



## 9th Liver Interest Group Annual Meeting

# HCC guidance



Eduard Jonas

Surgical Gastroenterology Unit

University of Cape Town and Groote Schuur Hospital

Cape Town

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[eduard.jonas@uct.ac.za](mailto:eduard.jonas@uct.ac.za)

# Introduction

- Most common primary hepatic malignancy
- Annual incidence of 782000\*
- Globally accounts for 9.2% of all new cancer cases
- 5<sup>th</sup> most common cancer in males and 8<sup>th</sup> in females
- Around 84% occur in less developed regions
- Annual mortality is 746000\*
- Worldwide it is the second leading cause of cancer-related death

\*IARC. *Liver Cancer: Estimated Incidence, Mortality, Prevalence Worldwide in 2012*.  
[http://globocaniarcfr/Pages/fact\\_sheets\\_cancer.aspx](http://globocaniarcfr/Pages/fact_sheets_cancer.aspx). 2012. Accessed December 12, 2013.



Clinical Practice Guidelines



JOURNAL  
OF HEPATOLOGY

## **EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma<sup>☆</sup>**

European Association for the Study of the Liver<sup>\*</sup>

**HEPATOLOGY**



PRACTICE GUIDELINE | HEPATOLOGY, VOL. 67, NO. 1, 2018

## **AASLD Guidelines for the Treatment of Hepatocellular Carcinoma**

Journal of Hepatology 2018, Vol. 69  
Hepatology, 2018, Vol. 67

- Addressing key questions
- Assessment of level of evidence
- Grade of recommendations

- Prevention strategies
- Diagnostic algorithms
- Treatment algorithms

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# Prevention strategies

## **Primary prevention**

- HBV vaccination: birth dose, high risk groups
- Safe injection and transfusion practices
- Decrease toxin exposure (Aflatoxin B1)
- Education on risk factors
- Control of obesity, diabetes and NAFLD
- Management of iron overload
- Limit alcohol ingestion
- Treatment for HBV and HCV

## **Secondary prevention**

- Screening for and surveillance of high-risk populations

## **Tertiary prevention**

- Follow-up of treated patients especially HBV-infected and cirrhotic patients

# Prerequisites for surveillance

- ☐ disease with high prevalence, mortality and morbidity
- ☐ effective therapies should be available
- ☐ the at-risk population must be readily identifiable
- ☐ screening tests - sensitive and specific, minimally invasive, widely available and inexpensive
- ☐ treatment of occult disease should offer advantages compared to treatment of symptomatic disease
- ☐ surveillance program with effective recall procedures
- ☐ screening need must be sanctioned by healthcare providers and accepted by patients

# At-risk population

Surveillance has been found to be cost-effective in

- Cirrhotics\*
  - prevalence of cirrhosis in HCC patients is 85%-95%
  - HCC incidence rate 2-4% per year (threshold  $\geq 1.5\%$ /year)
- Chronic hepatitis B
  - substantial differences in guidelines on subgroups based on clinical and ethnic criteria
- Stage 3 fibrosis or advanced/bridging fibrosis

