Management of Hepatocellular Carcinoma in Africa

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Disclosures

• Nothing to disclose
HCC in Africa

- Burden of HCC in Africa
- Management of HCC
- Prevention Strategies
HCC : Africa

HCC most common fatal malignancy in males & 3rd in women

Global Burden of Disease Study 2015: North Africa/Middle East & SSA
• 78,000 new cases, 86,000 deaths

Clinical Profile
• M:F ratio: 2-5 fold higher in males esp in HBV-HCC
• Socioeconomic: Rural >> Urban
• Median Age in SSA: 45 yrs (IQR 35–57) : HBV-HCC
  o 34.7yrs in rural born and living Blacks (20-40yrs)
  o 50.9 ys in rural Blacks migrating to cities in early adulthood
• Aggressive tumour with coexisting cirrhosis in only 60% in SSA
• HCC incidence matches mortality rate: 0.9

Risk factors: HCC in Africa

- Hepatitis B + Hepatitis D
- Hepatitis C
- Exposure to dietary Aflatoxin B1
- Alcohol-induced cirrhosis
- Dietary Iron overload
- NAFLD
- Obesity
- Diabetes Mellitus
- Insulin resistance
- Smoking
HCC in Africa: ASIR, ASMR and Age-standardized DALYs

<table>
<thead>
<tr>
<th>Region</th>
<th>Incident Cases, No. x 10^3 (95% UI)</th>
<th>ASIR per 100 000, No. (95% UI)</th>
<th>Deaths, No. x 10^3 (95% UI)</th>
<th>ASMR per 100 000, No. (95% UI)</th>
<th>DALYs x 10^3 (95% UI)</th>
<th>Age-Standardized DALYs Rate per 10^5 (95% UI)</th>
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<tbody>
<tr>
<td>North Africa and Middle East</td>
<td>21 (18 - 23)</td>
<td>6.3 (5.5 - 5.6)</td>
<td>24 (21 -26)</td>
<td>7.1 (6.3-7.8)</td>
<td>616 (502 - 683)</td>
<td>159.3 (133.2- 176.0)</td>
</tr>
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<td>West SSA</td>
<td>29 (22 - 39)</td>
<td>16.9 (13.0 - 22.4)</td>
<td>31 (24-41)</td>
<td>18.1 (14.1-23.4)</td>
<td>1 055 (804 -1422)</td>
<td>483.9 (372.3 -640.7)</td>
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<tr>
<td>Central SSA</td>
<td>7 (5 - 11)</td>
<td>16.9 (10.6 - 25.9)</td>
<td>8 (5-13)</td>
<td>19.9 (12.6-30.3)</td>
<td>234 (140 -373)</td>
<td>460.1 (278.1 - 723.4)</td>
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<tr>
<td>East SSA</td>
<td>17 (13 - 21)</td>
<td>10.3 (7.9 -12.8)</td>
<td>19 (14-24)</td>
<td>11.9 (9.0-15.0)</td>
<td>575 (433 -750)</td>
<td>306.3 (231.1 - 396.2)</td>
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<td>Southern SSA</td>
<td>4 (3-5)</td>
<td>8.6 (7.0 -10.6)</td>
<td>4 (4-5)</td>
<td>9.5 (7.9-11.4)</td>
<td>114 (94 -145)</td>
<td>218.3 (180.6 - 272.1)</td>
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</table>

JAMA Oncol 2017;3(12):1683
<table>
<thead>
<tr>
<th>Region</th>
<th>Cancer</th>
<th>ASIR 2015, male</th>
<th>95% UI ASIR 2015, male</th>
<th>ASIR 2015, female</th>
<th>95% UI ASIR 2015, female</th>
<th>Ratio ASIR Male/Female</th>
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<td>(1.6, 4.6)</td>
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<td>(1.1, 3.5)</td>
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<td>1.1</td>
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<td>0.9</td>
<td>(0.6, 1.4)</td>
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Contribution of HBV, HCV, Alcohol and Other Causes on Absolute Liver Cancer Deaths in Both Sexes: 2015

