



9th Liver Interest Group Annual Meeting

HCC guidance



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Introduction

- Most common primary hepatic malignancy
- Annual incidence of 782000*
- Globally accounts for 9.2% of all new cancer cases
- 5th most common cancer in males and 8th 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. 2012. Accessed December 12, 2013.

Clinical Practice Guidelines



**JOURNAL
OF HEPATOLOGY**

EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma[☆]

European Association for the Study of the Liver*

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

-

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

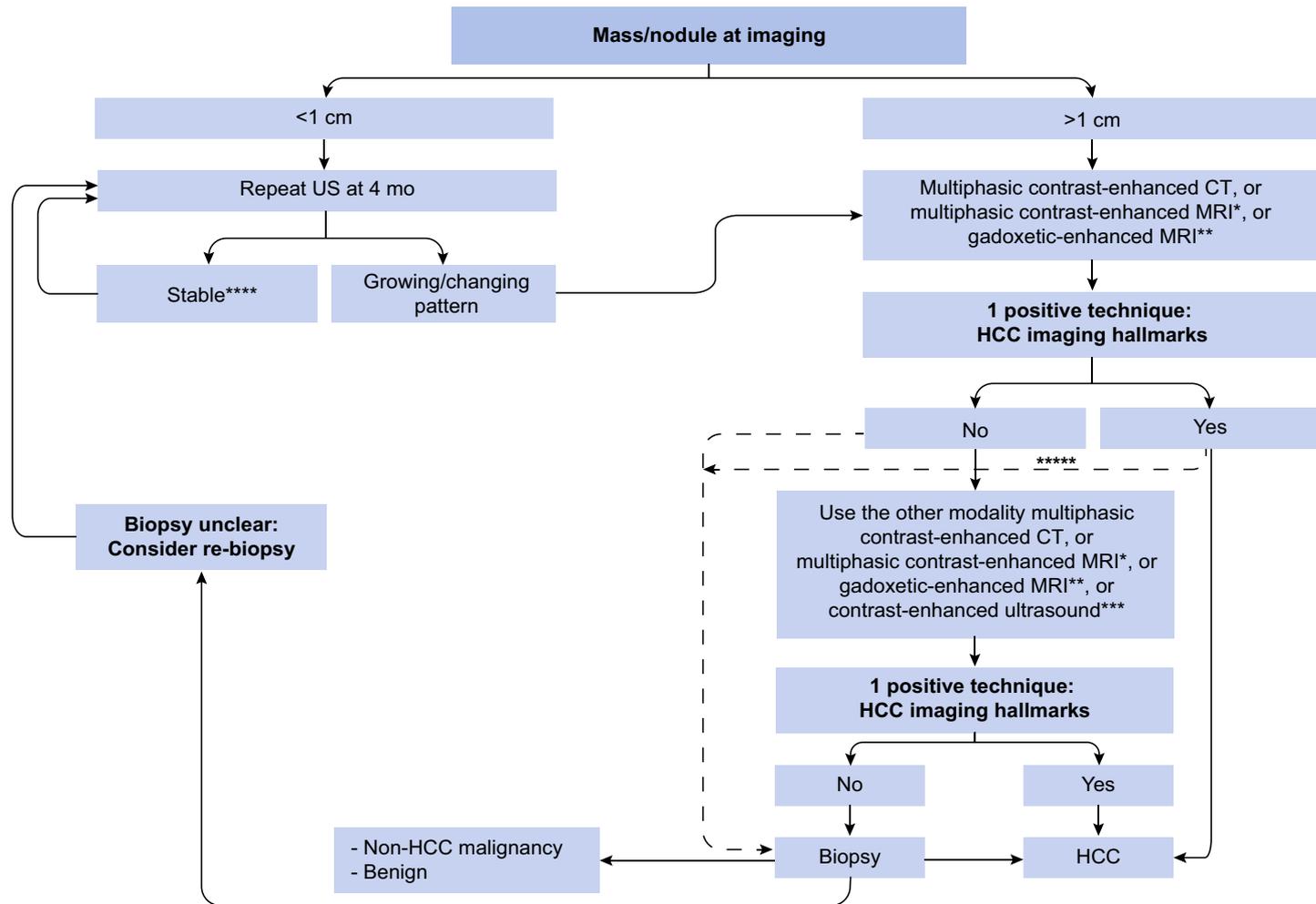
Screening tests

- 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%
 - ≥ 20 ng/ml- sensitivity 41-65%; specificity 80%-94%
- Combination of AFP and Ultrasound
 - AFP increase ≥ 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 ≤ 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

