography (once every 2 years for women aged 50-69 years) linked with timely diagnosis and treatment of breast cancer</td>
<td>Sensitivity</td>
<td>0.76</td>
<td>IARC, 2016 [19]</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>0.93</td>
<td>IARC, 2016 [19]</td>
</tr>
<tr>
<td></td>
<td>Frequency (per year)</td>
<td>1/2</td>
<td>WHO, 2014 [20]</td>
</tr>
<tr>
<td>Treatment of breast cancer stages I and II with surgery +/- systemic therapy, including diagnosis, staging, treatment and surveillance after completion of treatment</td>
<td>Stage I</td>
<td>0.14</td>
<td>Groot et al. 2006 [21]; Zelle et al. 2012 [16], Perez et al. 2014 [22]; Davies et al. [23]; Feng et al., 2014 [24]</td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>0.18</td>
<td></td>
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<tr>
<td></td>
<td>Stage III</td>
<td>0.23</td>
<td></td>
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<tr>
<td></td>
<td>Stage IV</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>Annual mortality rate without treatment</td>
<td>Stage I</td>
<td>0.006</td>
<td>Groot et al. 2006 [21]; Zelle et al. 2012 [16], Perez et al. 2014 [22]; Davies et al. [23]; Feng et al., 2014 [24]</td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>0.039</td>
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<tr>
<td></td>
<td>Stage III</td>
<td>0.093</td>
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<tr>
<td></td>
<td>Stage IV</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>Annual mortality with treatment</td>
<td>Stage I</td>
<td>95.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>78.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stage III</td>
<td>59.6%</td>
<td></td>
</tr>
</tbody>
</table>
### TABLE 2: COSTING ASSUMPTIONS¹ USED IN WHO CHOICE ANALYSIS

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Major costing assumptions</th>
</tr>
</thead>
</table>
| Treatment of breast cancer stages I and II with surgery +/- systemic therapy, incl. diagnosis, staging, treatment and surveillance after completion of treatment | **Diagnosis and staging:**
Diagnostic imaging with bilateral mammogram  
Biopsy equipment, specimen fixative and staining,  
Pre-treatment tests and staging studies when indicated including x-ray and ultrasound.

**Treatment:**  
Modified radical mastectomy including pre-operative antibiotics,  
wound drainage kit  
Adjuvant systemic therapy including doxorubicin, cyclophosphamide and paclitaxel [28]  
Hormone therapy with tamoxifen [28]  
Management of neutropenia and chemotherapy-associated nausea including filgrastim, ondansetron and dexamethasone [28]  
Health workforce costs for treatment including surgery and systemic therapy  
Inpatient visit days: 2 days  
Outpatient visit days: 8 days for stage I, 10 days for stage II  
Surveillance with annual mammogram and clinical exam for 5 years |
| Screening with mammography (once every 2 years for women aged 50-69 years) linked with timely diagnosis and treatment of breast cancer | **Screening:**  
Screening mammogram  
Programme monitoring and evaluation, call and recall mechanism [29]  
Management of screen-positive mammograms with subsequent diagnostic studies  
**Diagnosis and staging:**  
Biopsy equipment, specimen fixative and staining,  
Pre-treatment tests and staging studies when indicated including x-ray and ultrasound  
**Treatment:**  
Modified radical mastectomy including pre-operative antibiotics,  
wound drainage kit  
Adjuvant systemic therapy including doxorubicin, cyclophosphamide and paclitaxel [28]  
Hormone therapy with tamoxifen [28]  
Management of neutropenia and chemotherapy-associated nausea including filgrastim, ondansetron and dexamethasone [28]  
Health workforce costs for treatment including surgery and systemic therapy  
Inpatient visit days: 2 days  
Outpatient visit days: 8 days for stage I, 10 days for stage II  
Surveillance with annual mammogram and clinical exam for 5 years |
| Palliative care                                                              | Symptom management including amitriptyline, stool softener, morphine (slow release, immediate release), bisphosphonates [30]  
Outpatient or home visit days: 2 visits |

¹ Prices are taken from the MSH drug price database as median buyer price: http://mshpriceguide.org/en/drug-search-page-2/  
List of consumables identified from WHO Priority Medical Devices in Cancer Management (2017).  
Systemic therapy treatment regimen taken from WHO List of Essential Medicines.  
Consumables required include those required for treatment-related complications and surveillance after treatment completion.
References


6. International Agency for Research on Cancer. IARC Registry Data. [link]


20. World Health Organization. WHO position paper on mammography screening. 2014. [link]


IDENTIFICATION OF INTERVENTIONS

The package of interventions for Cervical Cancer are based on those contained in the publication “Comprehensive cervical cancer control: a guide to essential practice – 2nd edition” of the World Health Organization (WHO) as well as the first Appendix 3 [1] and [2].