<table>
<thead>
<tr>
<th>Region</th>
<th>HBV</th>
<th>HCV</th>
<th>Alcohol</th>
<th>Other</th>
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<tbody>
<tr>
<td>Global</td>
<td>33%</td>
<td>21%</td>
<td>30%</td>
<td>16%</td>
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<tr>
<td>North Africa &amp; Middle East</td>
<td>27%</td>
<td>44%</td>
<td>13%</td>
<td>16%</td>
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<td>Western SSA</td>
<td>45%</td>
<td>11%</td>
<td>29%</td>
<td>15%</td>
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<td>Central SSA</td>
<td>20%</td>
<td>37%</td>
<td>29%</td>
<td>13%</td>
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<td>Eastern SSA</td>
<td>26%</td>
<td>28%</td>
<td>32%</td>
<td>14%</td>
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<tr>
<td>Southern SSA</td>
<td>29%</td>
<td>20%</td>
<td>40%</td>
<td>11%</td>
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</table>

JAMA Oncol 2017;3(12):1683
In 2015, Globally, at country level, HBV contributed the largest proportion to liver cancer mortality in The Gambia, at 60%.
Africa Liver Cancer Consortium

9 countries: 21 tertiary referral centres

- 2,566 patients
- Egypt (1251) vs 9 SSA countries (1315)
- **No Southern African countries**

Described: Aug 2006 - April 2016

- Demographic characteristics
- Clinical features
- Management
- Outcomes

Lancet Gastroenterol Hepatol 2017;2:103
Africa Liver Cancer Consortium

Overall median age: 54 yrs (IQR 44-61)

**Egypt:** 58 yrs (IQR 53-63)  
**SSA:** 46 yrs (IQR 36-58)

**Aetiology**

**Egypt**
- HCV 84% (1054/1251)
- HBV 1%
- Other 12%
- Cirrhosis 100%

**SSA**
- HBV 55% (597/1082)
- HCV 6%
- Alcohol 13%
- Other 22%
- Cirrhosis 66%

**Median Age**
- **HCV-HCC:** 58 yrs (IQR 53-63)  
- **HBV-HCC:** 42 yrs (IQR 34-51)

**Treatment**

**Egypt:** 76% (956/1251)  
**SSA:** 3% (43/1315)

**Median Overall Survival**

**Egypt:** 10.9 months (9.6-12)  
**SSA:** 2.5 months (2-3.1)

Lancet Gastroenterol Hepatol 2017;2:103
**HCC BCLC stage at presentation**

<table>
<thead>
<tr>
<th>BCLC stage</th>
<th>Sub-Saharan Africa*</th>
<th>Europe**</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-B</td>
<td>5%</td>
<td>40.4%</td>
</tr>
<tr>
<td>C</td>
<td>23%</td>
<td>43.9%</td>
</tr>
<tr>
<td>D</td>
<td>72%</td>
<td>14.5%</td>
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</tbody>
</table>


### Primary Treatment of HCC in Africa

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Egypt (n=1251)</th>
<th>Other African countries (n=1315)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any specific treatment</td>
<td>956 (76%)</td>
<td>43 (3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Curative treatment (transplantation or resection or local ablation)</td>
<td>442 (35%)</td>
<td>8 (&lt;1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Transplantation</td>
<td>10 (&lt;1%)</td>
<td>0</td>
<td>0.001</td>
</tr>
<tr>
<td>Resection</td>
<td>26 (2%)</td>
<td>8 (&lt;1%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Local radiofrequency ablation</td>
<td>406 (32%)</td>
<td>0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TACE</td>
<td>451 (36%)</td>
<td>5 (&lt;1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>63 (5%)</td>
<td>12 (1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other systemic treatment</td>
<td>0</td>
<td>18 (1%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are n (%). Primary treatment was reported per each patient in the following order of treatment option: transplantation > resection > local radiofrequency ablation > transcatheter arterial chemoembolisation (TACE) > sorafenib > other systemic treatment.