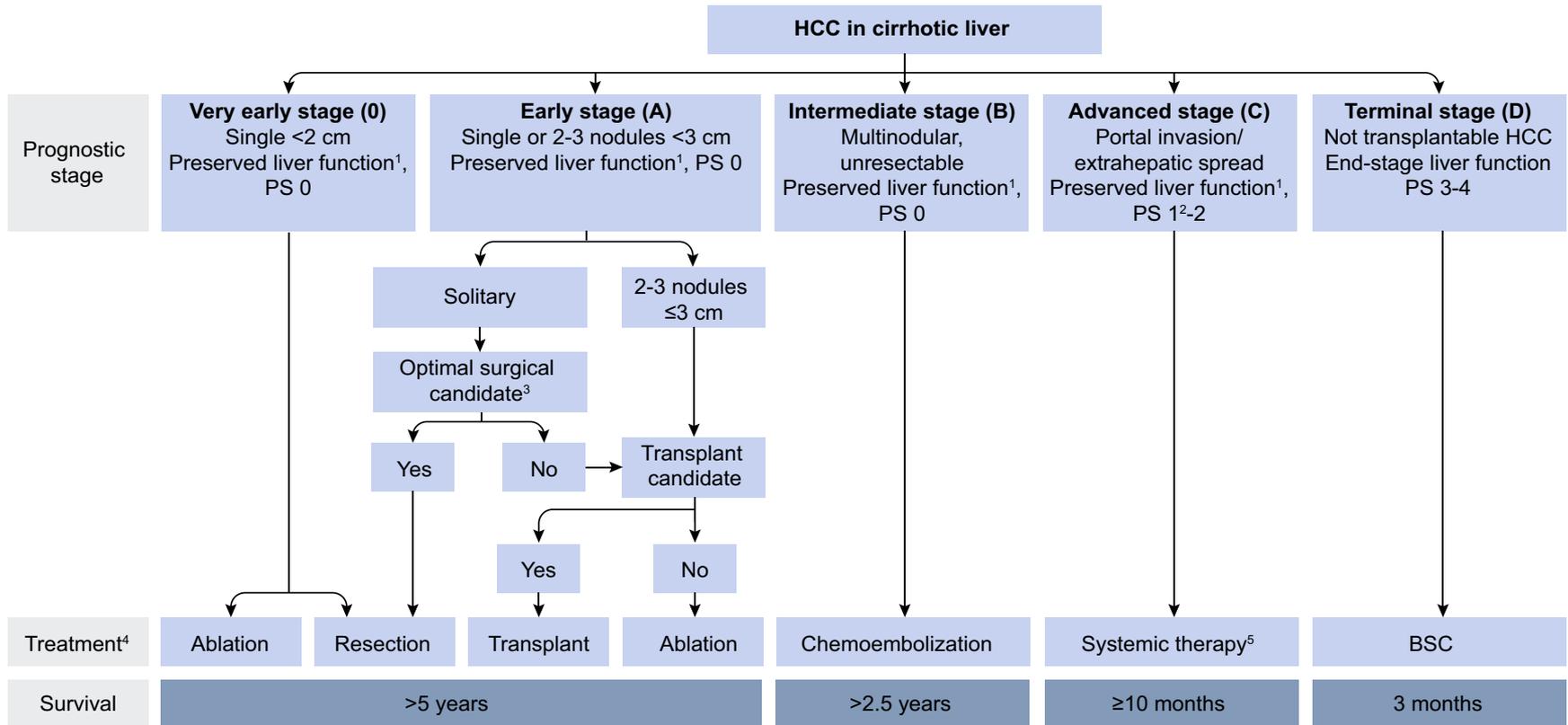
- **Curative treatment rates**

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