\*Child-Pugh C - only if on transplant list

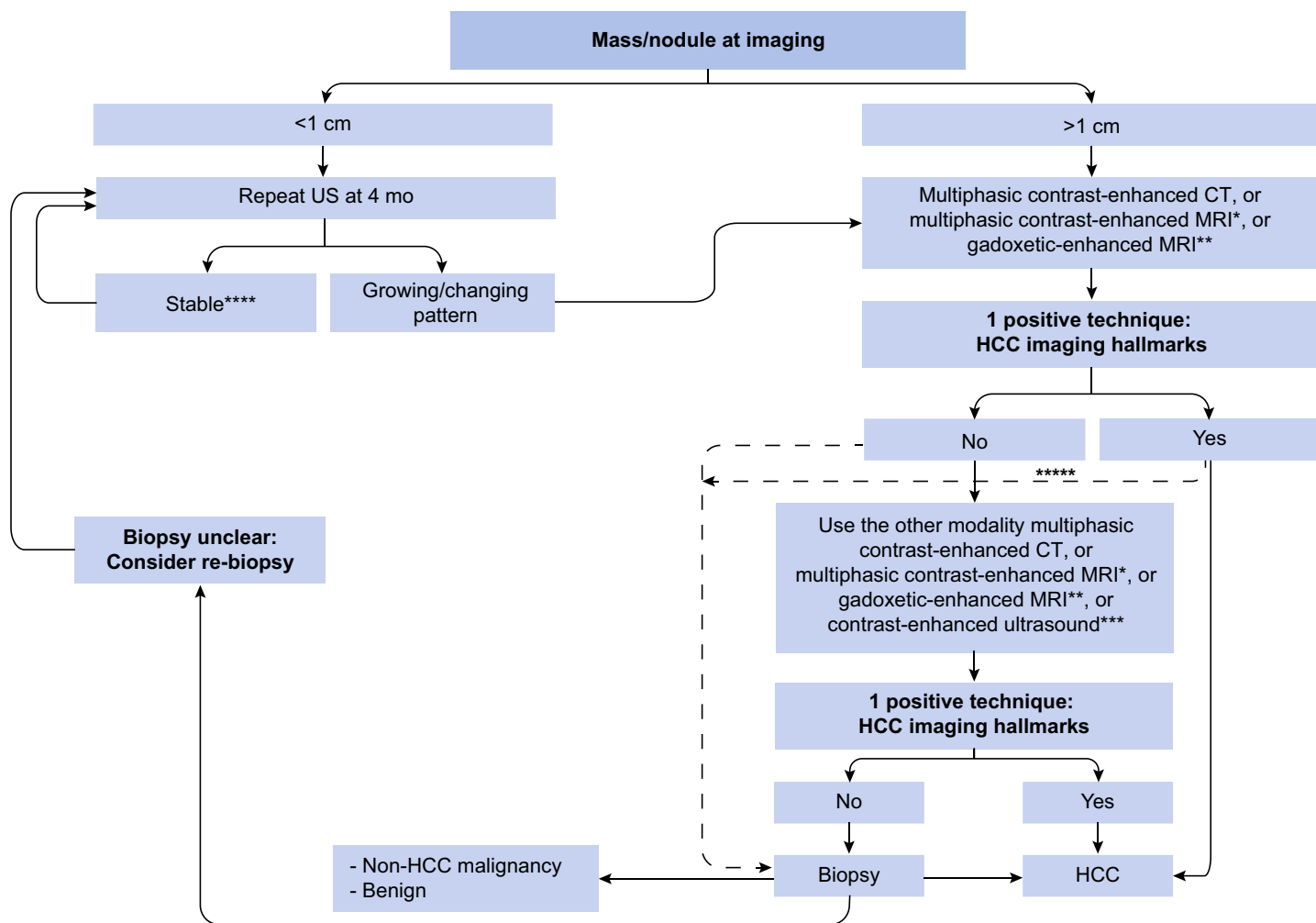
# Screening tests

- Ultrasound
  - sensitivity of 93 % (63% for early stage HCC)
- AFP
  - 10-11 ng/ml - sensitivity 80%; specificity 70%
  - 17-21 ng/ml - sensitivity 65%; specificity 85%
  - $\geq 20$  ng/ml- sensitivity 41-65%; specificity 80%-94%
- Combination of AFP and Ultrasound
  - AFP increase  $\geq 2$  times from 12 month nadir and US - sensitivity 99.2%; specificity 71.5%

# Screening interval

- 6 versus 12 monthly US (meta-analyses)
  - significantly higher sensitivity with 6 monthly for detecting early HCC
- 3 versus 6 monthly (randomized controlled trial)
  - no difference in HCC incidence ( $p=0.13$ ) or in prevalence of tumours  $\leq 30$  mm in diameter ( $p=0.30$ ) was seen