Lancet Gastroenterol Hepatol 2017;2:103
Africa Liver Cancer Consortium

Overall survival according to BCLC stage

• BCLA stage A-B: HR 0.63 (95% CI 0.22-1.4)
  o No difference between Egypt and other SSA countries

Survival worse in other SSA countries if:

• BCLA stage C: HR 2.07 (95% CI 1.42-2.92)
• BCLA stage D: HR 3.37 (95% CI 2.31-5.07)
• BCLA stage unknown: HR 5.96 (95% CI 4.16-8.67)

Median age range for HCC diagnosis younger in SAA countries

• 46 yrs (IQR 36-58) vs 58 yrs (IQR 53-63)
• Role of environmental, biological or genetic factors

Lancet Gastroenterol Hepatol 2017;2:103
Factors independently associated with poor survival

- **SSA vs Egypt:** HR 1.59 (95% CI 1.13–2.20)
- **Hepatic encephalopathy:** HR 2.81 (1.72–4.42)
- **Largest tumour diameter:** HR 1.07 per cm increase (1.04–1.11)
- **log α-fetoprotein:** HR 1.10 per unit increase (1.02–1.20)
- **Eastern Cooperative Oncol Grp performance status 3-4:** HR 2.92 (2.13–3.93)
- **No specific treatment:** HR 1.79 (1.44–2.22)

**Tumour size information:** Missing in 62% of SSA countries

- **Increased chance of receiving Rx:** OR 2.3 (95% CI 1.2–4.3)
- **Better overall survival:** HR 0.83 (95% CI 0.66-1.04)

Lancet Gastroenterol Hepatol 2017;2:103
Clinical Presentations: SSA

- Aggressive tumour – diagnosed late in advanced stage
- **Triad**: Abdominal pain, swelling and Jaundice

Clinical Presentations in West African Countries

Ladep et al, World J Hepatol 2014;6(11):783
Models predicting HBV-related HCC development

<table>
<thead>
<tr>
<th>Models</th>
<th>Authors</th>
<th>Developed area</th>
<th>Number of patients</th>
<th>Including cirrhosis</th>
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<tr>
<td>CU-HCC(^{37})</td>
<td>Wong et al</td>
<td>Hong Kong</td>
<td>1005</td>
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<td>GAG-HCC(^{38})</td>
<td>Yuen et al</td>
<td>Hong Kong</td>
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<td>REACH-B(^{39})</td>
<td>Yang et al</td>
<td>Taiwan</td>
<td>3584</td>
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<td>LSM-HCC(^{40})</td>
<td>Wong et al</td>
<td>Hong Kong</td>
<td>1035</td>
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<tr>
<td>PAGE-B(^{41})</td>
<td>Papatheodoridis et al</td>
<td>Europe</td>
<td>1325</td>
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</tr>
</tbody>
</table>

NONE OF THE HCC RISK SCORES VALIDATED IN AFRICA

- Weighted for Age and Cirrhosis
- 40% HCC occurs in young non-cirrhotic HBV pts in SSA
HCC Screening & surveillance programmes

AFP & ultrasound every 6 months in high risk individuals

- Enables early detection at a treatable stage
- Improves overall survival

Dependent on:

- Recall policies - need programmes
- Access to therapy
  - Reducing morbidity & mortality

Need Guidelines for North Africa & SSA

Small hypoechoic mass
HCC surveillance programmes

The Surveillance Gap

China
Europe
Japan
North America
South Korea
Taiwan

Survival time from treatment initiation (month)

Survival probability

L Roberts; Liver Int 2015; 35(9): 2155
Web-based survey: HCC surveillance in SSA

14 African Countries: 58 referral centres: 63 participants

Nov 2016 - Feb 2017: Burkina Faso, Cameroon, Cote D’Ivoire, Egypt, Ethiopia, Gambia, Ghana, Kenya, Malawi, Mauritania, Nigeria, South Africa, Sudan, Uganda, Tanzania and Zambia