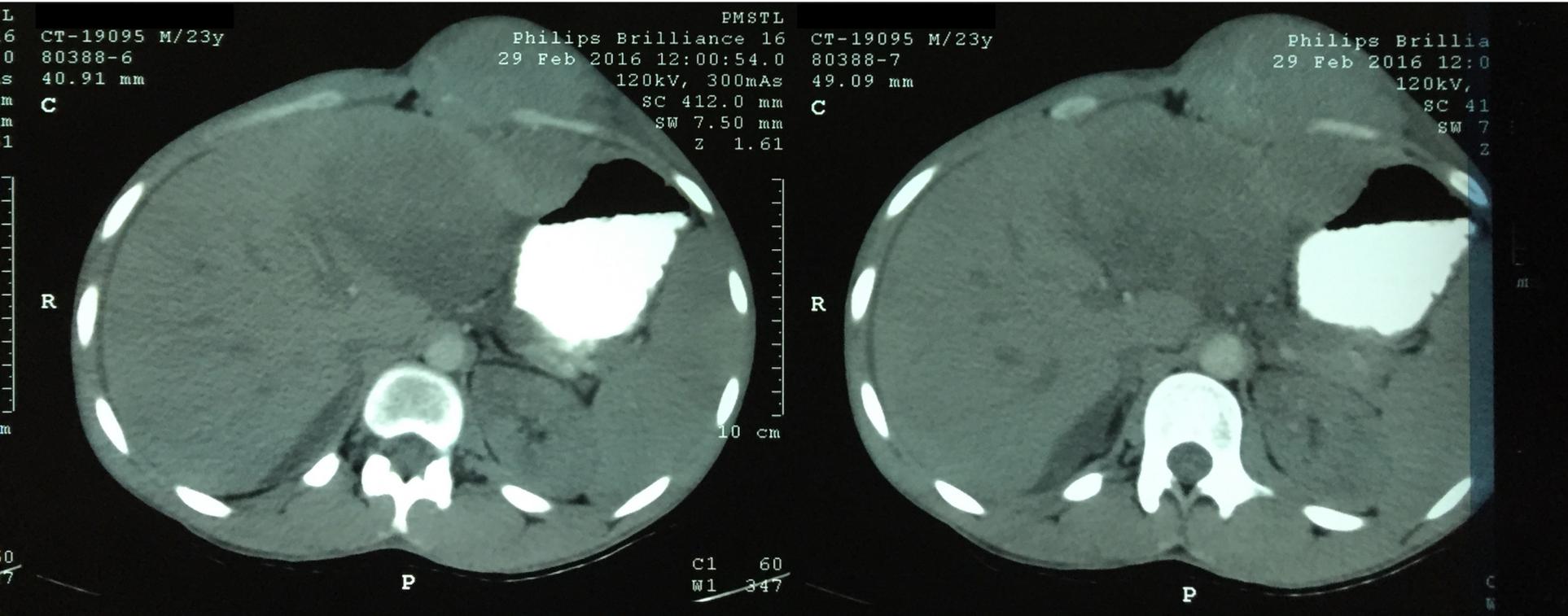
Guidance in sub-Saharan Africa

- 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