METHODOLOGICAL ASSUMPTIONS

- Incidence estimates and age at diagnosis of cervical cancer are sourced from Globocan [3];
- Estimates of HPV distribution by types taken from [4], [5] and [6];
- Region-specific data on stage-distribution were used when available [7], [8], [9], [10], and [11];
- Transition rates from dysplasia (CIN) to carcinoma are taken from [7];
- Disability weights for each health state were drawn from the Global Burden of Disease 2010 disability weight study [12];
- Treatment includes diagnosis, staging, treatment and post surveillance after completion of treatment;
- Modelled interventions effect changes in:
  - rates of incidence to invasive cancer (e.g. screening);
  - rates of diagnosis of invasive cancer (e.g. screening);
  - rates of mortality (e.g. surgery).
<table>
<thead>
<tr>
<th>Procedures</th>
<th>Variable</th>
<th>Assumptions</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination against human papillomavirus (2 doses) of 9–13 year old girls</td>
<td>Effectiveness of HPV vaccination for types 16 and 18 (reduction in incidence)</td>
<td>90%</td>
<td>WHO position paper, Oct 2014 [13]; WHO position paper, Sept 2014 [14], PRIME [15]</td>
</tr>
<tr>
<td>Prevention of cervical cancer by screening women aged 30–49 through visual inspection with acetic acid linked with timely treatment of pre-cancerous lesions</td>
<td>Sensitivity</td>
<td>0.66</td>
<td>IARC, 2005 [16], Goldie et al.2001 [17]</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>0.77</td>
<td>IARC, 2005 [16]</td>
</tr>
<tr>
<td></td>
<td>Frequency (per year)</td>
<td>1/3</td>
<td>WHO, 2014 [1]</td>
</tr>
<tr>
<td>Prevention of cervical cancer by screening women aged 30–49 through “Pap” smear (cervical cytology) every 3 years linked with timely treatment of pre-cancerous lesions</td>
<td>Sensitivity</td>
<td>0.62</td>
<td>IARC, 2005 [16]</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>0.95</td>
<td>Goldie et al., 2001 [17]</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>1/3</td>
<td>WHO, 2014 [1]</td>
</tr>
<tr>
<td>Prevention of cervical cancer by screening women aged 30–49 through Human papillomavirus test every 5 years linked with timely treatment of pre-cancerous lesions</td>
<td>Sensitivity</td>
<td>0.88</td>
<td>WHO,2014 [1]; IARC, 2005 [16]; Goldie et al., 2001 [17]</td>
</tr>
<tr>
<td></td>
<td>Specificity</td>
<td>0.75</td>
<td>WHO,2014 [1]</td>
</tr>
<tr>
<td>Treatment of cervical cancer stages I and II with either surgery or radiotherapy +/- chemotherapy, incl. diagnosis, staging, treatment and post surveillance after completion of treatment</td>
<td>Stage I</td>
<td>0.120</td>
<td>Goldie et al.,2003 [7], NCCN 2016 [18], and Chuang 2016 [19]</td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>0.196</td>
<td></td>
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<tr>
<td></td>
<td>Stage III</td>
<td>0.4766</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stage IV</td>
<td>1.266</td>
<td></td>
</tr>
<tr>
<td>Annual mortality with treatment</td>
<td>Stage I</td>
<td>0.027</td>
<td>Goldie et al.,2003 [7], NCCN 2016 [18], and Chuang 2016 [19]</td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>0.062</td>
<td></td>
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<tr>
<td></td>
<td>Stage III</td>
<td>0.167</td>
<td></td>
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<tr>
<td></td>
<td>Stage IV</td>
<td>0.316</td>
<td></td>
</tr>
<tr>
<td>Impact of treatment (% reduction mortality)</td>
<td>Stage I</td>
<td>77.5%</td>
<td>Goldie et al.,2003 [7], NCCN 2016 [18], and Chuang 2016 [19]</td>
</tr>
<tr>
<td></td>
<td>Stage II</td>
<td>68.4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stage III</td>
<td>65.0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stage IV</td>
<td>75.0%</td>
<td></td>
</tr>
</tbody>
</table>

3 90% effectiveness for types 16 and 18 [13]. Assumption made that vaccines provide lifelong protection, as suggested by the absence of vaccine failures in long-term follow-up of vaccinated cohorts, and statistical extrapolation of immunogenicity data [15, 24]. The quality of the data is limited [24]. WHO is moderately confident that administration of primary HPV vaccination to young adolescent girls prevents cervical cancer later in life [13]. Estimated Incidence of HPV types 16 and 18 taken from [4], [5] and [6].