# Diagnostic algorithm and recall policy





# Efficacy of HCC surveillance

HCC surveillance is associated with improved

- **Early stage detection**

70.9% vs 29.9% if diagnosed incidentally or if presenting with symptoms

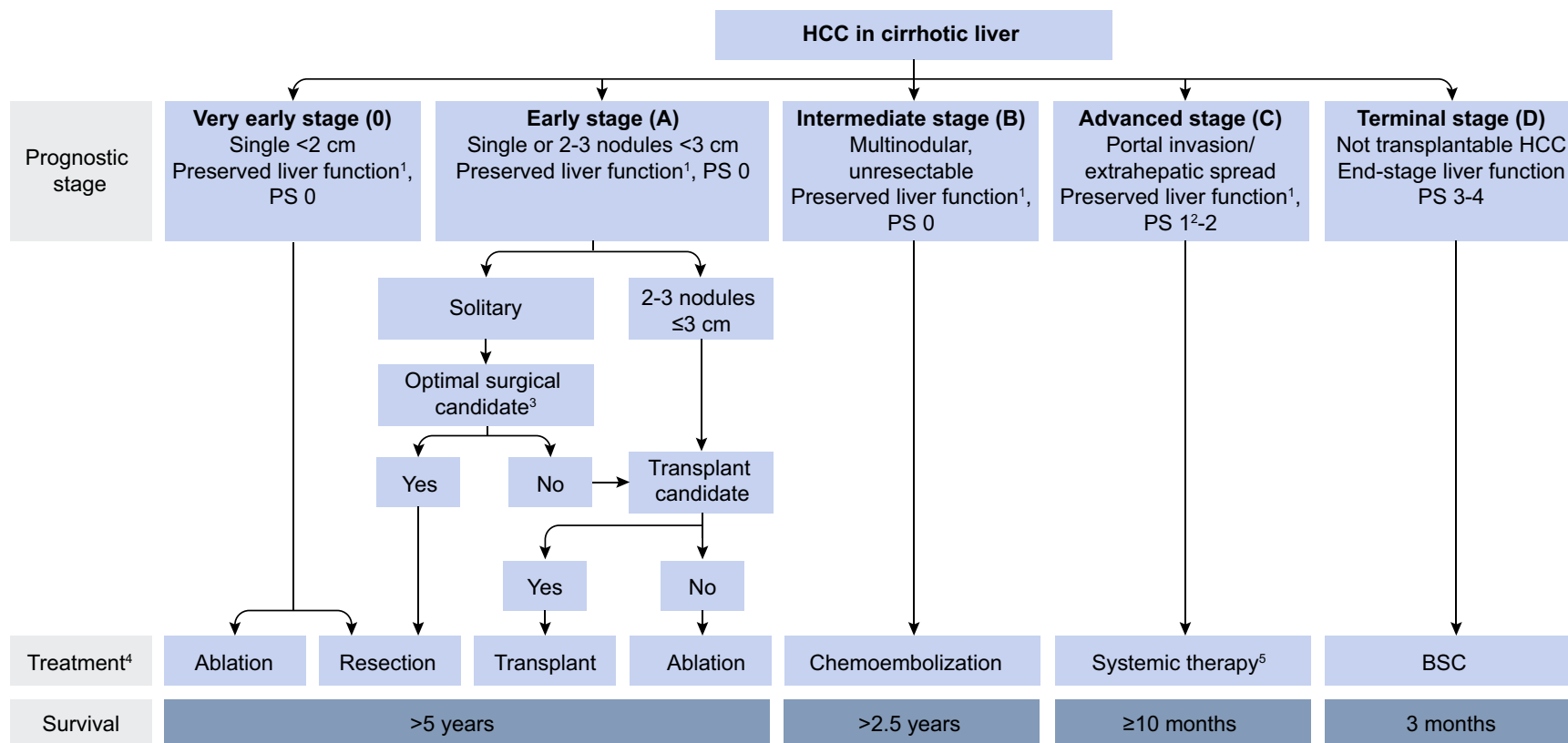
- **Curative treatment rates**

51.3% vs. 23.8% if diagnosed incidentally or if presenting with symptoms

- **Significantly prolonged survival**

50.8% vs. 28.2% 3-year survival if diagnosed incidentally or if presenting with symptoms

# Treatment strategy



# Prognosis of untreated HCC

Median survival as per Barcelona Clinic Liver Cancer (BCLC) stage

- Stages 0/A 13.4 months
- Stages B 9.5 months
- Stages C 3.4 months
- Stages D 1.6 months

# Prognosis of treated HCC

- Liver resection\* >70% 5 year survival
- Local ablation\* >70% 5 year survival
- Transplantation\* >75% 5 year survival
- TACE 20 mo improved survival
- Sorafenib 2.9 mo improved survival

\*Treated within the Barcelona criteria

Guglielmi A, et al. World J Gastroenterol.2014;20:7525-7533  
Yao FY. American Journal of Transplantation 2008;8:1982–1989  
Tiong L, et al. British Journal of Surgery 2011;98:1210–1224  
Llovet JM, Bruix J. Hepatology 2003;37:429–42  
Llovet JM, et al. N Engl J Med 2008;359:378-90



# Guidance in sub-Saharan Africa

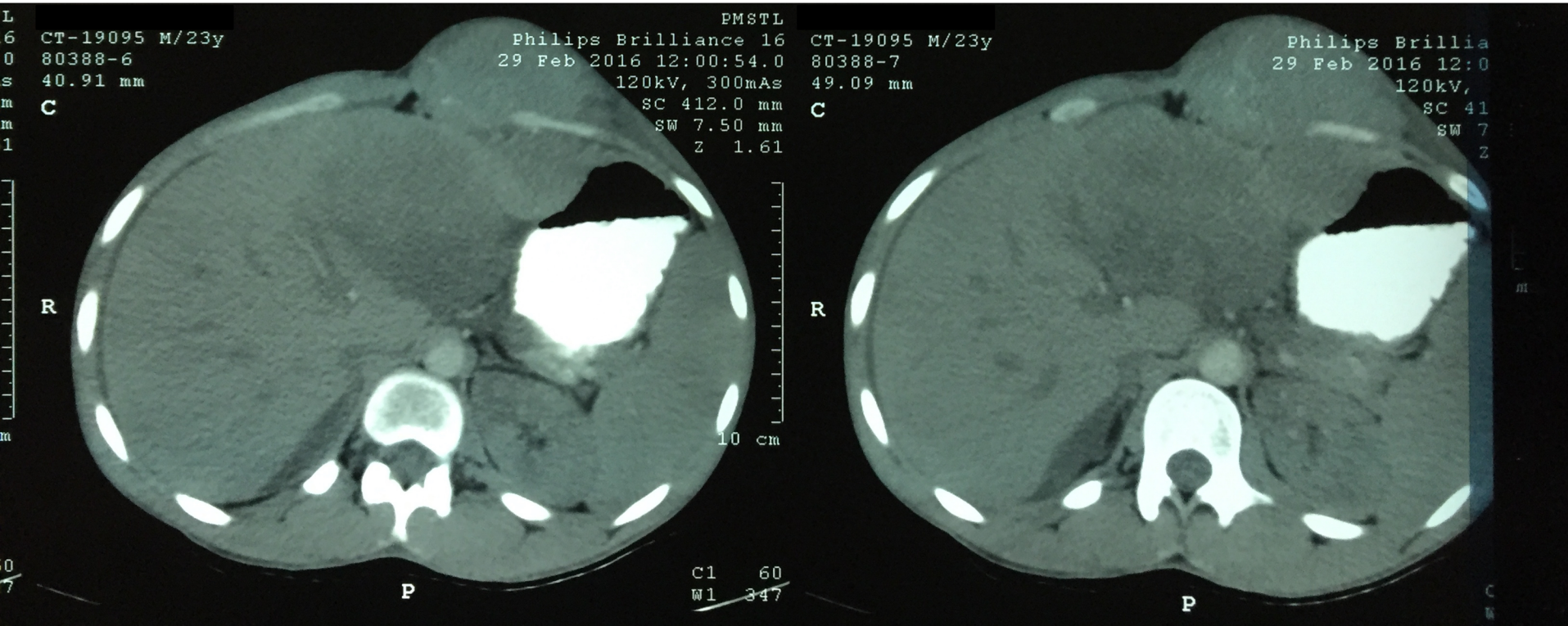
- Current guidelines are exclusively based on data from well-resourced countries and are tailored for the disease spectrum as seen in these populations
- Assume that medicine is practiced in a standard well-resourced environment and that imaging and treatment options are generally available