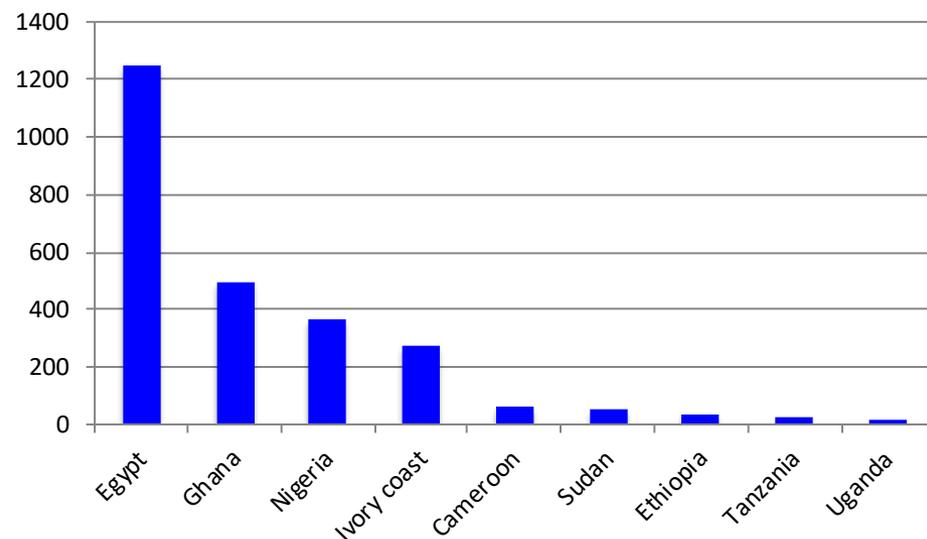
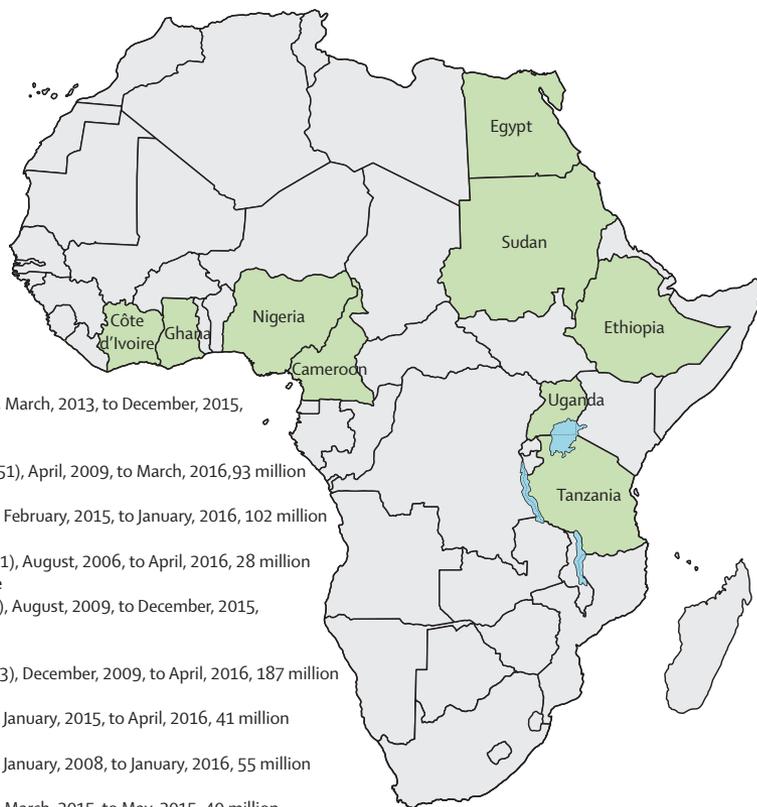
Is it a different disease?