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### TABLE 2: COSTING ASSUMPTIONS USED IN WHO-CHOICE ANALYSIS

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Major costing assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination against human papillomavirus (2 doses) of 9–13 year old girls</td>
<td>Vaccine price&lt;sup&gt;4&lt;/sup&gt; Vaccine delivery costs&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Prevention of cervical cancer by screening women aged 30–49 through visual inspection with acetic acid linked with timely treatment of pre-cancerous lesions</td>
<td><strong>Screening</strong>: visual inspection with acetic acid (VIA) performed by trained provider&lt;sup&gt;3&lt;/sup&gt;  <strong>Treatment</strong>: same-day treatment with cryotherapy for individuals with positive findings on VIA  Programme monitoring and evaluation, call and recall mechanism [20]  Outpatient visit: one day&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Prevention of cervical cancer by screening women aged 30–49 through “Pap” smear (cervical cytology) every 3 years linked with timely treatment of pre-cancerous lesions</td>
<td><strong>Screening</strong>: cervical smear obtained by trained provider&lt;sup&gt;5&lt;/sup&gt; and subsequently reviewed by cytopathologist  <strong>Treatment</strong>: recall and subsequent treatment with cryotherapy for individuals with positive findings on Pap smear  Programme monitoring and evaluation, call and recall mechanism [20]  Outpatient visits: two days&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Prevention of cervical cancer by screening women aged 30–49 through Human papillomavirus test every 5 years linked with timely treatment of pre-cancerous lesions</td>
<td><strong>Screening</strong>: provider obtained HPV test&lt;sup&gt;7&lt;/sup&gt;  Recall for positive HPV test with subsequent visual inspection with acetic acid  <strong>Treatment</strong>: same-day treatment for those with positive findings on VIA with cryotherapy  Programme monitoring and evaluation, call and recall mechanism [20]  Outpatient visit: two days&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Treatment of cervical cancer stages I and II with either surgery or radiotherapy +/- chemotherapy, incl. diagnosis, staging, treatment and post surveillance after completion of treatment</td>
<td><strong>Diagnosis and staging</strong>:  Diagnostic evaluation with biopsy, specimen fixative and staining, Pre-treatment tests and staging studies when indicated including cross-sectional imaging and ultrasound.  <strong>Treatment</strong> [1], [18], [19] and [21]:  Cone biopsy or simple hysterectomy for microinvasive disease  Radical hysterectomy for early invasive surgery  Concurrent chemoradiotherapy with cisplatin and stage IB2 or stage II [22]  Management of chemotherapy-associated nausea including ondansetron  Health workforce costs for treatment  Inpatient visit days: 6 days for stage I, 2 days for stage II  Outpatient visit days: 6 days for stage I, 30 days for stage II  Surveillance with imaging as indicated for 5 years [18]</td>
</tr>
<tr>
<td>Palliative care</td>
<td>Symptom management including amitriptyline, stool softener, morphine (slow release, immediate release), and urinary catheter, as needed [23]  Outpatient or home visit days: 2 visits</td>
</tr>
</tbody>
</table>

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<sup>5</sup> Referral for subsequent colposcopy and/or biopsy for lesions suspicious for invasive carcinoma

<sup>6</sup> Costing includes health workforce time and one or two outpatient facility visits.
References

24. Duration of protection conferred by HPV vaccination in immunocompetent females [Internet]. World Health Organization. 2014. http://www.who.int/immunization/position_papers/hpv_grad_duration_immunocompetent.pdf?ua=1
CANCER INTERVENTIONS TECHNICAL BRIEFING

COLORECTAL CANCER INTERVENTIONS FOR THE APPENDIX 3 OF THE GLOBAL ACTION PLAN FOR THE PREVENTION AND CONTROL OF NONCOMMUNICABLE DISEASES

IDENTIFICATION OF INTERVENTIONS

The interventions considered for colorectal cancer analysis are based on WHO guidance and emphasizes comprehensive cancer control including diagnosis, staging, multi-modality treatment, survivorship care and palliative care as well as the first Appendix 3 [1], [2], [3] and [4].