# HCC in sub-Saharan Africa

- Annual incidence 103.8 per 100 000 vs. 1 - 7 per 100 000
- Male predominance 8:1 vs. 2.5:1
- Mean age of onset 33.4 - 47.5 years vs. 60 - 80 years
- Present more often with tumour-related symptoms
- Present more often with complicated disease
- More rapid tumour growth and larger tumour burdens
- Very low resectability rates



# Is it a different disease?

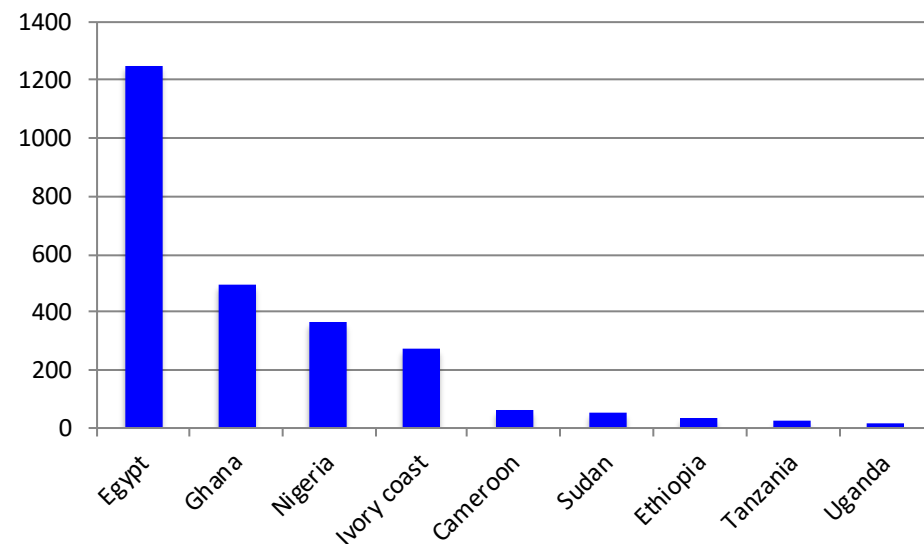
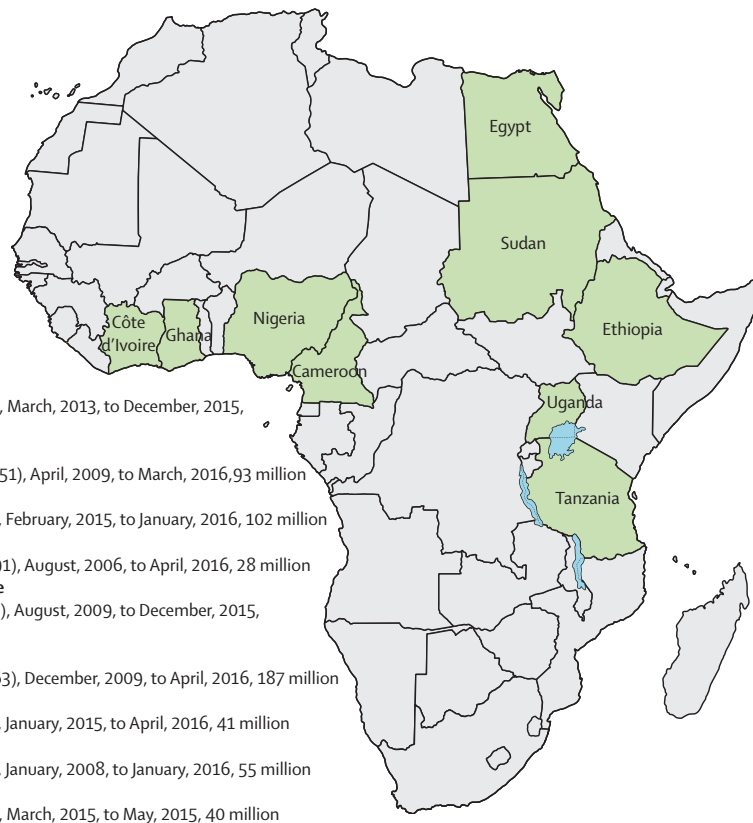