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

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

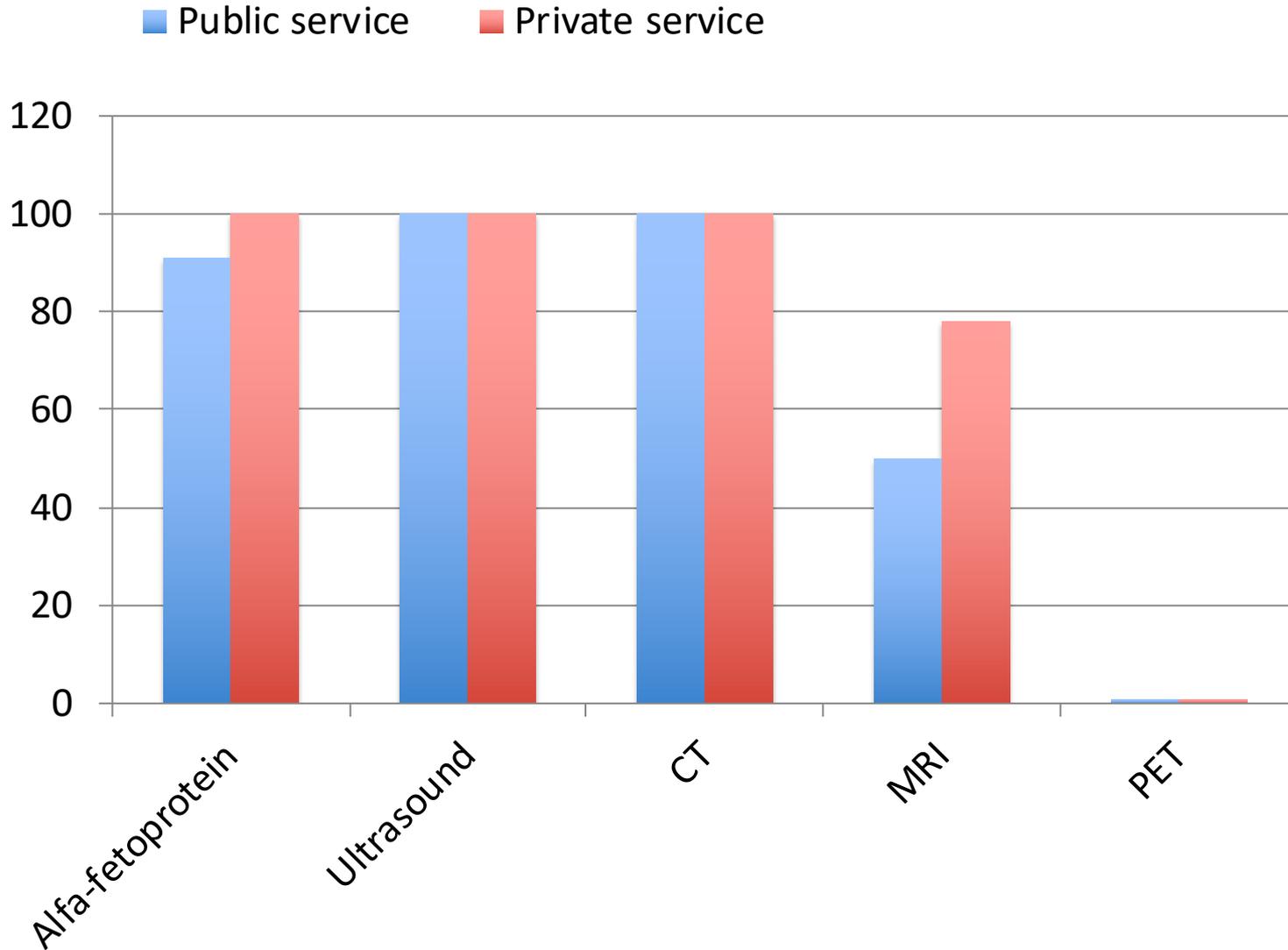
Curative treatment	8 (<1%)
Resection	8 (<1%)
Local ablation	0 (0%)
Transplantation	0 (0%)
Palliative	17 (1%)
TACE	5 (<1%)
Sorafenib	12 (<1%)