METHODOLOGICAL ASSUMPTIONS

- Estimates of incidence of colorectal cancer and age of diagnosis are sourced from Globocan [5];
- Region-specific data on stage-distribution and ratio of colon cancer to rectal cancer of 2:1 were based on [6], [7], [8], [9], [10], [11], [12] and [13];
- Disability weights for each health state were drawn from the Global Burden of Disease 2010 disability weight study [14];
- Modelled intervention effect changes in rates of mortality (e.g. surgery).

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Variable</th>
<th>Assumptions</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of colorectal cancer stages I and II with surgery +/- chemotherapy and radiotherapy, incl. diagnosis, staging, treatment and surveillance after completion of treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual mortality rate without treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>0.18</td>
<td></td>
<td>Liu et al., 2014 [15]; NCCN, 2017 [16]</td>
</tr>
<tr>
<td>Stage II</td>
<td>0.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage III</td>
<td>0.58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>0.90</td>
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<tr>
<td>Annual mortality with treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>0.01</td>
<td></td>
<td>Frazier et al., 2000 [17]; Wu et al., 2006 [18]; Chadder et al., 2016 [19]; NCIN, 2009 [20]</td>
</tr>
<tr>
<td>Stage II</td>
<td>0.01</td>
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</tr>
<tr>
<td>Stage III</td>
<td>0.05</td>
<td></td>
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</tr>
<tr>
<td>Stage IV</td>
<td>0.57</td>
<td></td>
<td></td>
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<tr>
<td>Impact of treatment (% reduction on mortality)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stage I</td>
<td>94.4%</td>
<td></td>
<td>Liu et al., 2014 [15]; NCCN, 2017 [16]; Frazier et al., 2000 [17]; Wu et al., 2006 [18]; Chadder et al., 2016 [19]; NCIN, 2009 [20]</td>
</tr>
<tr>
<td>Stage II</td>
<td>94.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage III</td>
<td>91.4%</td>
<td></td>
<td></td>
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<tr>
<td>Stage IV</td>
<td>36.7%</td>
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</tbody>
</table>
**TABLE 2: COSTING ASSUMPTIONS USED IN WHO-CHOICE ANALYSIS**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Major costing assumptions</th>
</tr>
</thead>
</table>
| Treatment of colorectal cancer stages I and II with surgery +/- chemotherapy and radiotherapy, incl. diagnosis, staging, treatment and surveillance after completion of treatment | **Diagnosis and staging:**
- Diagnosis with colonoscopy, biopsy, specimen fixative and staining
- Pre-treatment tests and staging studies when indicated including cross-sectional imaging

**Treatment:**
- Colectomy including pre-operative antibiotics
- Adjuvant systemic therapy for colon cancer such as capecitabine and oxaliplatin for select patients with Stage II colon cancer [16] and [21]
- Neoadjuvant systemic therapy for rectal cancer such as capecitabine and radiotherapy for select patients with Stage II rectal cancer [16], [21] and [22]
- Adjuvant chemotherapy with 5-FU, oxaliplatin and leucovorin for select patients with Stage II rectal cancer [16] and [21]
- Management of complications and toxicities including surgical infection, neutropenia and chemotherapy-associated nausea that includes antibiotics, filgrastim and ondansetron [16] and [21]
- Health workforce costs for treatment including surgery and systemic therapy
- Inpatient visit days: 7 days
- Outpatient visit days: 8 days for stage I, 30 days for stage II
- Surveillance including laboratory test, cross-sectional imaging and endoscopy as indicated for 5 years

| Palliative care | Symptom management including amitriptyline, stool softeners, morphine (slow release, immediate release), amitriptyline [22]
<table>
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<tbody>
<tr>
<td></td>
<td>Outpatient or home visit days: 2 visits</td>
</tr>
</tbody>
</table>

**References**

   http://apps.who.int/iris/bitstream/10665/94384/1/9789241506236_eng.pdf?ua=1


   http://apps.who.int/iris/bitstream/10665/43827/1/9789241547406_eng.pdf

   http://apps.who.int/iris/bitstream/10665/254500/1/9789241511940-eng.pdf?ua=1


6. Comparative statistics by cancer registry - SurvCan [Internet]. Cancer Survival in Africa, Asia, the Caribbean and Central America. 2017 [cited 7 April 2017]. Available from:
   http://survcan.iarc.fr/survivalstats.php?country=chiangmai&table=Table5b&submission=submit

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