# Epidemiology

- In order of prevalence
  1. Western Africa
  2. Central Africa
  3. Eastern Africa
  4. Southern Africa
- Incidences  $>20/100\ 000$  inhabitants reported in a number of African Countries

# Characteristics, management, and outcomes of patients with hepatocellular carcinoma in Africa: a multicountry observational study from the Africa Liver Cancer Consortium



2566 patients  
21 referral centres

Yang JD, et al. Lancet Gastroenterol Hepatol 2016

Published Online December 2, 2016 [http://dx.doi.org/10.1016/S2468-1253\(16\)30161-3](http://dx.doi.org/10.1016/S2468-1253(16)30161-3)

# BCLC stage at presentation

BCLC stage	Sub-Saharan Africa*	Europe**
A-B	5%	40.4%
C	23%	43.9%
D	72%	14.5%

\* Yang JD, et al. Lancet Gastroenterol Hepatol 2016

\*\* Weinmann A, et al. J Clin Gastroenterol. 2014;48:279-89

# Treatment in sub-Saharan Africa

n=1315

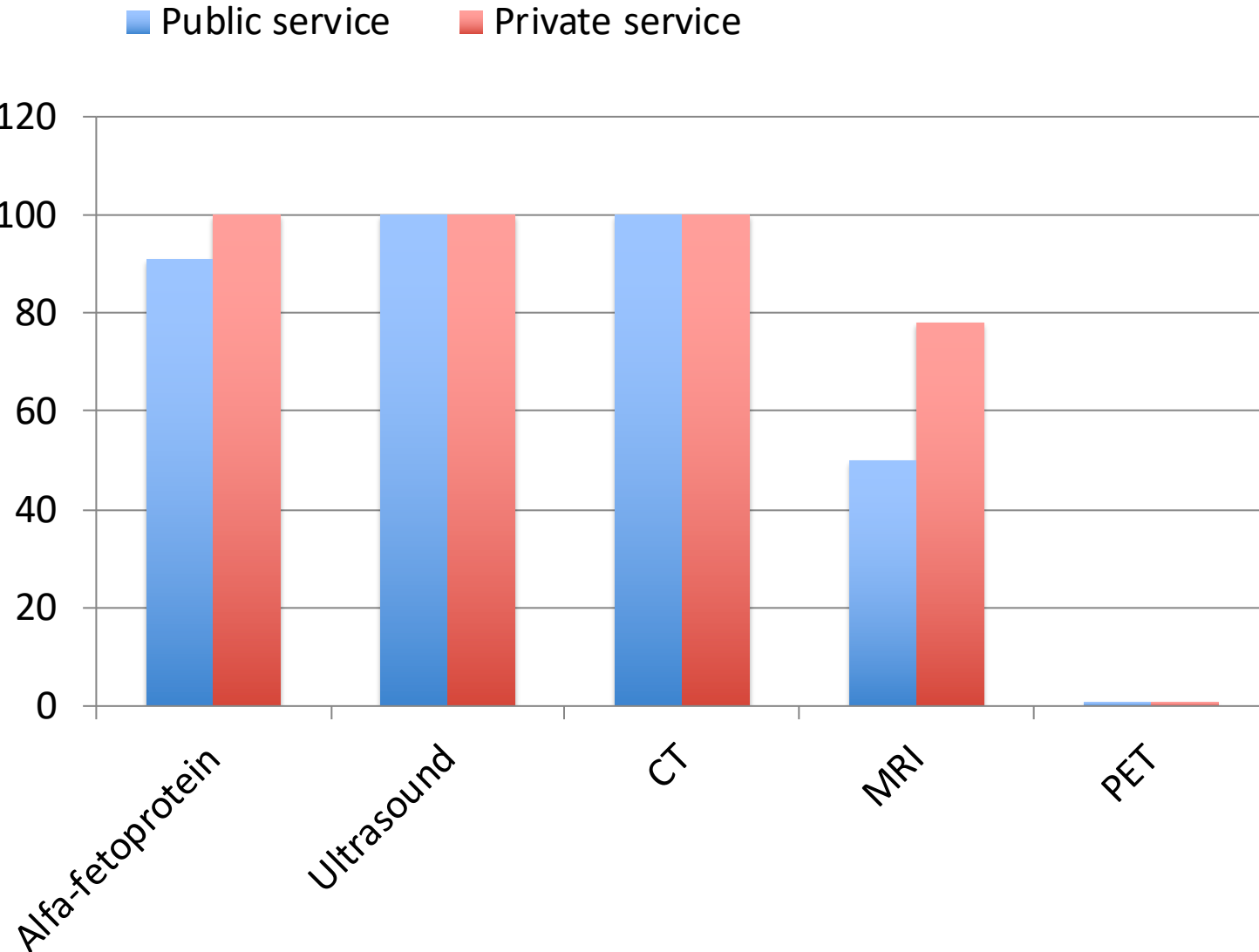
<b>Curative treatment</b>	<b>8 (&lt;1%)</b>
Resection	8 (<1%)
Local ablation	0 (0%)
Transplantation	0 (0%)
<b>Palliative</b>	<b>17 (1%)</b>
TACE	5 (<1%)
Sorafenib	12 (<1%)