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

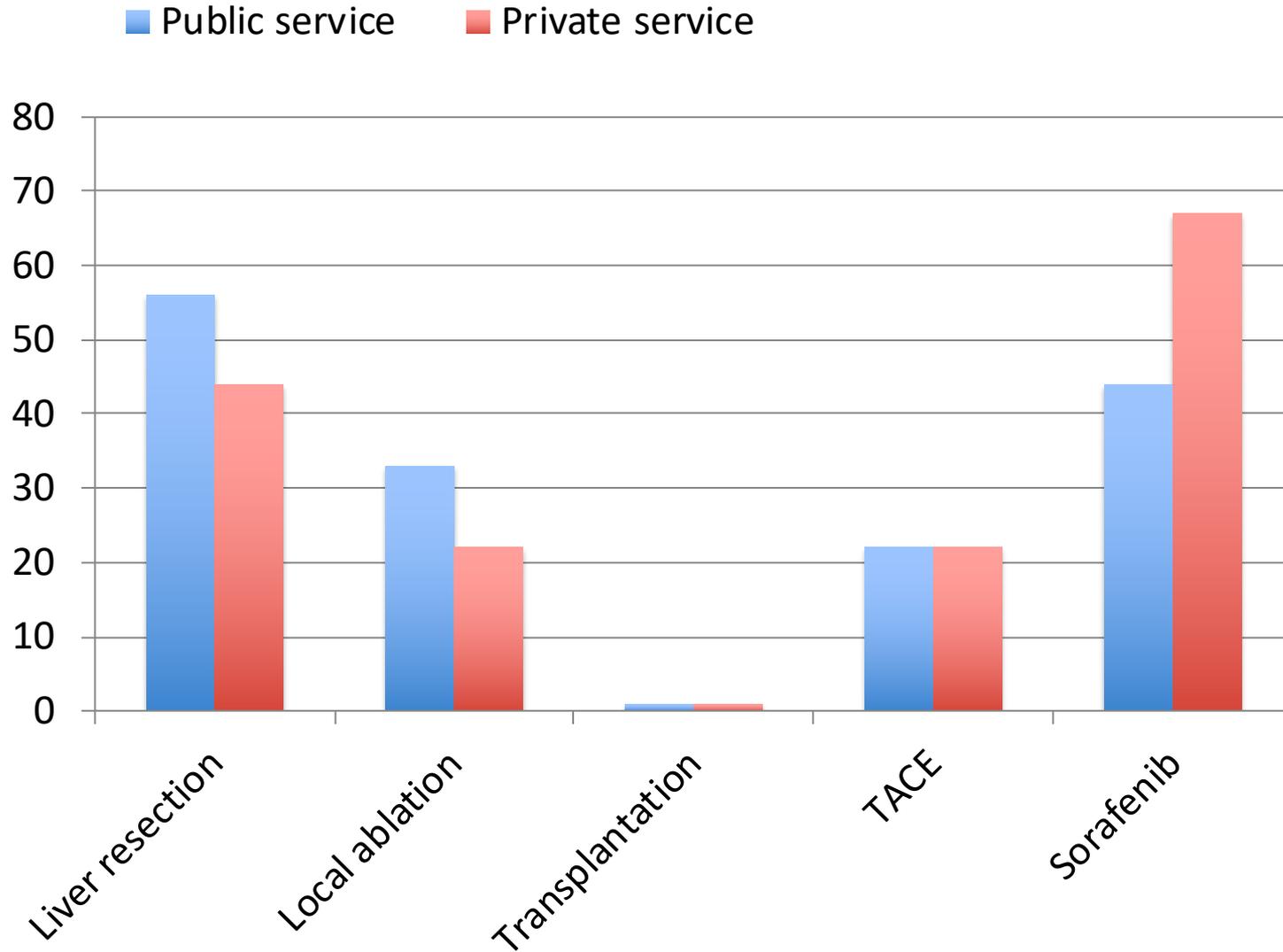
Diagnosis and treatment in sub-Saharan SA