HCC surveillance at time of diagnosis
- 76% reported that <10% pts were under surveillance at diagnosis

HBV diagnosis before HCC diagnosis
- 62% reported that HBV was diagnosed before HCC diagnosis in <10%

Barriers to HCC surveillance
- 90% lack of liver disease diagnosis
- 59% lack of symptoms
- 44% poverty

Lewis Roberts: GASLIDD 2018 Meeting, Accra Ghana, August 2018
Web-based survey: HCC surveillance in SSA

Available treatment options for HCC
- Surgery: 56%
- Local Ablation: 37%
- Locoregional therapy: 30%

Reasons for no treatment
- Advanced stage: 98%
- Poverty: 59%
- Lack of clinical expertise: 57%

Population-based HBV screening in endemic countries such as SSA is a critical strategy for identifying candidates for HCC surveillance

Lewis Roberts: GASLIDD 2018 Meeting, Accra Ghana, August 2018
Diagnostic algorithm for HCC

Mass detected on surveillance ultrasonography in a cirrhotic liver

<1 cm

• Stable over 18–24 months
  - Return to standard surveillance

• Enlarging
  - Proceed according to lesion style

>1 cm

• Four-phase MDTC or dynamic MRI
  - Arterial hypervascularisation and venous or delayed phase washout

Negative

• Other imaging modality (CT or MRI)
  - Arterial hypervascularisation and venous or delayed phase washout

Positive

Biopsy

Negative

Inconclusive

Diagnosis requires:
• Sophisticated Imaging
• Experienced radiologists

Lancet 2018; 391: 1301-14
Management of HCC

WHO Africa region

- 27 are low-income and 14 lower-middle-income countries

Management options depend on:

1. Access to Healthcare
   - 0.7 (low-income) and 5.5 (lower-middle income) surgical care providers per 100 000 population
     - 22.6 and 56.9 per 100 000 for upper-middle-income and high-income countries respectively

2. Stage of HCC

3. Performance status
Management Options: HCC

**Curative**
- Local ablation
- Resection
- Liver Transplantation

**Palliative**
- TACE
- Systemic therapy: Sorafenib
- Best Supportive care

**Prevention Strategies**
Liver Resection

WHO Global Health Estimate: Estimated need for surgery (GBD 2010 study)

Highest rates of surgical need:

- **Western SSA**: 6,495 operations per 100,000 inhabitants
- **Central SSA**: 6,255 operations per 100,000 inhabitants
- **Eastern SSA**: 6,145 operations per 100,000 inhabitants

2017 Online survey: SSA outside of SA

- Hepatobiliary surgeons at 13 tertiary centres
- Nigeria, Senegal, Ghana, Cameroon, Kenya, Uganda, Namibia, Zimbabwe