**Screening for HCC when treatment options are not in place is bound to be an expensive failure**

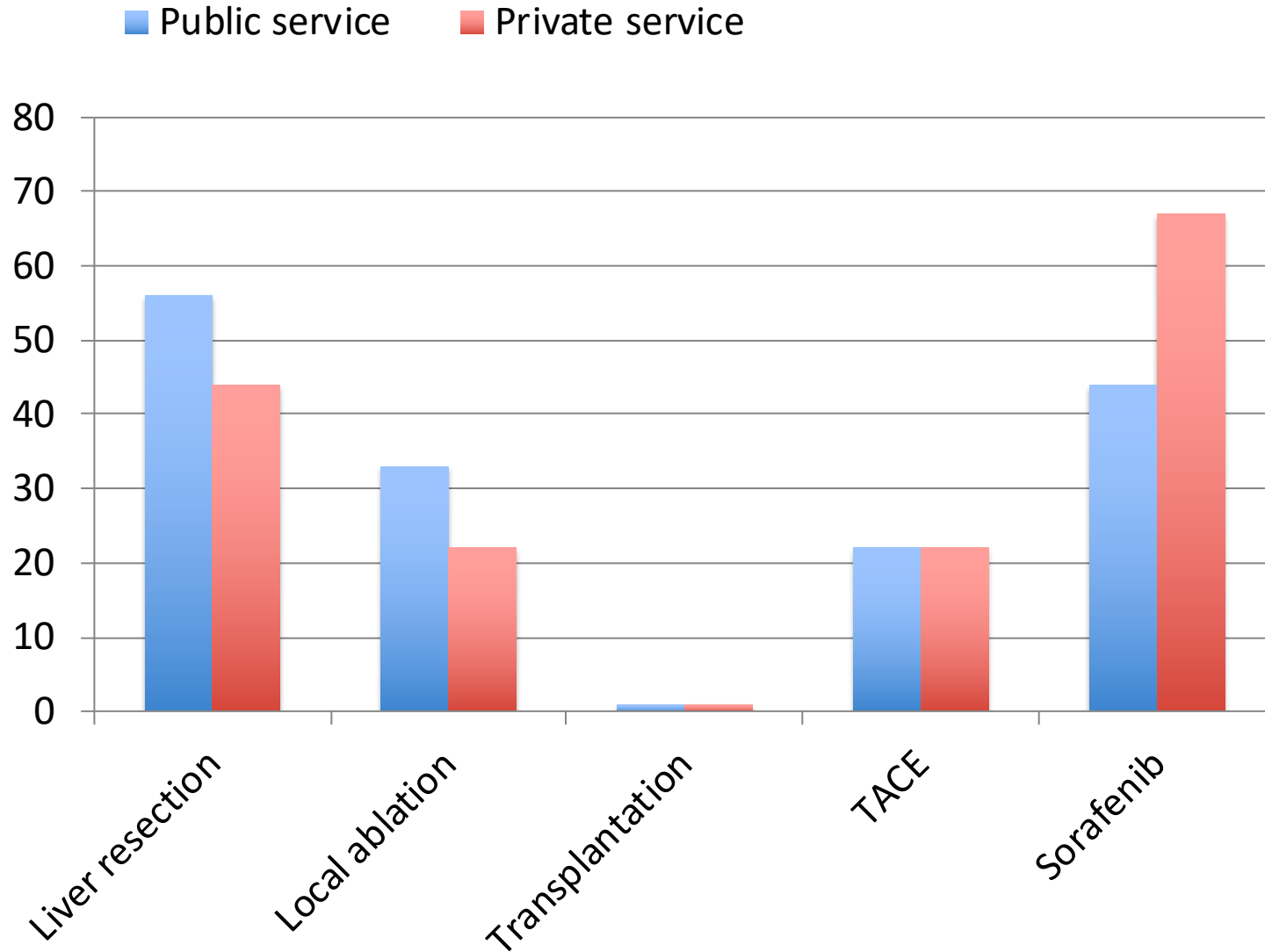
# Diagnosis and treatment in sub-Saharan SA