- 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

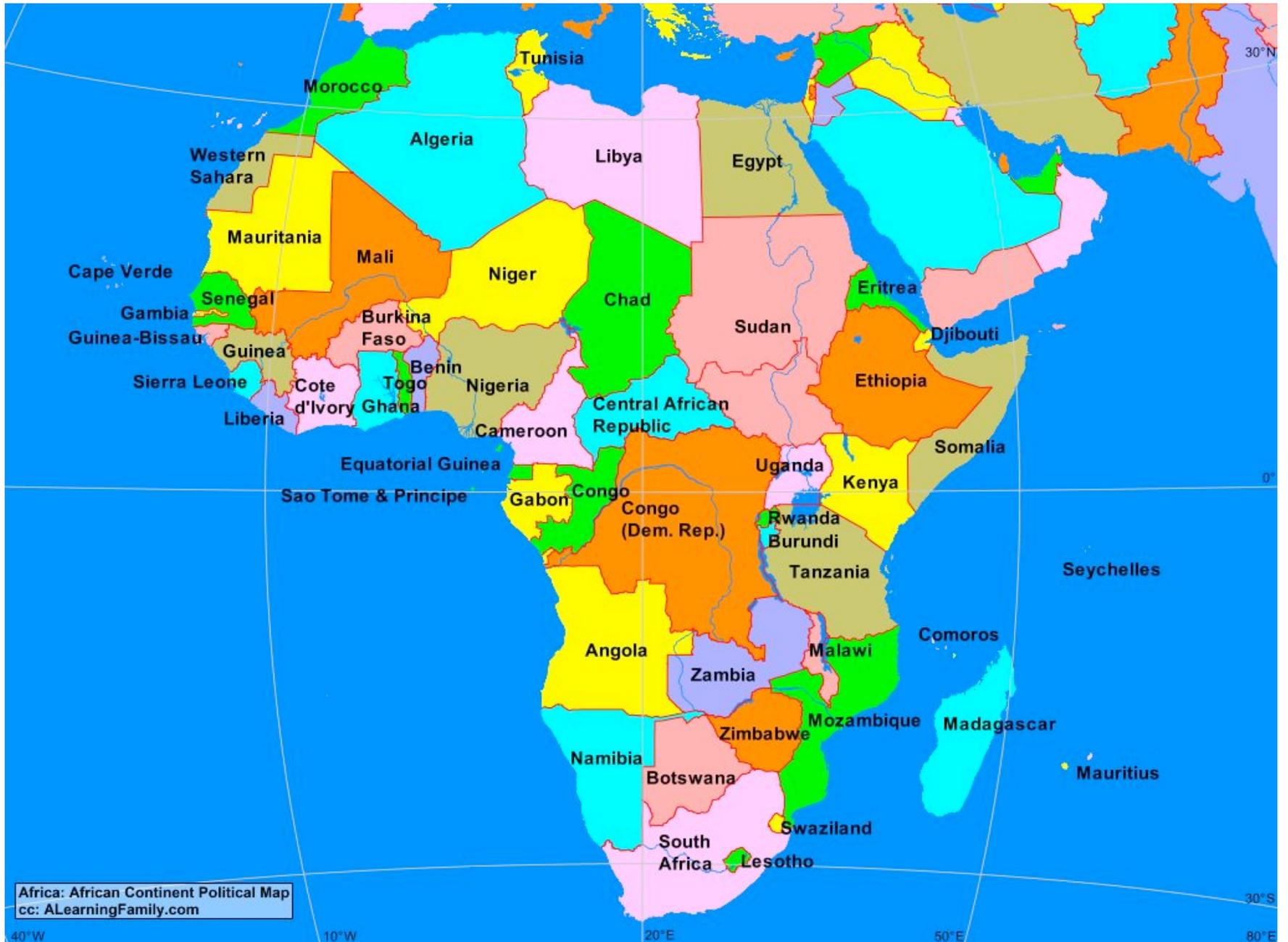
- Treatment
 - Best supportive care
 - Referral of early tumours
- Diagnostics
 - Confirming the diagnosis
- Prevention
 - Primary prevention