Liver Transplantation

Established Liver Transplantation centres in Africa

- Egypt
- South Africa

Planning Liver Transplant Programmes

- Sudan
- Ghana
**Radiology**

Limited access to diagnostic imaging: CT scan, MRI

CT scan: Arterial phase  
Delayed portal venous phase  
MRI Primovist

Lack of trained interventional radiologists: RFA
## Systemic Therapy

Targeted therapies evaluated in phase 3 trials in HCC

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Randomisation</th>
<th>Time to progression</th>
<th>Survival</th>
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<td></td>
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<td>Months</td>
<td>p value</td>
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<td><strong>First line</strong></td>
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<tr>
<td>Sorafenib*</td>
<td>Llovet et al (2008)&lt;sup&gt;71&lt;/sup&gt; Sorafenib (n=299) vs placebo (n=303)</td>
<td>5.5 vs 2.8</td>
<td>&lt;0.001</td>
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<tr>
<td>Sorafenib*</td>
<td>Cheng et al (2009)&lt;sup&gt;24&lt;/sup&gt; Sorafenib (n=150) vs placebo (n=76)</td>
<td>2.8 vs 1.4</td>
<td>&lt;0.001</td>
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<tr>
<td>Sunitinib</td>
<td>Cheng et al (2013)&lt;sup&gt;125&lt;/sup&gt; Sunitinib (n=550) vs sorafenib (n=544)&lt;sup&gt;†&lt;/sup&gt;</td>
<td>3.6 vs 3.6</td>
<td>NS</td>
</tr>
<tr>
<td>Brivanib</td>
<td>Johnson et al (2013)&lt;sup&gt;126&lt;/sup&gt; Brivanib (n=577) vs sorafenib (n=578)</td>
<td>4.2 vs 4.1</td>
<td>NS</td>
</tr>
<tr>
<td>Sorafenib plus erlotinib</td>
<td>Zhu et al (2015)&lt;sup&gt;131&lt;/sup&gt; Sorafenib plus erlotinib (n=362) vs sorafenib (n=358)</td>
<td>3.2 vs 4.0</td>
<td>NS</td>
</tr>
<tr>
<td>Linifanib</td>
<td>Cainap et al (2015)&lt;sup&gt;132&lt;/sup&gt; Linifanib (n=514) vs sorafenib (n=521)</td>
<td>5.4 vs 4.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Sorafenib plus doxorubicin</td>
<td>Abou-Alfa et al (2016)&lt;sup&gt;133&lt;/sup&gt; Sorafenib plus (n=173) doxorubicin vs sorafenib (n=173)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Lenvatinib*</td>
<td>Kudo et al (2017)&lt;sup&gt;135&lt;/sup&gt; Lenvatinib (n=478) vs sorafenib (n=476)&lt;sup&gt;††&lt;/sup&gt;</td>
<td>8.9 vs 3.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Second line</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regorafenib*</td>
<td>Bruix et al (2016)&lt;sup&gt;136&lt;/sup&gt; Regorafenib (n=379) vs placebo (n=194)</td>
<td>3.9 vs 1.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Brivanib</td>
<td>Llovet et al (2013)&lt;sup&gt;137&lt;/sup&gt; Brivanib (n=263) vs placebo (n=132)</td>
<td>4.2 vs 2.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Everolimus</td>
<td>Zhu et al (2014)&lt;sup&gt;138&lt;/sup&gt; Everolimus (n=362) vs placebo (n=184)</td>
<td>2.9 vs 2.6</td>
<td>NS</td>
</tr>
<tr>
<td>Ramucirumab</td>
<td>Zhu et al (2015)&lt;sup&gt;139&lt;/sup&gt; Ramucirumab (n=283) vs placebo (n=282)</td>
<td>3.5 vs 2.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tivantinib</td>
<td>Rimassa et al (2017)&lt;sup&gt;140&lt;/sup&gt; Tivantinib (n=226) vs placebo (n=114)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

NS = non-significant. NA = not available. *Agents with survival benefit. †Open-label trial. ††Non-inferiority design.

Only 1% of current ongoing clinical HCC trials conducted in Africa

Lancet 2018; 391: 1301-14
Palliative treatment in Africa

- 95% HCC pts in SSA treated with palliative intent

SSA Countries with access to oral morphine in 2012

- Regulatory restrictions
- Lack of Healthcare training
  - Opioids for palliation
- Opioid phobia
  - Side-effects
  - Addiction

At least 88% of cancer deaths with moderate to severe pain are untreated

Lancet Oncol. 2013;14:e76-82; Lancet Oncol 2017;18(9):e522
Resource-sensitive Approach to HCC

Resources differ within and between countries in Africa

**Minimal resources**

- Hardly any treatment options are available
  
- *Primary and secondary prevention strategies*

**Medium resources**

- *Resection and ablation available* but not transplantation
  
- Improve access to Hepatobiliary surgery and Interventional radiology

**High resources**

- Liver transplant available

Prevention Strategies

Sustainable Development Goals and World Health Organization strategies for noncommunicable diseases and viral hepatitis