- Online survey
- Questions on diagnostic and treatment resources in public and private facilities
- HPB surgeons at 13 tertiary centres
- Nigeria, Senegal, Ghana, Cameroon, Kenya, Uganda, Namibia, Zimbabwe

# Diagnostic tools in SSA



# Treatment in SSA





# Curative liver intervention

The Lancet Commission on Global Surgery identified Western, Eastern and Central Sub-Saharan Africa respectively as the regions with the highest, second highest and third highest rates of surgical need per population in the world

# Resource-sensitive guidelines

Treatment capability

Diagnostic capabilities

Prevention strategies

# Minimal resources

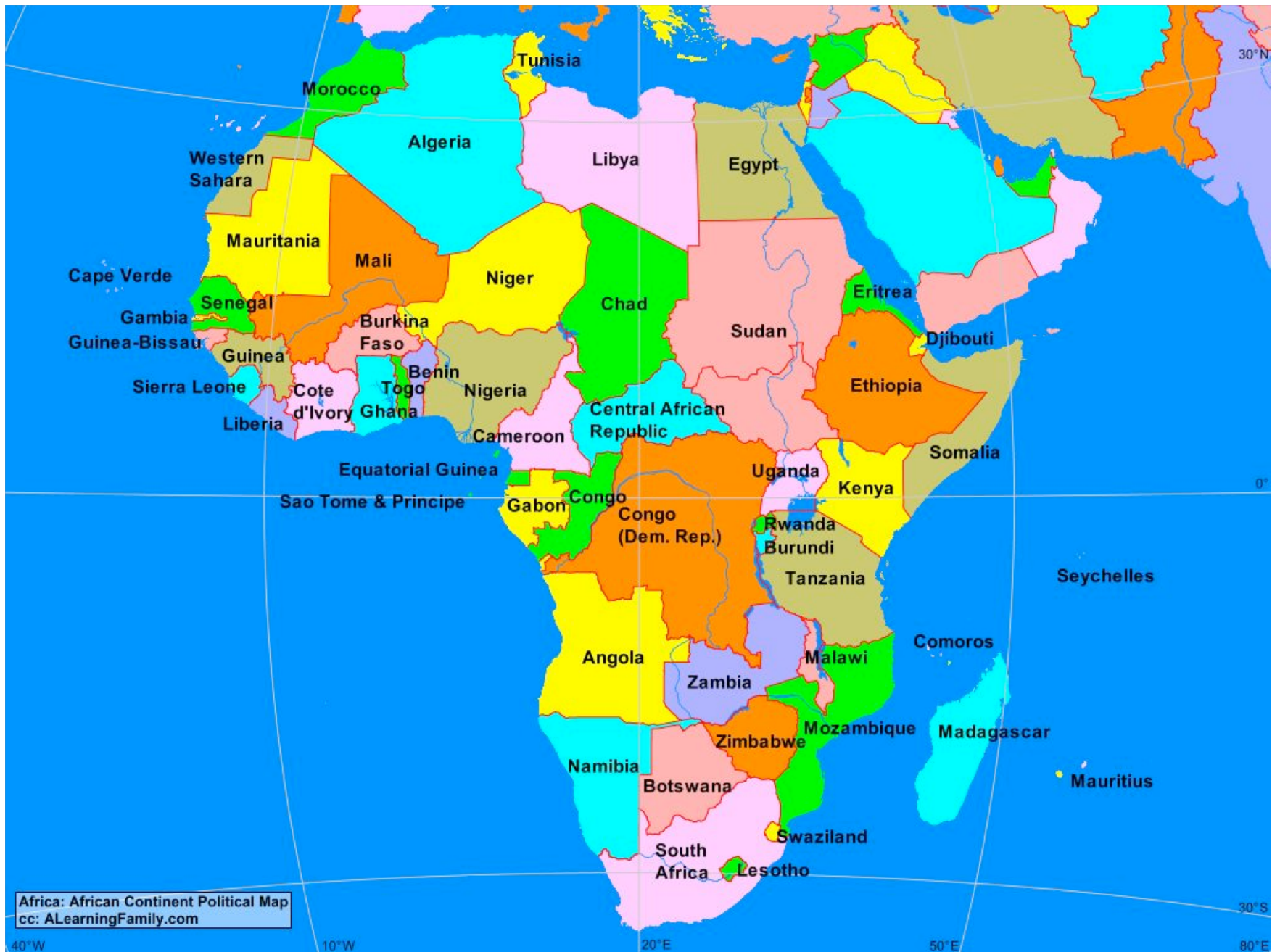
- Treatment
  - Best supportive care
  - Referral of early tumours
- Diagnostics
  - Confirming the diagnosis
- Prevention
  - Primary prevention

# Medium resources

- Treatment
  - Liver resection
  - Local ablation
- Diagnostics
  - Definitive diagnosis
  - Staging
- Prevention
  - Primary prevention
  - Secondary prevention