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



Africa: African Continent Political Map
cc: ALearningFamily.com

Review

Hepatocellular carcinoma: Exploring the impact of ethnicity on molecular biology

Angela Lamarca^a, Marta Mendiola^b, Jorge Barriuso^{c,*}

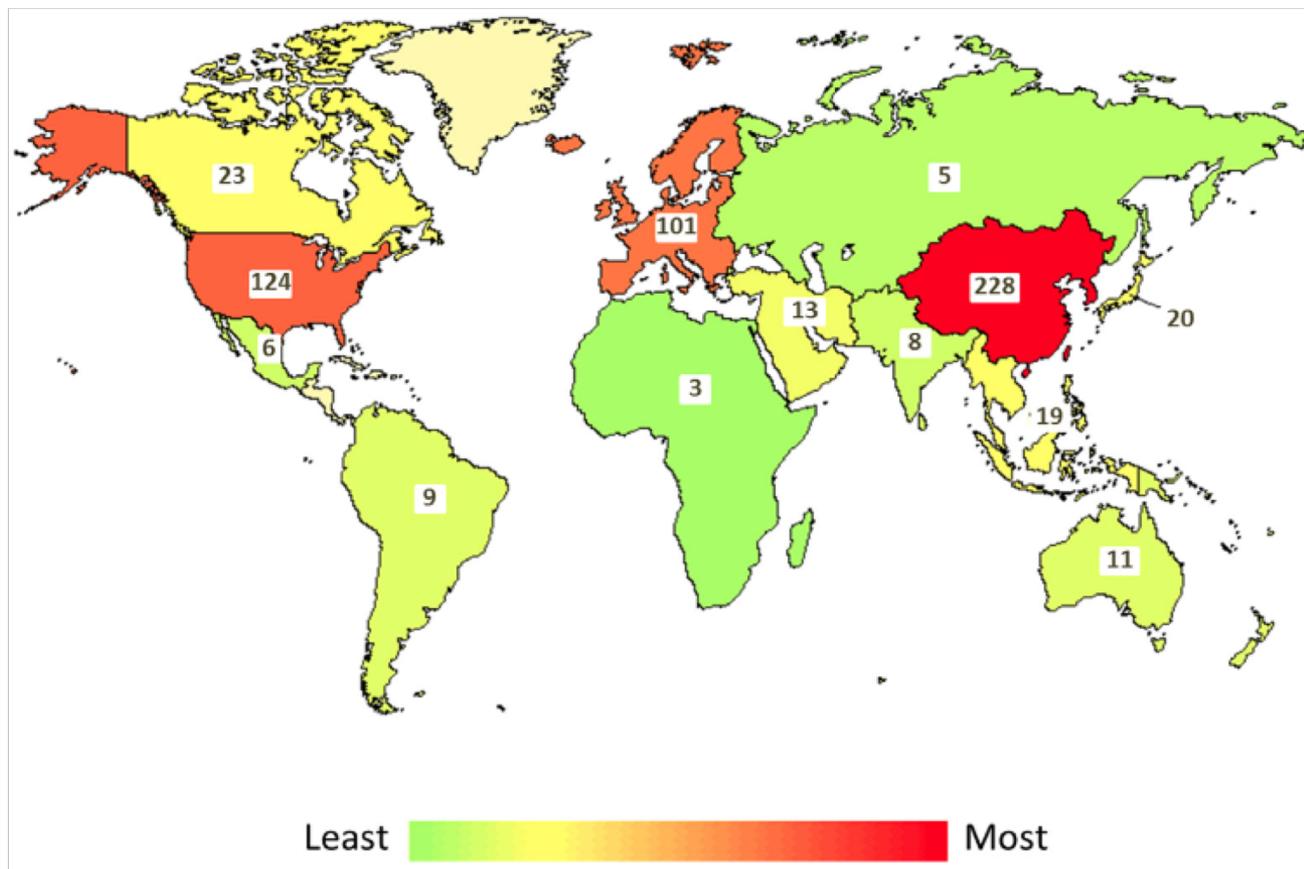
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^b Cancer Molecular Pathology and Therapeutic Targets Research Group, IdiPAZ, La Paz University Hospital, Madrid, Spain

^c 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



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