**Primary prevention targets include**

- Eliminating viral hepatitis as a major public health threat by 2030
  - HBV Immunization: Birth dose, Universal vaccination, high risk groups
  - Safe injection and transfusion practices
  - Avoidance of parenteral treatments
- Decrease aflatoxin exposure
- Reducing the harmful use of alcohol and tobacco
- Controlling diabetes and obesity
- Community and patient education programmes
  - Risk factors for viral hepatitis
  - Aflatoxin and associated liver disease
  - Healthy lifestyle options

Prevention of Perinatal Infection

Systematic review:
Earlier age at infection associated with:
- Increasing probability of chronic HBV infection
- Increased risk of HCC

Shimakawa et al; PlosOne 2013; 8(7): e69430

Longitudinal study in The Gambia: HBV MTCT was a risk factor for:
- Persistent high viral replication
- Significant fibrosis
- HCC

Shimakawa et al; Gut 2016;65(12):2007
Prevention Strategies: HBV vaccination

Taiwan: 1509 HCC patients: 1343 were born before & 166 were born post HBV vaccination program

Taiwan: HCC incidence per 10⁵ person-years decreased from 0.92 in unvaccinated to 0.23 in vaccinated cohorts

Global and regional infant vaccination rates

WHO/UNICEF estimates of third dose of HBV vaccine coverage 1990-2015

- Global coverage: 84%
- Africa region: 77%

Taiwan (Hepatology 2014;60:125)
- Incomplete vaccination is an important predictor for HCC
- HR 2.52 after correction for maternal HBsAg status
Prevention Strategies: Aflatoxin Control

Aflatoxin B1 & HBV - synergistic hepatocarcinogenic effects

• RR 54.1 (95% CI 21.3-137.7) with dual exposure

Address both routes of contamination: Growth & storage of crops

• Replace crops with those that are less susceptible to AFB1
  ❖ Rice-based diet in China decreased exposure

• Damaged plants more susceptible to fungal contamination
  ❖ Pre-harvest prevention with adequate irrigation and use of fungicides
  ❖ Sun-drying on cloth not ground; hand-sorting and removing mouldy crops

• Improved storage facilities

• Decrease AFB1 below detectable limits: Decreases HCC incidence in general population by 14-19% and in HBsAg population by 10-29%

HCC : Prevention Strategies

Secondary prevention

*Treatment for HBV and HCV*

- Decrease HCC risk including those with advanced liver fibrosis, even leading to regression of fibrosis
- **Dependent on diagnosis and linkage to care**
  - Affordable WHO-pre-qualified point-of-care diagnostics

*Screening and surveillance of high-risk populations*

*Establish centres of excellence for HCC management*
Significant reduction in HCC with ETV compared with controls in cirrhotic patients

**No cirrhosis**

<table>
<thead>
<tr>
<th>Treatment duration (years)</th>
<th>Cumulative HCC rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>1.6%</td>
</tr>
<tr>
<td>2</td>
<td>3.2%</td>
</tr>
<tr>
<td>3</td>
<td>4.9%</td>
</tr>
<tr>
<td>4</td>
<td>7.0%</td>
</tr>
<tr>
<td>5</td>
<td>9.5%</td>
</tr>
<tr>
<td>6</td>
<td>11.4%</td>
</tr>
</tbody>
</table>

Log-rank test:
- ETV vs LAM: $P=0.126$
- ETV vs control: $P=0.440$
- LAM vs control: $P=0.879$