# High resources

- Treatment
  - International guidelines apply (AASLD/EASL)
- Diagnosis
  - International guidelines apply (AASLD/EASL)
- Prevention
  - Primary
  - Secondary
  - Tertiary



# Hepatocellular carcinoma: Exploring the impact of ethnicity on molecular biology

Angela Lamarca<sup>a</sup>, Marta Mendiola<sup>b</sup>, Jorge Barriuso<sup>c,\*</sup>

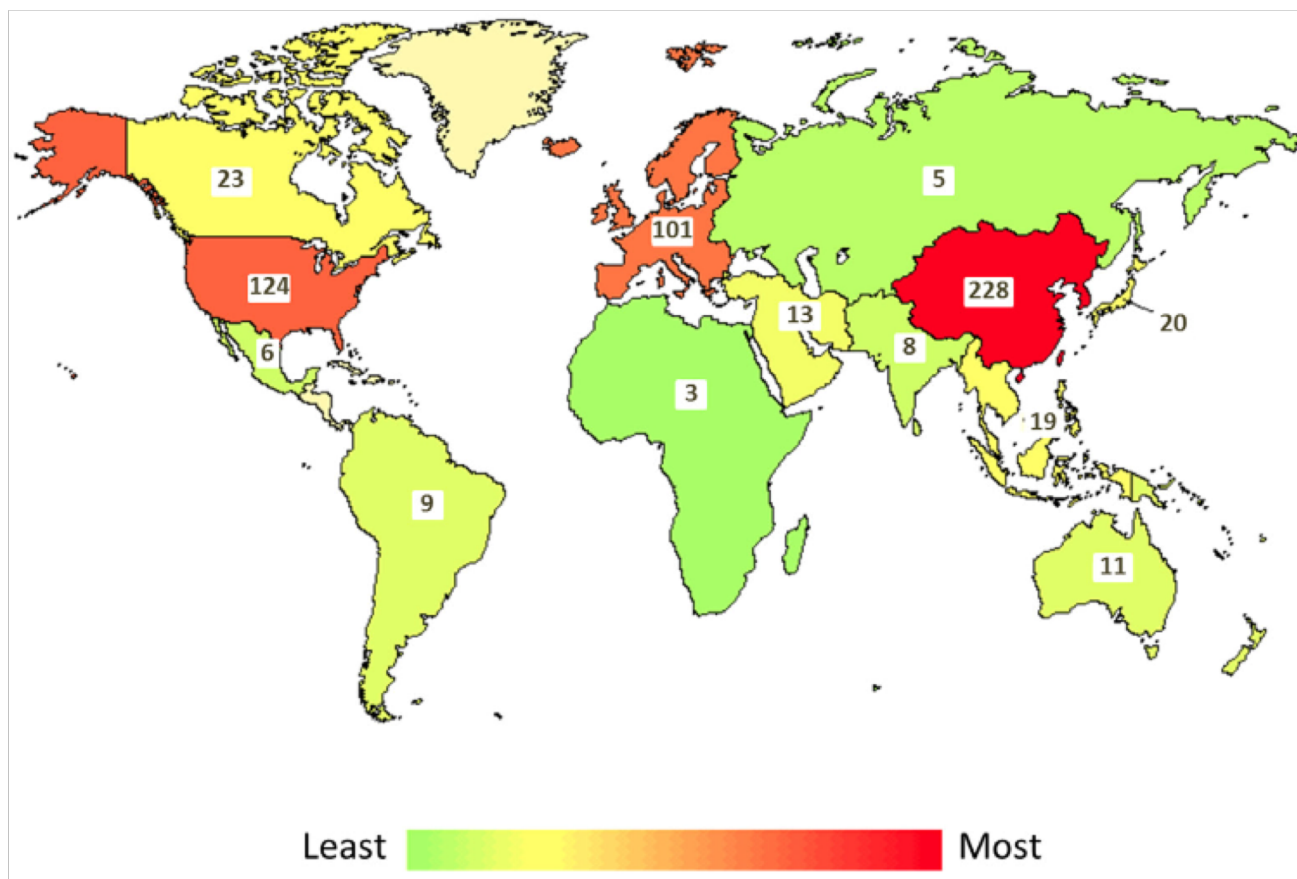
<sup>a</sup> Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK

<sup>b</sup> Cancer Molecular Pathology and Therapeutic Targets Research Group, IdiPAZ, La Paz University Hospital, Madrid, Spain

<sup>c</sup> Faculty of Life Sciences, University of Manchester, Manchester, UK



# Research in Africa



Less than 1% of currently ongoing clinical HCC trials are conducted on the continent



# Conclusion

- Implementation of resource-sensitive guidance algorithms in sub-Saharan Africa is a realistic and feasible approach
- However, the endeavour will be eroded by geographical and economic between and within country variations in the quality and accessibility of health care
- Accounting for, minimizing, or at best eradicating these inequalities will be a prerequisite for the successful implementation of these algorithms
- These inequalities are a powerful political tool to bring about change and stimulate improvement of health care

# Thank you