**Cirrhosis**

<table>
<thead>
<tr>
<th>Treatment duration (years)</th>
<th>Cumulative HCC rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>2.6%</td>
</tr>
<tr>
<td>2</td>
<td>4.3%</td>
</tr>
<tr>
<td>3</td>
<td>7.0%</td>
</tr>
<tr>
<td>4</td>
<td>7.0%</td>
</tr>
<tr>
<td>5</td>
<td>11.4%</td>
</tr>
<tr>
<td>6</td>
<td>20.9%</td>
</tr>
</tbody>
</table>

Log-rank test:
- ETV vs LAM: $P=0.043$
- ETV vs control: $P<0.001$
- LAM vs control: $P=0.019$

Cumulative HCC incidence rates at 5 years: 3.7% (Entecavir) 13.7% (controls), $p <0.001$

Secondary Prevention: HBV Treatment

The Polaris Observatory HBV Modelling Study : Africa

- 78 M (68–89 M) estimated to be HBV-infected
- 1 486 000 diagnosed (2%)
- 21 356 000 (27%) eligible for Rx
- 33 700 treated (<1% accessed therapy)
- Target 1M by 2020

Lancet Gastroenterol Hepatol 26 March 2018
Secondary Prevention: HCV Treatment

Cumulative incidence of HCC

Retrospective cohort study

- **22,500 pts treated with DAAs**
- **129 Veterans Health Administration hospitals: 1 Jan - 31 Dec 2015**
- **271 new HCC cases**
  - 183 patients with SVR

SVR: significantly reduced risk of HCC (0.90 vs 3.45 HCC/100 person-yrs)

- Adjusted HR 0.28 (95% CI 0.22–0.36)

Cirrhotics had highest annual HCC incidence after SVR

- 1.82 vs 0.34/100 person-yrs in non-cirrhotics; adjusted HR 4.73 (95% CI, 3.34-6.68)
- **Ongoing surveillance required**
Access to HCV Therapy

Net cure by region in 2016

Negative net cure = epidemic size is increasing

Net cure worldwide in 2016: 0.43%
Tertiary Prevention

Hepatitis B
Systemic review and meta-analysis of NA therapy: Reducing HCC recurrence after curative therapy

• 13 trials with 6 350 patients

• Improvement in recurrence-free survival in NA group
  o HR 0.66, 95% CI 0.54–0.80; p<0.0001

• Improvement in overall survival in NA group
  o HR 0.56, 95% CI 0.43–0.73; p<0.0001

Nationwide claim database study in Taiwan

• NAs therapy was independently associated with reduced risk of HCC recurrence after:
  o Surgical resection: HR 0.67; P < 0.001
  o Radiofrequency ablation: HR 0.69; P < 0.005

The PROLIFICACA Project

Prevention of Liver Fibrosis and Cancer in Africa

*Reduce the incidence of HBV-related HCC in West Africa*

- **Validated 3 point-of-care rapid diagnostic tests (Determine, Vikia and Espline), both in the field and laboratory settings in the Gambia**
  - Enables upscaling of diagnosis and linkage to care

- **Demonstrated that large scale test-and-treat HBV programmes are feasible and cost-effective in endemic countries such as SSA**

- **Validated a urinary metabolite panel**: Inosine, indole-3-acetate, galactose, and an N-acetylated amino acid (NAA)
  - High sensitivity (86.9% [75.8-94.2]) & specificity (90.3% [74.2-98.0]) in discrimination of HCC from cirrhosis
  - Diagnostically outperforms serum AFP

Management of HCC in Africa

- Public health approach with primary prevention
  - Remains the cornerstone of management of HCC in SSA

- HCC fulfills the criteria for a successful surveillance program
  - Enabling earlier diagnosis of a curable HCC

- Improved surveillance requires improved access to:
  - Point-of-care viral hepatitis testing
  - Diagnostic imaging modalities: Fibroscan, US, CT scan, MRI
  - Interventional Radiology
  - Curative Surgery
  - Palliative Interventions

- Need to develop adaptable resource-sensitive HCC Guidelines for Africa and establish HCC registries

- Develop centres of excellence within African countries
  - Academic training centres
  - Sites for Clinical Trials